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U.S. FOOD & DRUG ADMINISTRATION

August 28, 2020

Alydia Health
% Cindy Domecus, R.A.C.
Principal
Domecus Consulting Services LLC
1171 Barroilhet Drive
Hillsborough, CA 94010

Re: K201199
Trade/Device Name: Jada® System
Regulation Number: 21 CFR§ 884.4530
Regulation Name: Obstetric-gynecologic specialized manual instrument
Regulatory Class: II
Product Code: OQY
Dated: July 27, 2020
Received: July 29, 2020

Dear Cindy Domecus:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Monica D. Garcia -S

Monica D. Garcia, Ph.D.
Acting Assistant Director
DHT3B: Division of Reproductive,
Gynecology and Urology Devices
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K201199

Device Name
Jada® System

Indications for Use *(Describe)*
The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary – K201199

I. SUBMITTER

510(k) Owner
Colby Holtshouse
Alydia Health
3495 Edison Way
Menlo Park, CA 94025
Phone: 650-275-3772
Fax: 415-354-3473
Email: colby@alydiahealth.com

Submission Correspondent
Cindy Domecus, R.A.C. (US & EU)
Domecus Consulting Services LLC
Phone: (650) 343-4813
Fax: (650) 343-7822
Email: DomecusConsulting@comcast.net

Date Prepared
August 28, 2020

II. DEVICE

Name of Device:	Jada® System
Common or Usual Name:	Vacuum-induced Hemorrhage Control
Regulation Name:	Obstetric-Gynecologic Specialized Manual Instrument
Regulation Number:	21 CFR § 884.4530
Regulatory Class:	II
Product Code:	OQY (Intrauterine Tamponade Balloon)

III. PREDICATE DEVICE

The predicate device is the Bakri® Postpartum Balloon, Bakri® Postpartum Balloon with Rapid Instillation Components, K170622. The predicate device has not been subject to a design-related recall.

IV. DEVICE DESCRIPTION

The Jada® System is a 41 cm long intrauterine device primarily made of silicone. The vacuum connector and seal valve are made of polyvinylchloride and acrylonitrile-butadiene-styrene. The device consists of an intrauterine loop on the distal end of a translucent tube. The proximal end of the tube has a vacuum connector for connection to a vacuum tube. Proximal to the connection of the Intrauterine Loop is

a donut-shaped cervical seal. The cervical seal is filled with and emptied of 60-120 mL of sterile fluid by attaching a syringe to the seal valve. The intrauterine loop has 20 vacuum pores oriented toward its inside diameter. The outer surface of the intrauterine loop is a silicone shield which overhangs the vacuum pores to protect tissue from vacuum and to prevent the vacuum pores from plugging with tissue and blood clots.

Before placing the Jada® System device inside the uterus, the intrauterine loop is compressed. The compressed loop is inserted into the uterus transvaginally. The cervical seal is placed within the vagina, at the external cervical os, and inflated. Vacuum is then applied to a maximum value of 90 mmHg until bleeding is controlled. The device should be fixed to the thigh along the tube.

V. INDICATIONS FOR USE

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

VI. COMPARISON OF INTENDED USE AND TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Attribute	**K201199 Subject Device: Jada® System**	**K170622 Predicate Device: Bakri® Postpartum Balloon** **Bakri® Postpartum Balloon with Rapid Instillation Components**	**Comparison**
Manufacturer	Alydia Health	Cook Incorporated	N/A
Product Code	OQY	OQY	Same
Indications for Use	The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.	Bakri® Postpartum Balloon is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted. Bakri® Postpartum Balloon with Rapid	Different

		Instillation Components is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.	
Principle of Action	Inserted into the uterus and establishes a vacuum to cause the uterine walls to press against one another, producing a tamponade of the bleeding vessels	Inserted into the uterus and is inflated to press outward on the uterine walls, producing tamponade of the bleeding vessels	Different
Design	Inflatable cervical seal and intrauterine loop with vacuum pore	Inflatable uterine balloon and a single drainage side port	Different
Rx/OTC	Rx	Rx	Same
Materials	Silicone, Polyvinylchloride (PVC), Acrylonitrile-Butadiene-Styrene (ABS)	Silicone	Different
Sterile	SAL 10^{-6}	SAL 10^{-6}	Same
Single-use	Yes	Yes	Same

The Indications for Use statement for the Jada® System is not identical to the predicate device; however, the differences do not alter the intended use of the device. Both the subject and predicate devices have the same intended use for the treatment of abnormal uterine bleeding when conservative management is warranted.

The following technological differences exist between the subject and predicate devices:

- Principle of Operation: The subject device utilizes vacuum to affect tamponade on uterine walls, whereas the predicate device utilizes the fluidic pressure of an expanding balloon to affect tamponade
- Design: The subject device's intrauterine loop has a looped (drain) tube with a series of Vacuum Pores on the inside surface. The intrauterine loop features an elliptical pattern that lays flat on the uterine tissue bed, whereas the

predicate device has a single opening drain tube protruding out of the middle of the inflated balloon
- Materials: The patient contacting portions of both devices are made of silicone. However, the subject device includes a seal valve and vacuum connector made of ABS and PVC, respectively. All patient contacting devices are made of silicone for the subject and predicate device.

These differences in technological characteristics do not raise different questions of safety and effectiveness. Non-clinical and clinical data provided by Alydia Health were used to address the differences related to design and principle of operation to demonstrate substantial equivalence to the predicate device.

VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Mechanical Testing

The following mechanical tests were performed:

- Cervical Seal and Tube Dimensions: Verification of tube and seal dimensions
- Intrauterine Loop Portion Dimensional Test – Verification of intrauterine loop dimensions
- Removal of Intrauterine Portion Test – Verification that intrauterine loop and shield remain intact during removal
- Vacuum Pore Diameter – Verification of vacuum pore size
- No Sharp Edges – Verification of smooth edges and surfaces of device
- Attaining Pressure Drop – Verification that cervical seal withstands pressure differential of 180 mmHg vacuum
- Static Load Test – Verification that the cervical seal withstands a static load of 1 lb. applied axially along the tube without failure
- Overfill Capacity – Verification that cervical seal does not fail when filled with 180 mL water.
- Cervical Seal Inflation – Verification that cervical seal can be filled with 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Impact Load Test – Verification that the cervical seal withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Connection Tube Junction Impact Load Test - Verification that the intrauterine loop withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Flow Rate – Verification that the device with vacuum is able to evacuate 400 mL of simulated blood in 1 minute or less
- Device Integrity Leak Test – Verification that the joints of the device do not leak when 180 mmHg of vacuum is applied

- Integration to Hospital Vacuum Line – Verification that the device connects to a vacuum tube
- Inflation Tube Geometry – Verification that the cervical seal inflation lumen is functional
- Syringe Accommodation – Verification that a luer tapered syringe can be attached to the seal valve
- Cervical Seal Deflation – Verification that cervical seal can be emptied of 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Cervical Seal Diameter and Bond Stability – Verification that the seal maintains a diameter of 70 mm and maintains integrity after 48 hours
- Clotted Blood Test – Verification that the device can evacuate simulated blood in the presence of clotted blood without occluding
- Vacuum Connector Bond Test – Verification that the vacuum connector withstands a tensile load of 8.8 lbf
- Seal Valve Bond Test – Verification that the seal valve withstands a tensile load of 3.7 lbf

Biocompatibility Testing

The Jada® System is a surface device in contact with a breached surface, with limited duration (≤ 24 hours).

The biocompatibility evaluation for the Jada® System was conducted in accordance with the FDA June 2016 guidance *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process", Guidance for Industry and Food and Drug Administration Staff*. The battery of testing included the following tests:

- Cytotoxicity (ISO 10993-5:2009)
- Maximization Sensitization (ISO 10993-10:2010)
- Vaginal Irritation (ISO 10993-10:2010)
- Systemic toxicity (ISO 10993-11:2017)
- Material Mediated Pyrogenicity (ISO 10993-11:2017)

Sterilization and Shelf-Life Testing

The Jada® System is sterilized using gamma radiation to a SAL = 10^{-6}, according to ISO 11137-2: 2013. A shelf-life of 4 years has been established based on real-time aging.

Clinical Studies

Clinical testing of the Jada® System included an initial pilot study of 10 women in Indonesia, an initial phase of the pivotal study of 13 women in Uganda, and an IDE pivotal study of 107 women in the U.S. Substantial equivalence was based in part on the pivotal study, as described below.

Pivotal Study

The pivotal study was a prospective, multicenter, single-arm, open label, literature-controlled study at 12 sites in the U.S. A total of 107 subjects were enrolled into the study, of which 106 subjects were evaluable. Study entrance criteria included the following estimated blood loss (EBL) ranges:

Vaginal delivery: 500 – 1500 mL EBL or
C-section delivery: 1000 – 1500 mL EBL

Primary Effectiveness Endpoint

The primary effectiveness endpoint was as follows:
Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line or surgical intervention to control uterine hemorrhage after the use of the Jada® System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada® System use is standard of care and does not constitute failure of the primary effectiveness endpoint.

Primary Safety Endpoint

The primary safety endpoint was the incidence, severity and seriousness of device-related adverse events.

Effectiveness Results

The analysis of effectiveness was based on the 106 subjects in the ITT Cohort. Results from the 104 subjects in the mITT and 97 subjects in the PP Cohort are also presented. The treatment success rate in the ITT Cohort was 94.3% (100/106, $p<0.001$), with a lower bound 95% confidence limit of 88.1%. The success rate performance goal was 82.0% (95% CI: 73.4% to 89.2%), based on a meta-analysis of data from literature assessing the performance of the Bakri Postpartum Balloon. The treatment success rate in the mITT Cohort was 96.2% (100/104; 95% CI: 90.4%, 98.9%). The treatment success rate in the PP Cohort was 99% (96/97; 95% CI: 94.4% to 100%).

Safety Results

There were no adverse events judged definitely related to the device or the procedure and there was a low rate of possibly related adverse events, all of which were anticipated in this patient population and with introduction of an intrauterine device. Five possibly device-related adverse events were rated as “mild” and three were rated as “moderate” without any event in this group rated “severe”. The three moderate events were cases of endometritis, which is a known risk of long labor, vaginal exam, and postpartum hemorrhage.

Summary

In summary, the pivotal trial of the Jada® System demonstrates the device's safety and effectiveness in the treatment of abnormal postpartum uterine bleeding and hemorrhage.

VIII. CONCLUSIONS

The nonclinical and clinical performance data described above demonstrate that the Jada® System is as safe and effective as the predicate device and supports a determination of substantial equivalence.

To: Reginald Avery
Cc: Monica Garcia
From: Kelly Colden
Subject: Clinical review of the sponsor's responses for the Jada System, Alydia Health (K201199/S001)
Date: August 24, 2020

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(b)(5) FDA Reviewer Notes

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Kelly Colden -S

Kelly Colden -S
2020.08.24
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Hello,

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(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received:
https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

Hello Reginald,

(b)(4) Deficiencies

Thank you for your continued reivew of our file.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

Exhibit B: Redlined copy of revised Jada System Instructions for Use

(b)(4) Draft Manual

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July 2, 2020</br></br> We have reviewed your submission. Please see attached.

If you have any questions, please contact the lead reviewer assigned to your submission, Poulomi Nandy.

 *** This is a system-generated email notification ***

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Appendix A. Acceptance Checklist for Traditional 510(k)s

(Should be completed within 15 days of DCC receipt)

The following information is not intended to serve as a comprehensive review.
FDA recommends that the submitter include this completed checklist as part of the application.

510(k)#: **Date Received by DCC:**

510(k) Lead Reviewer:

Center: **Office:** **Division:**

Decision: **Accept_____ Refuse to Accept_____**

If Accept, notify the submitter.

If Refuse to Accept, notify submitter electronically and include a copy of this checklist.

Is an Addendum attached?: Yes No

Note: If an element is left blank on the checklist, it does not mean the checklist is incomplete; it means the reviewer did not assess the element during the RTA review and that the element will be assessed during substantive review.

Preliminary Questions			
Answers in the shaded blocks indicate consultation with an identified Center advisor is needed. (Boxes checked in this section represent FDA's preliminary assessment of these questions at the time of administrative review.)	**Yes**	**No**	**N/A**
1. Is the product a device (per section 201(h) of the FD&C Act) or a combination product (per 21 CFR 3.2(e)) with a device constituent part subject to review in a 510(k)? If it appears not to be a device (per section 201(h) of the FD&C Act) or such a combination product (per 21 CFR 3.2(e)), or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action, and inform management. *Provide a summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* If the product does not appear to be a device or such a combination product, mark	X	☐	

"No."			
Comments: The subject device is a medical device per 21 CFR 884.4530 and IDE G150265.			
2. Is the submission with the appropriate Center? If the product is a device or a combination product with a device constituent part, is it subject to review by the Center in which the submission was received? If you believe the submission is not with the appropriate Center or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide a summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* If submission should not be reviewed by your Center mark "No."	X	☐	
Comments: The subject device is a medical device per 21 CFR 884.4530 and IDE G150265. The subject device is not a combination product.			
3. If a Request for Designation (RFD) was submitted for the device or combination product with a device constituent part and assigned to your center, identify the RFD # and confirm the following: **(a) Is the device or combination product the same (e.g., design, formulation) as that presented in the RFD submission?** **(b) Are the indications for use for the device or combination product identified in the 510(k) the same as those identified in the RFD submission?** If you believe the product or the indications presented in the 510(k) have changed from the RFD, or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide a summary of Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* If the answer to either question above is no, mark "No." If there was no RFD, mark "N/A."	☐	☐	X
Comments:			
4. Is the submission for a combination product that contains as a constituent part a drug that has the same active moiety as an approved drug with exclusivity as described in 21 USC 503(g)(5)(C)(ii)-(v) (section 503(g)(5)(C)(ii)-(v) of the FD&C Act)? If "Yes," then contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide the summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.*	☐	X	☐
Comments: The subject device is a medical device per 21 CFR 884.4530 and IDE G150265. The subject device is not a combination product.			

5. Is this device type eligible for a 510(k) submission? If a 510(k) does not appear to be appropriate (e.g., Class III type and PMA required, or Class I or II type and 510(k)-exempt), consult with the appropriate CDRH or CBER staff during the acceptance review, provide a summary of the discussion with them, and indicate their recommendation/action in the comment section below. If 510(k) is not the appropriate regulatory submission, mark "No."	X	☐	
Comments: The subject device falls under 21 CFR 884.4530, Product Code OQY. The submission type for OQY is a 510(k).			
6. Is there a pending PMA for the same device with the same indications for use? If "Yes," consult your management and CDRH Office of Product Evaluation and Quality/Office of Regulatory Programs/Division of Regulatory Programs 1 (Submission Support) (OPEQ/ORP/DRP1) or appropriate CBER staff to determine the appropriate action.	☐	X	
Comments: There is no PMA pending for the same device.			
7. If clinical studies have been submitted, is the submitter the subject of an Application Integrity Policy (AIP)? If "Yes," consult with the CDRH Office of Product Evaluation and Quality/Office of Clinical Evidence and Analysis/Division of Clinical Science and Quality (OPEQ/OCEA/DCEA1) or CBER Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Bioresearch Monitoring Branch (OCBQ/DIS/BMB) to determine the appropriate action, provide a summary of the discussion with them, and indicate their recommendation/action. If no clinical studies have been submitted, mark "N/A." Check on the AIP list at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/application-integrity-policy/application-integrity-policy-list.	☐	X	☐
Comments: The 510(k) submitter is not the subject of an AIP.			

- **If the answer to 1 or 2 appears to be "No," then stop review of the 510(k) and contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.**
- **If the answer to 3a or 3b appears to be "No," then stop the review and contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.**
- **If the answer to 4 is "Yes," then contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer, provide a summary of the discussion with them, and indicate their recommendation/action.**
- **If the answer to 5 is "No", the lead reviewer should consult division management and other Center resources to determine the appropriate action.**

- **If the answer to 6 is "Yes," then stop review of the 510(k), contact CDRH/OPEQ/ORP/DRP1, or appropriate CBER staff.**
- **If the answer to 7 is "Yes," then contact CDRH/OPEQ/OCEA/DCEA1 or CBER/OCBQ/DIS/BMB, provide a summary of the discussion with DCEA1 or BMB Staff, and indicate their recommendation/action.**

Organizational Elements Failure to include these items should not result in an RTA designation.				
***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**		**Yes**	**No**	***Page #**
1.	Submission contains a Table of Contents.	X	☐	1
2.	Each section is labeled (e.g., headings or tabs designating Device Description section, Labeling section, etc.).	X	☐	
3.	All pages of the submission are numbered. *All pages should be numbered in such a manner that information can be referenced by page number. This may be done either by consecutively numbering the entire submission, or numbering the pages within a section (e.g., 12-1, 12-2...).*	X	☐	
4.	Type of 510(k) is identified (i.e., Traditional, Abbreviated, or Special) *If type of 510(k) is not designated, review as a Traditional 510(k).*	X	☐	Page 1, Cover Sheet, and page 3-1
Comments:				

Elements of a Complete Submission (RTA Items) **(21 CFR 807.87 unless otherwise indicated)** Submission should be designated RTA if not addressed.
• Any "No" answer will result in a "Refuse to Accept" decision; however, FDA staff has discretion to determine whether missing items are needed to ensure that the submission is administratively complete to allow the submission to be accepted or to request missing checklist items interactively from submitters during the RTA review. • Each element on the checklist should be addressed within the submission. The submitter may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criterion is considered present (Yes). An assessment of the rationale will be considered during the review of the submission.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
A.	**Administrative**						
	1.	All content used to support the submission is written in English (including translations of test reports, literature articles, etc.).		X	☐		
		Comments:					
	2.	Submission identifies the following (FDA recommends use of the CDRH Premarket Review Submission Cover Sheet form (Form 3514, available at https://www.fda.gov/media/72421/download)):					
		a.	Device trade/proprietary name	X	☐		Cover Sheet
		b.	Device class and panel OR Classification regulation OR Statement that device has not been classified with rationale for that conclusion	X	☐		Cover Sheet
		Comments:					
	3.	Submission contains an Indications for Use Statement with Rx and/or OTC designated (see also 21 CFR 801.109, and FDA's guidance "Alternative to Certain Prescription Devices Labeling Requirements," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/alternative-certain-prescription-device-labeling-requirements.) *See recommended format (https://www.fda.gov/media/86323/download).*		X	☐		5-1
		Comments:					
	4.	Submission contains a 510(k) Summary or 510(k) Statement. *Refer to 21 CFR 807.92 and 21 CFR 807.93 for contents of 510(k) Summary and Statement, respectively. Adequacy of the content will be assessed during substantive review.*		X	☐		6-1
		Comments:					

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
	5.	Submission contains a Truthful and Accuracy Statement per 21 CFR 807.87(*l*). *See recommended format (https://www.fda.gov/medical-devices/premarket-notification-510k/premarket-notification-truthful-and-accurate-statement).*		X	☐		7-1
		Comments:					
	6.	Submission is a Class III 510(k) Device. *Select "N/A" only if submission is not a Class III 510(k).*		☐		X	8-1
		a.	Contains Class III Summary and Certification per 21 CFR 807.87(k). *See recommended content (https://www.fda.gov/medical-devices/premarket-notification-510k/premarket-notification-class-iii-certification-and-summary). Select "N/A" only if submission is not a Class III 510(k).*	☐	☐	☐	
		Comments:					
	7.	Submission contains clinical data. *Select "N/A" if the submission does not contain clinical data. If "N/A" is selected, parts a, b, and c below are omitted from the checklist.*		X		☐	21-1
		a.	Submission includes completed Financial Certification (FDA Form 3454, available at https://www.fda.gov/media/70465/download) or Disclosure (FDA Form 3455, available at https://www.fda.gov/media/69872/download) information for each covered clinical study included in the submission. *Select "N/A" if the submitted clinical data is not a "covered clinical study" as defined in the guidance entitled "Financial Disclosures by Clinical Investigators," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/financial-disclosure-clinical-investigators.*	X	☐	☐	9-1

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**					**Yes**	**No**	**N/A**	***Page #**
		b.		Submission includes completed Certification of Compliance with requirements of ClinicalTrials.gov Data Bank (FDA Form 3674, available at https://www.fda.gov/media/69901/download) (42 U.S.C. 282(j)(5)(B)) for each applicable device clinical trial included in the submission. *Select "N/A" if the submitted clinical data is not an "applicable device clinical trial" as defined in Title VIII of FDAAA, Sec. 801(j).*	X	☐	☐	9-1
		c.		Statements of Compliance for Clinical Investigations *Select "N/A" if the submission does not contain any clinical data from investigations (as defined in 21 CFR 812.3(h)) to demonstrate substantial equivalence.* *For multicenter clinical investigations involving both United States (US) and outside United States (OUS) sites, part (i) should be addressed for the US sites and part (ii) should be addressed for the OUS sites. 21 CFR 812.28 applies to all OUS clinical investigations that enroll the first subject on or after February 21, 2019.* *Please refer to the guidance document entitled "Acceptance of Clinical Data to Support Medical Device Applications and Submissions - Frequently Asked Questions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-clinical-data-support-medical-device-applications-and-submissions-frequently-asked for more information.*	X		☐	9-1
			i.	For each clinical investigation conducted in the US, the submission includes a statement of compliance with 21 CFR parts 50, 56, and 812. **OR** The submission includes a brief statement of the reason for noncompliance with 21 CFR parts 50, 56, and 812. *Select "N/A" if the clinical investigations were conducted solely OUS.*	X	☐	☐	9-1

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.					Yes	No	N/A	*Page #
			ii.	For each clinical investigation conducted OUS, the submission includes a statement that the clinical investigations were conducted in accordance with good clinical practice (GCP) as described in 21 CFR 812.28(a)(1). **OR** The submission includes a waiver request in accordance with 21 CFR 812.28(c). **OR** The submission includes a brief statement of the reason for not conducting the investigation in accordance with GCP and a description of steps taken to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of subjects have been adequately protected. *Select "N/A" if the clinical investigations were conducted solely inside the US.*	☐	☐	X	9-1
			Comments:					
	8.	The submission identifies prior submissions for the same device included in the current submission (e.g., submission numbers for a prior not substantially equivalent [NSE] determination, prior deleted or withdrawn 510(k), Q-Submission, IDE, PMA, etc.). **OR** States that there were no prior submissions for the subject device. *Prior submissions (or no prior submissions) for this device should be included in Section F (prior related submissions) of the CDRH Premarket Review Submission Cover Sheet form (Form 3514, available at https://www.fda.gov/media/72421/download). This information may also be included in the Cover Letter (i.e., as a statement that there were no prior submissions for the device or a listing of the number(s) of the prior submissions).*				X	☐		(b)(4)

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		a.	If there were prior submissions, the submitter has identified where in the current submission any issues related to a determination of substantial equivalence from prior submissions for this device are addressed. *To address this criterion, it is recommended that the submission include a separate section with the prior submission number(s), a copy of the FDA feedback (e.g., letter, meeting minutes), and a statement of how or where in the submission this prior feedback was addressed. Note that adequacy of how the feedback was addressed will be assessed during the substantive review.* *Select "N/A" if the submitter states there were no prior submissions.*	X	☐	☐	10-1
			Comments:				
	9.	The submission utilizes voluntary consensus standard(s) (See section 514(c) of the FD&C Act). *This includes both FDA-recognized and non-recognized consensus standards. Select "N/A" if the submission does not utilize voluntary consensus standards.*		X		☐	11-1
		a.	The submission cites FDA-recognized voluntary consensus standard(s).	X		☐	11-1

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**					**Yes**	**No**	**N/A**	***Page #**
			i.	The submission includes a Declaration of Conformity (DOC) as outlined in FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices. **OR** If citing general use of a standard as noted in FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," the basis of such use is included along with the underlying information or data that supports how the standard was used.	X	☐		11-1
		b.	The submission cites non-FDA-recognized voluntary consensus standard(s).		☐		X	
			i.	The basis of use is included along with the underlying information or data that supports how the standard was used.	☐	☐		
		Comments:						
	Combination Product Provisions – Per 503(g) of the FD&C Act. Select "N/A" if the product is not a combination product. 21 CFR 3.2(e). The remaining criteria in this section will be omitted from the checklist if "N/A" is selected. If you are unsure if the product is a combination product, consult with the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.						X	
	10.	Submission identifies the product as a combination product.			☐	☐		
	11.	The combination product contains as a constituent part an approved drug as defined in section 503(g)(5)(B) of the FD&C Act. Select "N/A" if the combination product does not contain as a constituent part an approved drug. Please also select "N/A" if a right of reference or use for the drug constituent part(s) is included with the submission. If "N/A" is selected, part a below is omitted from the checklist.			☐		☐	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.				Yes	No	N/A	*Page #
		a.	The submission includes appropriate patent statement or certification and a statement that the submitter will give notice, as applicable. See 503(g)(5)(A)&(C).	☐	☐		
			Comments:				
B.	**Device Description**						
	12.		The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding the device description that is applicable to the subject device. *If "N/A" is selected, parts a and b below are omitted from the checklist.*	☐		X	
		a.	The submission addresses device description recommendations outlined in the device-specific guidance. **OR** The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria. *Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not includea rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.*	☐	☐	X	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		b.	The submission includes device description information that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device. **OR** The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness. *Select "N/A" if there are no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.*	☐	☐	X	
			Comments:				
	13.	Descriptive information is present and consistent within the submission (e.g., the device description section is consistent with the device description in the labeling).		X	☐		12-1, 15-1
		Comments:					
	14.	The submission includes descriptive information for the device, including the following:					
		a.	A description of the principle of operation or mechanism of action for achieving the intended effect.	X	☐		12-3
		b.	A description of proposed conditions of use, such as surgical technique for implants; anatomical location of use; user interface; how the device interacts with other devices; and/or how the device interacts with the patient.	X	☐		12-4
		c.	A list and description of each device for which clearance is requested. *Select "N/A" if there is only one device or model. "Device" may refer to models, part numbers, various sizes, etc.*	X	☐	☐	12-5

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		d.	Submission contains representative engineering drawing(s), schematics, illustrations, photos and/or figures of the device. **OR** Submission includes a statement that engineering drawings, schematics, etc. are not applicable to the device (e.g., device is a reagent and figures are not pertinent to describe the device). *In lieu of engineering drawings, schematics, etc. of each device to be marketed, "representative" drawings, etc. may be provided, where "representative" is intended to mean that the drawings, etc. provided capture the differences in design, size, and other important characteristics of the various models, sizes, or versions of the device(s) to be marketed.*	X	☐		12-1, 12-2, and 12-6 – 12-9
			Comments:				
	15.	Device is intended to be marketed with accessories and/or as part of a system. *Select "N/A" if the device is not intended to be marketed with accessories and/or as part of a system. If "N/A" is selected, parts a-c below are omitted from the checklist.*		☐		X	
		a.	Submission includes a list of all accessories to be marketed with the subject device.	☐	☐		
		b.	Submission includes a description (as detailed in item 14a., 14b., and 14d. above) of each accessory. *Select "N/A" if the accessory(ies) has been previously cleared, or is exempt, and the proposed indications for use are consistent with the cleared indications.*	☐	☐	X	
		c.	A 510(k) number is provided for each accessory that received a prior 510(k) clearance. **AND** A statement is provided that identifies accessories that have not received prior 510(k) clearance.	☐	☐		
			Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
C.	**Substantial Equivalence Discussion**						
	16.	Submitter has identified a predicate device(s), including the following information:					
		a.	Predicate device identifier provided (e.g., 510(k) number, De Novo number, reclassified PMA number, classification regulation reference, if exempt (e.g., 21 CFR 872.3710), or statement that the predicate is a preamendment device). For predicates that are preamendments devices, information is provided to document preamendments status. *Information regarding documenting preamendment status is available online (https://www.fda.gov/medical-devices/quality-and-compliance-medical-devices/preamendment-status).*	X	☐		13-1
		b.	The identified predicate(s) is consistent throughout the submission (e.g., the predicate(s) identified in the Substantial Equivalence section is the same as that listed in the 510(k) Summary (if applicable) and that used in comparative performance testing.	X	☐		13-1, 6-1, 20-1
			Comments:				
	17.	Submission includes a comparison of the following for the predicate(s) and subject device and a discussion why any differences between the subject and predicate(s) do not impact safety and effectiveness [see section 513(i)(1)(A) of the FD&C Act and 21 CFR 807.87(f)]. *See the FDA guidance document "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k for more information on comparing intended use and technological characteristics.*				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		a.	Indications for use *If there are no differences between the subject device and the predicate(s) with respect to indications and intended use, this should be explicitly stated.*	X	☐		13-2
		b.	Technology, including technical specifications, features, materials, and principles of operation *Examples of technological characteristics include, but are not limited to design, features, materials, energy source, and principle of operation.* *FDA recommends a tabular format for comparing technological characteristics. Any characteristic that is the same as the predicate(s) should be explicitly stated. Differences in technological characteristics should be identified and a rationale provided why they do not raise different questions of safety and effectiveness.*	X	☐		13-3
			Comments:				
D.	**Proposed Labeling (see also 21 CFR parts 801 and 809 as applicable)**						
	18.		Submission includes proposed package labels and labeling (e.g., instructions for use, package insert, operator's manual).	X	☐		Exhibits 14.A-14.C
		a.	Indications for use are stated in labeling and are identical to Indications for Use form and 510(k) Summary (if 510(k) Summary provided).	X	☐		
		b.	Labeling includes: - Statements of conditions, purposes or uses for which the device is intended (e.g., hazards, warnings, precautions, contraindications) (21 CFR 801.5) **AND** - Includes adequate directions for use (see 21 CFR 801.5) **OR** - Submission states that device qualifies for exemption per 21 CFR 801 Subpart D	X	☐		14-1

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
			Comments:				
	19.		Labeling includes name and place of business of the manufacturer, packer, or distributor (21 CFR 801.1).	X	☐		Exhibit 14.A
			Comments:				
	20.		Labeling includes the prescription statement (see 21 CFR 801.109(b)(1)) or Rx Only symbol (see also Section 502(a) of the FD&C Act and FDA's guidance "Alternative to Certain Prescription Device Labeling Requirements," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/alternative-certain-prescription-device-labeling-requirements. *Select "N/A" if not indicated for prescription use.*	X	☐	☐	Exhibit 14.A-14.C
			Comments:				
	21.		The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding labeling that is applicable to the subject device. *If "N/A" is selected, parts a and b below are omitted from the checklist.*	☐		X	
		a.	The submission addresses labeling recommendations outlined in the device-specific guidance. **OR** The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria. *Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not includea rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.*	☐	☐	X	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		b.	The submission includes labeling information that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device. **OR** The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness. *Select "N/A" if there are no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.*	☐	☐	X	
			Comments:				
	22.	If the device is an in vitro diagnostic device, provided labeling includes all applicable information required per 21 CFR 809.10. *Select "N/A" if not an in vitro diagnostic device.*		☐	☐	X	
		Comment:					
E.	**Sterilization** *If an in vitro diagnostic (IVD) device and sterilization is not applicable, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected.*					☐	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**			**Yes**	**No**	**N/A**	***Page #**
	Submission states that the device and/or accessories, if applicable, are: (*one of the below must be checked*) ☒ Provided sterile, intended to be single-use Requires processing during its use-life Non-sterile when used (and no processing required) ☐ Information regarding the sterility status of the device is not provided (if this box is checked, please also check one of the two boxes below) ☐ Sterility status not needed for this device (e.g., software-only device) ☐ Sterility status needed or need unclear This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *If "non-sterile when used" or "not provided and not needed" is selected, the sterility-related criteria below are omitted from the checklist.* *If information on sterility status is not provided, and it is needed or the need for this information is unclear, select "No."* *The "Requires processing during its use-life" option refers to devices falling into one of the four categories below:* • *Supplied sterile and requires reprocessing prior to subsequent patient use* • *Supplied non-sterile and requires user to process the device for initial use, as well as to reprocess the device after each use* • *Reusable medical device (single-user) reprocessed between each use* • *Single-use medical devices initially supplied as non-sterile to the user, and requiring the user to process the device prior to its use* *Please refer to the FDA guidance document "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/reprocessing-medical-devices-health-care-settings-validation-methods-and-labeling, for additional information.*			☐		15-1
	Comments:					
	23.	Assessment of the need for cleaning and subsequent disinfection or sterilization information.				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		a.	Identification of device and/or accessories, if applicable, that are provided sterile. *Select "N/A" if no part of the device or accessories are provided sterile.*	☐	☐	X	
		b.	Identification of device and/or accessories, if applicable, that are end user sterilized or disinfected. *Select "N/A" if no part of the device are accessories are end user sterilized or disinfected.*	☐	☐	X	
		c.	Identification of device and/or accessories, if applicable, that are reusable. *Select "N/A" if no part of the device or accessories, are reusable.*	☐	☐	X	
			Comments:				
	24.	If the device and/or accessories, if applicable, are provided sterile: *Select "N/A" if no part of the device or accessories are provided sterile, otherwise complete a-f below.*				☐	
		a.	Sterilization method is stated for each device (including dose for radiation sterilization)	X	☐		15-1
		b.	A description of method to validate the sterilization parameters is provided for each proposed sterilization method (e.g., half-cycle method and full citation of FDA-recognized standard, including date). *Note: the sterilization validation report is not required.*	X	☐		15-1
		c.	For devices sterilized using chemical sterilants such as ethylene oxide (EO) and hydrogen peroxide, submission states maximum levels of sterilant residuals remaining on the device and sterilant residual limits. *Select "N/A" if not sterilized using chemical sterilants.*	☐	☐	X	
		d.	Sterility Assurance Level (SAL) stated	X	☐		15-1
		e.	Submission includes description of packaging	X	☐		

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		f.	For products labeled "non-pyrogenic," a description of the method used to make the determination stated (e.g., limulus amebocyte lysate [LAL]). *Select "N/A" if not labeled "non-pyrogenic."*	X	☐		15-2
			Comments:				
	25.	If the device and/or accessory, if applicable, is reusable or end user sterilized or disinfected: *Select "N/A" if no part of the device or accessories are reusable or end user sterilized or disinfected, otherwise complete a-d below.*				X	
		a.	Cleaning method is provided in labeling for each device and/or accessory, if applicable. *Select "N/A" if not reusable and does not need cleaning prior to disinfection or sterilization.*	☐	☐	X	
		b.	Disinfection method is provided in labeling for each device and/or accessory, if applicable. *Select "N/A" if not disinfected (i.e., undergoes terminal sterilization) prior to use.*	☐	☐	X	
		c.	Sterilization method is provided in labeling for each device and/or accessory, if applicable. *Select "N/A" if not sterilized (i.e., undergoes disinfection) prior to use.*	☐	☐	X	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**					**Yes**	**No**	**N/A**	***Page #**
		d.	Device types in this submission are listed in the Federal Register (FR) Notice entitled "Validated Instructions for Use and Validation Data Requirements for Certain Reusable Medical Devices in Premarket Notifications" (Reprocessing FR Notice, available at https://www.federalregister.gov /documents/2017/06/09/2017-12007/medical-devices-validated-instructions-for-use-and-validation-data-requirements-for-certain-reusable). *Device types identified in the Reprocessing FR Notice represent devices posing a greater likelihood of microbial transmission and represent a high risk of infection. Select "N/A" if the device type in the submission is not included in the Reprocessing FR Notice.*		☐		X	
			i.	If device types in this submission are included in the Reprocessing FR Notice, the submission includes protocols and test reports for validating the reprocessing instructions. *Select "N/A" if the device type in the submission is not included in the Reprocessing FR Notice.*	☐	☐	X	
			Comments:					
	26.	The device has a device-specific guidance document, special controls, and/or requirement in a device-specific classification regulation regarding sterility and/or reprocessing that is applicable to the subject device. *If "N/A" is selected, parts a and b below are omitted from the checklist.*			☐		X	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		a.	The submission addresses sterility and/or reprocessing recommendations outlined in the device-specific guidance. **OR** The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria. *Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.*	☐	☐	X	
		b.	The submission includes sterility and/or reprocessing information that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device. **OR** The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness. *Select "N/A" if there are no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.*	☐	☐	X	
			Comments:				
F.	**Shelf-Life**						
	27.		Proposed shelf life/ expiration date stated **OR** Statement that shelf-life is not applicable because of low likelihood of time-dependent product degradation.	X	☐		16-1

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**			**Yes**	**No**	**N/A**	***Page #**
		Comments:				
	28.	For a sterile device, submission includes summary of methods used to establish that device packaging will maintain a sterile barrier for the entirety of the proposed shelf-life. *Select "N/A" if the device is not provided sterile.*	X	☐	☐	16-1
		Comments:				
	29.	Submission includes summary of methods used to establish that device performance is maintained for the entirety of the proposed shelf-life (e.g., mechanical properties, coating integrity, pH, osmolality, etc.). **OR** Statement why performance data is not needed to establish maintenance of device performance characteristics over the shelf-life period.	X	☐	☐	16-1
		Comments:				
G.	**Biocompatibility** *If an in vitro diagnostic (IVD) device, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected.*				☐	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**			**Yes**	**No**	**N/A**	***Page #**
	Submission states that there: (*one of the below must be checked*) X Are direct or indirect tissue-contacting components Are no direct or indirect tissue-contacting components ☐ Information regarding tissue contact status of the device is not provided (if this box checked, please also check one of the two boxes below) ☐ Tissue contact information not needed for this device (e.g., software-only device) ☐ Tissue contact information is needed or need unclear This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *If "are no" or "not provided and not needed" is selected, the biocompatibility-related criteria below are omitted from the checklist. If information on the tissue-contact status is not provided, and contact information is needed or its contact status is unclear, select "No."* *An example of a direct tissue-contacting device would be an implant that has direct contact with tissues during use. An example of an indirect tissue-contacting device would be fluid entering the body following passing through device/device components not in direct contact with the tissue.*			☐		17-1
	Comments:					
	30.	Submission includes a list identifying each tissue-contacting device component (e.g., implant, delivery catheter) and associated materials of construction for each component, including identification of color additives, if present.	X	☐		17-1
		Comments:				
	31.	Submission identifies contact classification (e.g., surface-contacting, less than 24 hour duration) for each tissue-contacting device component (e.g., implant, delivery catheter).	X	☐		17-1
		Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.			Yes	No	N/A	*Page #
	32.	For a biocompatibility assessment of tissue-contacting components, submission includes: • Each relevant endpoint for the device (as identified in device-specific guidance, or Attachment A of the FDA guidance document entitled "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and), has been addressed. • For any testing performed, test protocol (including identification and description of test article including whether the test article is the device in its final finished form using the recommended approach in Attachment F of "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'" methods, and pass/fail criteria), and analysis of results (including tables with data points and statistical analyses, where appropriate), as described in Attachment E of the guidance document entitled "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'" provided for each completed test. **OR** A statement that biocompatibility testing is not needed with a rationale that considers all relevant endpoints (e.g., materials and manufacturing/processing are identical to the predicate).	X	☐		17-1
		Comments:				
H.	**Software**					

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**			**Yes**	**No**	**N/A**	***Page #**
	Submission states that the device: (*one of the below must be checked*) Does contain software/firmware X Does not contain software/firmware ☐ Information on whether device contains software/firmware is not provided (if this box checked, please also check one of the two boxes below) ☐ Software/firmware information not needed for this device (e.g., surgical suture, condom) ☐ Software/firmware information is needed or need unclear This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *If "does not contain" or "not provided and not needed" is selected, the software-related criteria below are omitted from the checklist. If information on software is not provided, and this information is needed or the need is unclear, select "No."*			☐		
	Comments:					
	33.	Submission includes a statement of software level of concern and rationale for the software level of concern	☐	☐		
		Comments:				
	34.	All applicable software documentation provided based on level of concern identified by the submitter, as described in "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-devices, or the submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through an alternative approach (i.e., the submitter has identified an alternate approach with a rationale). *Note: This element is also applicable to non-internally generated or off-the-shelf (OTS) software used in the device.*	☐	☐		

		Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**	**Yes**	**No**	**N/A**	***Page #**
		Comments:				
I.	**Cybersecurity**					
	Submission states that the device: (*one of the below must be checked*) ☐ Does contain any external wired and/or wireless communication interfaces (Wired: USB, ethernet, SD, CD, RGA, etc. or Wireless: Wi-Fi, Bluetooth, RF, inductive, Cloud, etc.) ☐ X Does not contain external interfaces as described above ☐ Information on whether device has external interfaces is not provided (if this box is checked, please also check one of the two boxes below) ☐ Cybersecurity information not needed for this device (e.g., surgical suture, condom) ☐ Cybersecurity information is needed or need unclear This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *If "does not contain" or "not provided and not needed" is selected, the cybersecurity criteria below are omitted from the checklist. If information on cybersecurity is not provided, and this information is needed or the need is unclear, select "No."*			☐		
	35.	All applicable documentation identified by the submitter, as described in "Guidance for the Content of Premarket Submissions for Management of Cybersecurity in Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices-0. **OR** Submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through an alternative approach (i.e., the submitter has identified an alternate approach with a rationale).	☐	☐		
		Comments:				
J.	**Electrical Safety and EMC**					

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**			**Yes**	**No**	**N/A**	***Page #**
	Electrical Safety: Submission states that the device: (*one of the below must be checked*) Does require electrical safety evaluation X Does not require electrical safety evaluation ☐ Information on whether device requires electrical safety evaluation is not provided (if this box checked, please also check one of the two boxes below) ☐ Electrical safety information not needed for this device (e.g., surgical suture, condom) ☐ Electrical safety information needed or need unclear This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *If "does not require" or "not provided and not needed" is selected, the electrical safety criteria below are omitted from the checklist. If information on electrical safety is not provided, and it is needed or the need for this information is unclear, select "No."*			☐		
	36.	Submission includes evaluation of electrical safety (e.g., per IEC 60601-1, or equivalent FDA-recognized standard, and if applicable, a device-specific standard). **OR** Submission includes electrical safety evaluation using methods or standards that are not FDA-recognized and submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through this alternative approach (i.e., the submitter has identified alternate methods or standards with a rationale).	☐	☐		
		Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**			**Yes**	**No**	**N/A**	***Page #**
	EMC: Submission states that the device: (*one of the below must be checked*) Does require EMC evaluation X Does not require EMC evaluation ☐ Information on whether device requires EMC evaluation not provided (if this box checked, please also check one of the two boxes below) ☐ EMC information not needed for this device (e.g., surgical suture, condom) ☐ EMC information needed or need unclear This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *If "does not require" or "not provided and not needed" is selected, the EMC criteria below are omitted from the checklist. If information on EMC is not provided, and it is needed or the need for this information is unclear, select "No."*			☐		
	Comments:					
	37.	Submission includes evaluation of electromagnetic compatibility (e.g., per IEC 60601-1-2 or equivalent FDA-recognized standard and if applicable, a device-specific standard). **OR** Submission includes electromagnetic compatibility evaluation using methods or standards that are not FDA-recognized and submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through this alternative approach (i.e., the submitter has identified alternate methods or standards with a rationale).	☐	☐		
		Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.				Yes	No	N/A	*Page #
K.	**Performance Data General** *If an in vitro diagnostic (IVD) device, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected. Performance data criteria relating to IVD devices is addressed in Section L.*					☐	
	Comments:						
	38.		Summaries of the non-clinical laboratory studies and full test reports* are provided. *Summary and full test report content recommendations can be found in FDA's guidance "Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket. If a submitter chooses to declare conformity to a voluntary consensus standard that FDA has recognized, submission of a full test report may not be necessary. Refer to 9a. See FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices. *Select "N/A" if the submission appropriately does not include performance data or there are no completed tests without a Declaration of Conformity.*	X	☐	☐	20-1
		a.	Submission includes an explanation of how the data generated from each test supports a finding of substantial equivalence (e.g., comparison to predicate device testing, dimensional analysis, etc.). *Select "N/A" if the submission does not include performance data.*	X	☐	☐	20-18
			Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
	39.	The device has a device-specific guidance document, special controls, and/or requirement in a device-specific classification regulation regarding performance data that is applicable to the subject device. *If "N/A" is selected, parts a and b below are omitted from the checklist.*		☐		X	
		a.	The submission addresses performance data recommendations outlined in the device-specific guidance. **OR** The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria. *Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not includea rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.*	☐	☐	X	
		b.	The submission includes performance data that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device. **OR** The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness. *Select "N/A" if there are no applicable special controls or device-specific regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.*	☐	☐	X	
			Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
	40.	If literature is referenced in the submission, submission includes: *Select "N/A" if the submission does not reference literature. If "N/A" is selected, parts a and b below are omitted from the checklist.* *Note that the applicability of the referenced article to support a substantial equivalence finding should be assessed during the substantive review; only the presence of a discussion is required to support acceptance.*				X	
		a.	Legible reprints or a summary of each article.	☐	☐		
		b.	Discussion of how each article is applicable to support the substantial equivalence of the subject device to the predicate.	☐	☐		
			Comments:				
	41.	For each completed animal study, the submission provides the following: *Select "N/A" if no animal study was conducted. If "N/A" is selected, parts a-c below are omitted from the checklist. Note that this section does not address biocompatibility evaluations, which are assessed in Section G of the checklist.*				☐	
		a.	Submission includes a study protocol which includes all elements as outlined in 21 CFR 58.120	☐		X	20-18
		b.	Submission includes final study report which includes all elements outlined in 21 CFR 58.185	☐		X	20-18
		c.	Submission contains a statement that the study was conducted in compliance with applicable requirements in the GLP regulation (21 CFR Part 58), OR, if the study was not conducted in compliance with the GLP regulation, the submission explains why the noncompliance would not impact the validity of the study data provided to support a substantial equivalence determination.	X	☐		20-18
			Comments:				

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
L.	**Performance Characteristics – In Vitro Diagnostic Devices Only (see also 21 CFR 809.10(b)(12))**						
	Submission indicates that device: (*one of the below must be checked*) Is an in vitro diagnostic device X Is not an in vitro diagnostic device *If "is not" is selected, the performance data-related criteria below are omitted from the checklist.*						
	42.	Submission includes the following studies, as appropriate for the device type, including associated protocol descriptions, study results and line data:					
		a.	Precision/reproducibility	☐	☐	X	
		b.	Accuracy (includes as appropriate linearity; calibrator or assay traceability; calibrator and/or assay stability protocol and acceptance criteria; assay cut-off; method comparison or comparison to clinical outcome; matrix comparison; and clinical reference range or cutoff).	☐	☐	X	
		c.	Sensitivity (detection limits, LoB, LoD, LoQ where relevant for the device type).	☐	☐	X	
		d.	Analytical specificity	☐	☐	X	
			Comments:				
	43.	The device has a device-specific guidance document, special controls, and/or requirement in a device-specific classification regulation regarding performance data that is applicable to the subject device. *If "N/A" is selected, parts a and b below are omitted from the checklist.*		☐	☐	X	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.**				**Yes**	**No**	**N/A**	***Page #**
		a.	The submission addresses performance data recommendations outlined in the device-specific guidance. **OR** The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria. *Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not includea rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.*	☐	☐	X	
		b.	The submission includes performance data that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device. **OR** The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness. *Select "N/A" if there are no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.*	☐	☐	X	
			Comments:				

Digital Signature Concurrence Table	
Reviewer Sign-Off	
Management Sign-Off (digital signature optional)*	

*Management review of checklist and concurrence with decision required.

(b)(4) SAS FILEPROCEDURE3

(b)(4)

(b)(4) Clinical Studies

(b)(4) Clinical Studies

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July 10, 2020

Kathryn Wine
VP Clinical Operations
Alydia Health
3475 Edison Way, Ste J
Menlo Park, CA 94025

Re: Cesarean delivery experience with the Jada system for control of postpartum hemorrhage

Dear Ms. Wine:

(b)(4)

(b)(4) Clinical Studies

(b)(4)

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4)

Sponsor:
(b)(4)
Alydia Health, Inc.
3475 Edison Way, Suite J
Menlo Park, CA 94025

MEM Elution GLP Report

Test Article: (b)(4)
Purchase Order:
Study Number:
Study Received Date:
Testing Facility:

Test Procedure(s):
Deviation(s):

(b)(4)

(b)(4)

(b)(4) Testing

(b)(4) Testing

SECTION 12: DEVICE DESCRIPTION

There is no device-specific guidance document, special controls document or requirements in a device-specific classification regulation regarding the device description that is applicable to the subject device.

The device description information provided below is consistent with other sections of this submission that contain such information (510(k) Summary provided in **Section 6,** substantial equivalence discussion provided in **Section 13**, and labeling provided in **Section 14**).

A. Device Overview

The Jada System is a 41 cm long intrauterine device made of silicone **(Figure 1).** The device consists of an Intrauterine Loop on the distal end of the translucent Tube. The proximal end of the Tube has a Vacuum Connector for connection to sterile vacuum tubing. Proximal to the connection of the Intrauterine Loop is a donut-shaped Cervical Seal. The Cervical Seal is filled with and emptied of 60-120 mL of sterile fluid by attaching a sterile syringe to the Seal Valve. The Intrauterine Loop consists of a Loop Tube with 20 Vacuum Pores oriented toward the inside diameter of the Intrauterine Loop. The outer surface of the Intrauterine Loop is covered by a Shield which overhangs the Vacuum Pores to protect tissue from vacuum and to prevent the Vacuum Pores from plugging with tissue and blood clots. The Intrauterine Loop and other components are designed to be soft and smooth to mitigate the chance of tissue damage during insertion and removal of the device.

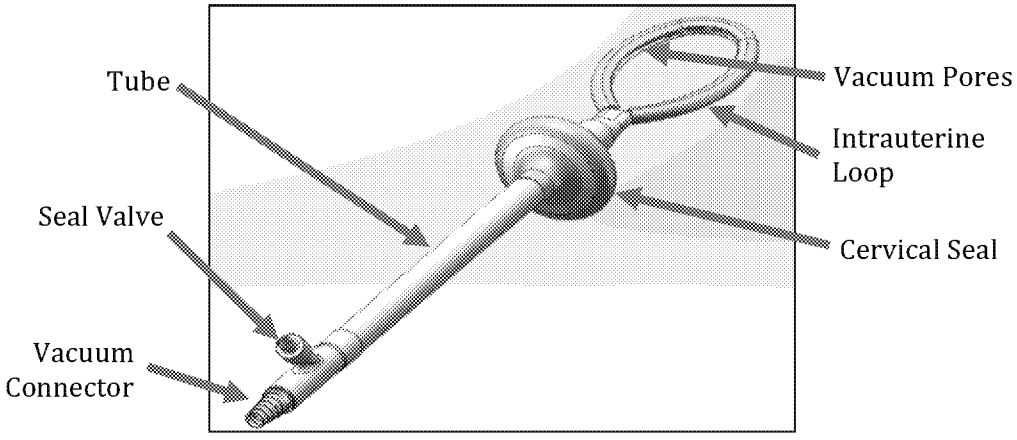


Figure 1: Jada System

During use, the Jada System is inserted transvaginally into the uterus of a woman who has had a vaginal delivery or Cesarean section, after the hysterotomy is closed. The user compresses the sides of the Intrauterine Loop and advances the tip of the Intrauterine Loop through the cervix

and into the uterine cavity. The device is advanced until the Cervical Seal is positioned in the upper vagina at the external cervical os. The Cervical Seal is then filled with sterile fluid using a sterile syringe at the Seal Valve.

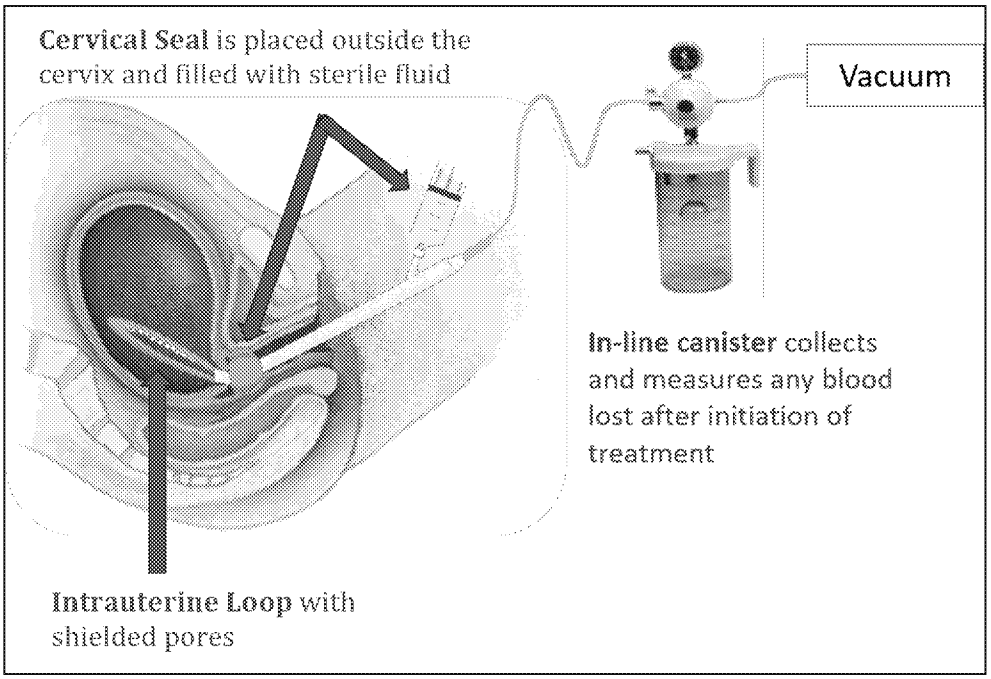


Figure 2: Jada System, Properly Positioned, Prior to Turning Vacuum On

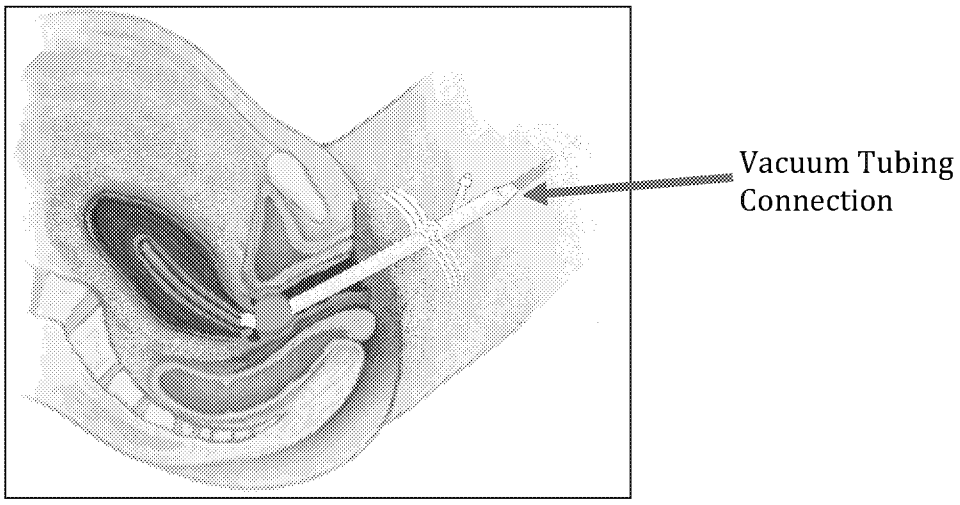


Figure 3: Jada System in Position with Vacuum

Vacuum is supplied via sterile vacuum tubing connected to both the Vacuum Connector on the device and to a regulated vacuum source. In line, between the device and vacuum source, is a graduated canister where any blood evacuated during treatment is both collected and measured (**Figure 2**). Treatment is initiated when vacuum is applied (**Figure 3)**.

B. Principles of Operation

(b)(4)

C. Mechanism of Action

(b)(4)

(b)(4)

D. Conditions of Use

Anatomical Location of Use: The Intrauterine Loop of the Jada System is inserted through the vagina and cervix and into the postpartum uterus after delivery and removal of the placenta.

User Interface: The Jada System is packaged on a backing card within a sterile sealed peel pouch. The distal end of the device is identified by the Intrauterine Loop while the proximal end is identified by the presence of a Vacuum Connector and Seal Valve. With the device in place in the patient, the proximal end of the device extends out of the vagina. When the Cervical Seal of the device is properly placed just outside the external cervical os, it is then filled with sterile fluid by a syringe attached to the Seal Valve. Sterile vacuum tubing is connected to the Vacuum Connector (**Figure 3**).

[1] SN Tripathy. The Uterus Manual. Jaypee Brothers Medical Publishers. First Edition 2009 Chapter 4, page 33

Interaction with Other Devices: The Jada System directly interacts with a sterile luer tapered syringe (used to fill and empty the seal), sterile fluid, tape to secure Jada to patient's leg, and sterile vacuum tubing (connecting Jada to the canister and finally to the source of vacuum).

Device Interaction with the Patient: The Jada System is placed transvaginally into the postpartum uterus. Application of vacuum collapses the uterine walls by removing any blood, body fluids and residual clots from the uterine space. Continued application of vacuum maintains the natural contracted state or involution of the uterus and controls bleeding. The device remains in place with vacuum applied for at least 1 hour until cessation of bleeding and uterine tone is achieved. The vacuum tubing is then disconnected from the device, the Cervical Seal is emptied and the device is left in place for an additional 30 minutes to confirm treatment is complete before removal. The device is removed by placing one hand on the abdomen to secure the uterine fundus while the other hand slowly withdraws the device. The device should not be left in place for more than 24 hours.

E. Detailed Device Description

Overall Device

The subject device, for which clearance is being requested, is the Jada System. The Jada System is manufactured with medical grade silicone and adhesives. The device consists of an Intrauterine Loop section, a Cervical Seal, a Tube and a Y-shaped interface section with a Seal Valve and Vacuum Connector (**Figure 1**). The overall dimensions of the device are: 41 cm long and 60 mm wide with a Cervical Seal diameter of 55 mm when filled with 60 mL of fluid (**Figure 5**). The Cervical Seal depicted in **Figure 5** shows the component shape when neither pressurized with fluid nor evacuated. The Tube of the Jada has a diameter of 15 mm. The Intrauterine Loop (60 mm wide) is flexible and can be folded and compressed to reduce the width to 20 mm (**Figure 6**).

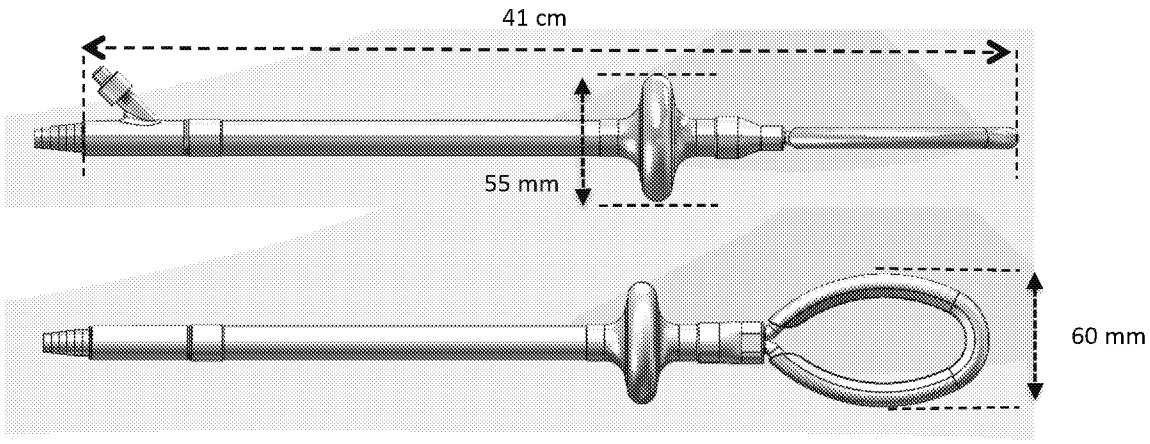


Figure 5: Device Model with Basic Dimensions

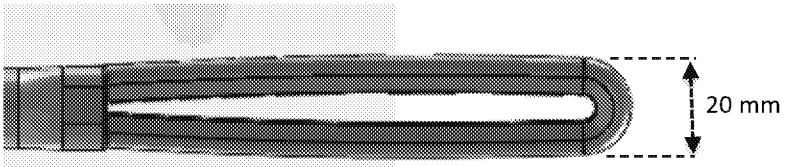


Figure 6: Intrauterine Loop Compressed

Intrauterine Loop

The Intrauterine Loop is an elliptical shape measuring 11 cm long, 60 mm wide (**Figure 7**) and 9 mm thick (**Figure 8**). (b)(4)

(b)(4)

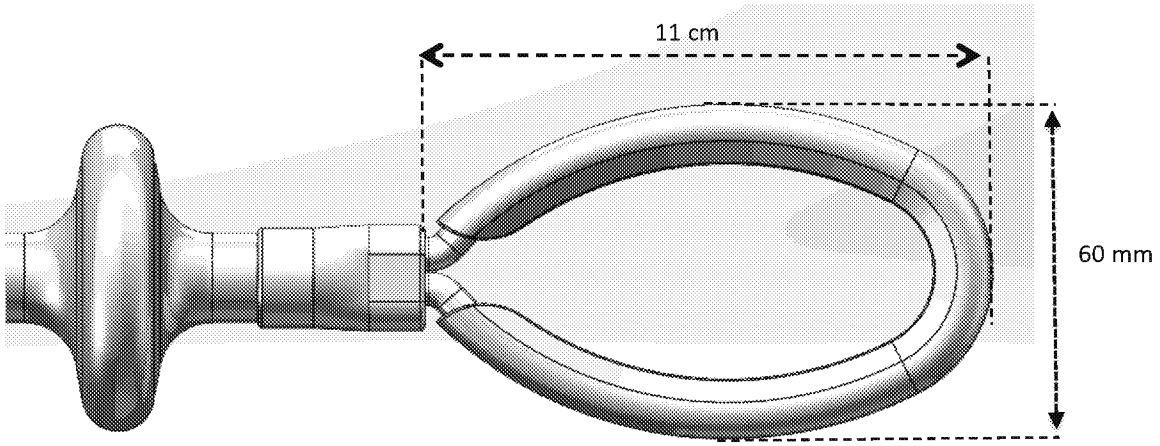


Figure 7: Intrauterine Loop with Basic Dimensions

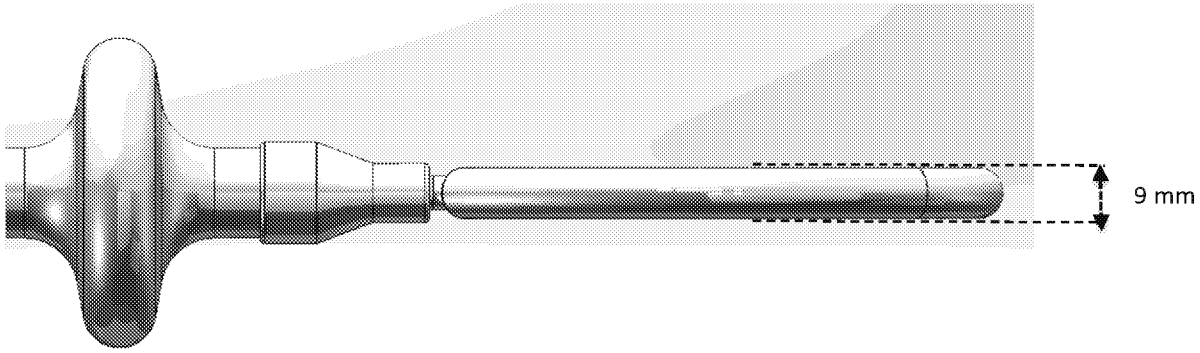


Figure 8: Intrauterine Portion Thickness

Cervical Seal and Tube

(b)(4)

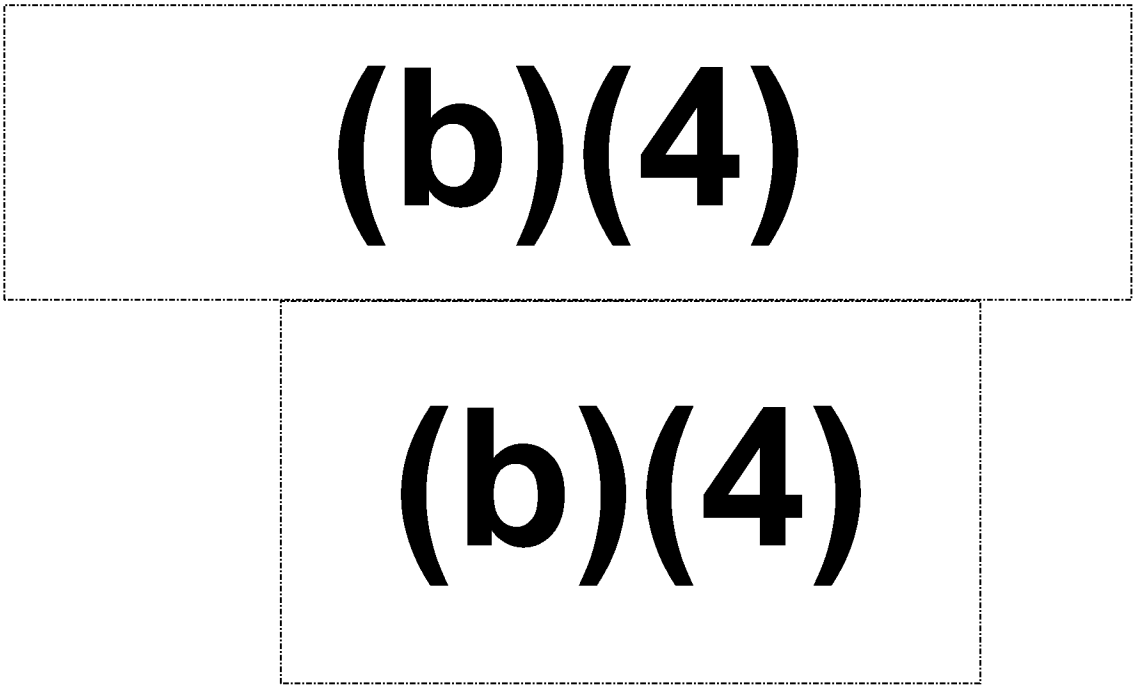


Figure 9: Cervical Seal

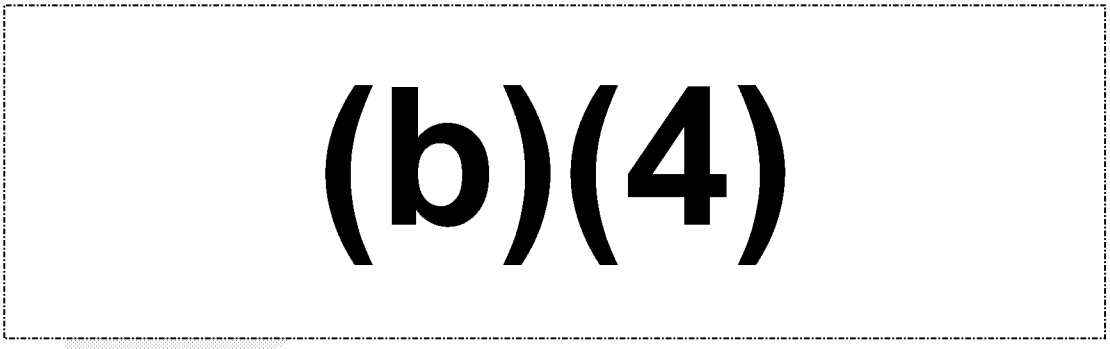


Figure 10: Proximal End of Bilumen Tubing

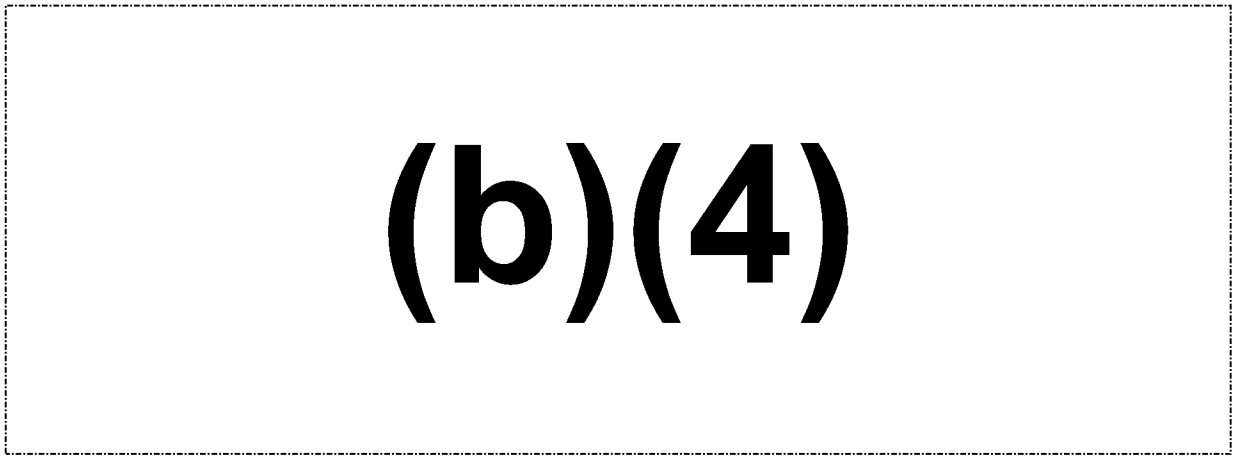
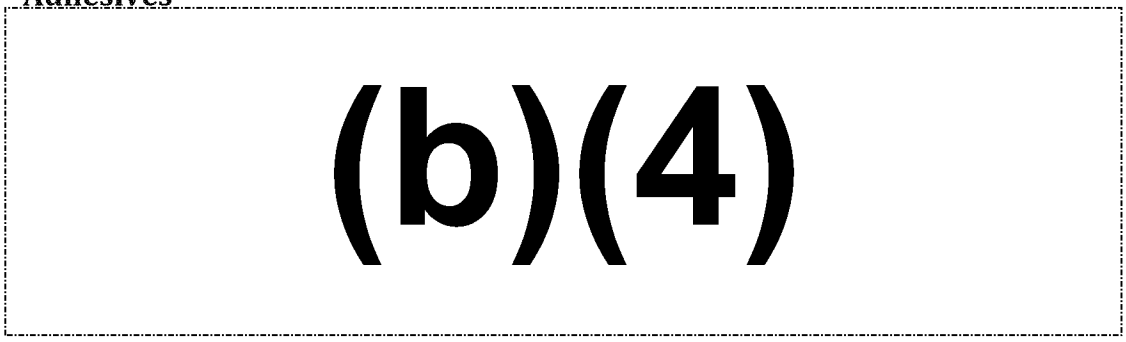


Figure 11: Section View of Vacuum and Inflation Lumens

Adhesives



Materials

All materials used in the Jada System are listed in **Table 12-1**.

Table 12-1 Material Summary.

Component	Material
Tube	Medical grade silicone, HCR, (b)(4)
Shield	Medical grade silicone, LSR,
Tubing Connector	Medical grade silicone, LSR,
Bilumen Tube	Medical grade silicone, HCR,
Y Connector (over-molded material only)	Medical grade silicone, LSR,
Seal Valve	White ABS body, silicone valve
Vacuum Connector	PVC, clear

Cervical Seal	Medical grade silicone, LSR, (b)(4)
Adhesive	Medical grade silicone adhesive, (b)(4) (b)(4)
Sealant	Medical grade silicone sealant, (b)(4) (b)(4)
Colorant for Shield and Cervical Seal	(b)(4)

F. Accessories

The Jada System is not marketed with any accessories. The Instructions for Use describes materials required but not supplied: sterile vacuum tubing (10' to 12'), a sterile 60 mL luer tapered syringe, sterile fluids, vacuum canister, regulated vacuum source, and tape.

Hello Cindy,

I did receive the email you sent on Saturday. Thank you for following up.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

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White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>

Sent: Monday, August 24, 2020 12:50 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov

Subject: Fwd: Request for information for Jada System (K201199/S001)

Hello Reginald,

Would you mind confirming receipt of my below email sent on Saturday? I have received a temporary delivery failure notice for the K number email address, but not yours. Nevertheless, I wanted to make sure you received it. Since the beginning of COVID, I have noticed that emails to FDA donâ€™t always get through on first attempt. I imagine that your servers are overloaded with pandemic-related communications.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

Begin forwarded message:

From: Cindy Domecus
<domecusconsulting@comcast.net<mailto:domecusconsulting@comcast.net>>

Subject: Re: Request for information for Jada System (K201199/S001)

Date: August 22, 2020 at 7:06:42 PM PDT

To: "Avery, Reginald" <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: "K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>"
<K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>>

Hello Reginald,

(b)(4) Deficiencies

Thank you for your continued reivew of our file.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? If possible, please provide a response by noon on Tuesday, August

25, 2020.

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

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Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

Obstetric Hemorrhage Care Guidelines

All patients are active participants in their care. Patients should be informed of any risk factors they may have or develop for PPH and advised of recommendations for their care. These recommendations may be individualized to reflect the patient's decisions.

Prenatal Assessment Planning

Identify and prepare for patients with special considerations: placenta previa/accrete, bleeding disorders or those who decline blood products (and have risk factors)

Admission Hemorrhage Risk Factor Evaluation

Low Risk	Medium Risk Treat 3 or more risk factors as "high risk"	High Risk
• No previous uterine incision • Singleton pregnancy • <4 previous births • No known bleeding disorder • No history of PPH	• Hct<30 • TOLAC • Multiple gestation • ≥ 4 previous births • History of previous PPH • Large uterine fibroids • Polyhydramnios • Estimated fetal weight > 4 kg • Magnesium Sulfate	• Placenta previa • Suspected placenta accreta or percreta • Platelets < 20,000 or ≤ 100,000 with potential for ↓ (i.e. HELLP syndrome) • Known coagulopathy – draw/send appropriate lab tests as specifically ordered for this patient

Admission Assessment & Planning

Type and Screen all patients on admission

- Evaluate for risk factors on admission
- It is strongly recommended that all women who meet criteria for medium/high risk have IV access
- If high risk, T&C for 2 units PRBC's & keep ahead 2; -keep these units available for 24 hours post delivery
- Identify women who may decline transfusion and counsel and consent
- If the patient has moderate/high risk for PPH:
- Review OB Hemorrhage Guideline

Ongoing Risk Assessment

- Evaluate for development of additional risk factors in labor:
  - Prolonged 2nd stage labor (4 hours, including time for "rest and descend")
  - Oxytocin use in labor ≥ 12 hours
  - Sustained antepartum bleeding
  - Suspected Triple I
  - Risk Factors in this column are considered medium risk and need to be added to admission risk factors
- **Treat 3 or more risk factors as "high risk"**
- **Nursing assessment of risk factors Q shift**

Stage 0: All Births – Prevention & Recognition of OB Hemorrhage

- Active management of the third stage of labor
- Administer all IV Pitocin per postpartum Pitocin guideline or give 10 U Pitocin IM
- Starting with delivery blood loss will be quantified for 24 hrs
- Ongoing evaluation of vital signs per guideline/orders
- Empty bladder; patients who have received an epidural/spinal are cathed (straight or Foley) prior to transfer to postpartum
- If patients fundus is not firm but BL <500:
  1. Vigorous crede for at least 15 seconds
  2. Empty her bladder
  3. Consider giving the ordered Methergine/Hemabate (must notify the OB Resident if this is given*)

Stage 1: Bleeding Concern

1. Vaginal deliveries with a cumulative blood loss between 501-999 Ml

AND

2. Sustained active bleeding with normal vital signs and lab values

MOBILIZE	ACT	THINK (differential diagnosis)
Pt's Primary Nurse - Initiate OB Rapid Response: *Team Alert: Bleeding Concern* **If in the OR – just page the CN to make her aware** Postpartum (MNBC or WSC units) – Initiate OB Rapid Response: *Team Alert: Bleeding Concern* ***Call 1-2222 or use Smartweb** Team to go immediately to the bedside to evaluate the patient If this is a CHC, UUHN, UFP, BCHC or private provider patient please notify	**Primary nurse / L&D Rapid Response team** • Constant crede until uterine tone improves • IV resuscitation • Increase Pitocin rate per guideline • Administer uteronics & TXA as ordered • Vital Signs q5 minutes • Empty bladder • Oxygen to maintain Sat≥95 • Keep patient warm **Charge Nurse:** • Assume Team Leader role for RR- initiate OB Hemorrhage Check-list • Ensure that the patient has a current T&S • Initiate OB Bleeding Concern Orderset **Physician or Midwife**: Initiate appropriate interventions and/or treatments	Consider potential etiology • Uterine atony • Trauma/laceration • Retained placenta • Amniotic fluid embolism • Coagulopathy • Placenta accreta • Uterine rupture

Routine Drugs	*Priority*	Dose	Route	Frequency	Contraindications	Possible Side Effects
Pitocin		30 units/ 500 ml	IV	Per Postpartum Pitocin Algorithm	Hypersensitivity to the drug	Usually none; potentially hypotension, nausea, vomiting, hyponatremia with prolonged IV admin.
Methergine		0.2 mg	IM	Q 2-4 hours	Hypertension	Severe hypertension, nausea, vomiting
Hemabate		250 mcg	IM	Q 15 minutes for 8 doses/24 hours	Asthma/bronchospasm	Bronchospasm, diarrhea, nausea, vomiting, fever/ chills
Tranexamic Acid		1 g	IV	Give over 10 min. via pump May repeat in 30 min.		Rare

Patients on the postpartum units should respond within 10 minutes from the initiation of interventions. If not the patient should transfer to Labor and Delivery.

Stage 2: OB Hemorrhage (criteria for PPH/ continue with the algorithm below)
Cumulative Blood Loss: ≥1000 – 2500 mL

MOBILIZE

Pt's Primary Nurse or designee

1) Ongoing patient assessments for S&S of significant hemorrhage such as:
    a) Sustained active bleeding
    b) Hypotension and/or tachycardia
2) If concern about ongoing hemorrhage:
    a) Send out the OB Rapid Response Stage 2 PPH (come now) page

- This alerts the whole team to respond

Recommend that the patient is moved to the OR at this time.

If this is a CHC, UUHN, UFP, BCHC or private provider patient please notify

ACT

Primary nurse/L&D Rapid Response Team

- Tasks/responsibilities as designated on the OB Rapid Response grid

Charge Nurse:

Assume Team Leader role for RR

- Initiate/Continue to fill in the *OB Hemorrhage Checklist*
- Ensure that CBC & Coags/ Rotem are drawn when #2 IV is started (T&S/T&C if not already done)
- Notify Anes. Tech to run the Rotem
- Delegate a nurse to call the Blood Bank and notify them of the need for emergency blood products as directed
- Delegate a nurse to initiate the OB Hemorrhage Orderset
- Delegate team member to have ongoing communication with the Blood Band as needed (1-2331)
- Ask Senior Provider if they would like IR notified.
- Ask if Antibiotics are needed

THINK (differential diagnosis)

Sequentially advance through procedures and other interventions based on etiology

Vaginal Birth

Evaluate for uterine atony:
- Initiate/Continue with uterotonics and TXA
- Uterine tamponade balloon
- Consider surgical interventions or IR

Evaluate for lacerations
- Visualize and repair

Evaluate for retained products of conception:
- Manual removal
- D&C

Evaluate for uterine inversion:
- General anesthesia or Nitroglycerine for uterine relaxation for manual reduction

Cesarean Section

- Initiate/Continue with uteronics and TXA
- B-Lynch
- Uterine tamponade balloon

If Amniotic Fluid Embolism (AFE):
Maximally aggressive respiratory, vasopressors and blood product support

Stage 3: OB Hemorrhage

Cumulative blood loss ≥ 2500 mL and/or need for rapid administration of blood products, hemodynamically unstable or suspicion of coagulopathy

MOBILIZE	ACT	THINK (differential diagnosis)
Patient must be moved to the OR at this time if she is not already there If this is a CHC, UUHN, UFP, BCHC or private provider patient please notify	**Primary nurse/L&D Rapid Response Team:** • Tasks/responsibilities as designated on OB Rapid Response grid **Charge Nurse:** • Assume Team Leader role for RR • Delegate team member to have ongoing communication with the Blood Band (1-2331)	• Prevention of hypothermia, acidemia • Conservative or definitive surgery: ◊ B-Lynch ◊ Hysterectomy ◊ O'Leary • Transfuse blood products as needed • Unresponsive coagulopathy

Once stabilized:
- **Consider ICU transfer (notify the House Supervisor)**
- **Vigilant postpartum management with increased surveillance**

Blood Products

• Massive Transfusion Protocol (6 PRBC &FFP/1Platelet) ➢ Call the blood bank @1-2331 ➢ Tell them you are initiating the MTP for: ➢ Pt's name, MRN and physician who is ordering the MTP • If cryoprecipitate is needed use the Emergency Release process ➢ Consider using fibrinogen concentrate (Riastap/3grams) as a bridge if fibrin is emergently needed and you are waiting for the cryoprecipitate to be ready.	A unit typically increases to Hct by 3 %
Packed Red Blood Cells (PRBC)	1 unit typically increased Hct by 3%
Fresh Frozen Plasma (FFP): Approximately 30 minutes to thaw	1 unit typically 180 ml and typically increased Fibrinogen by 10mg/dL
Platelets:	Provides a transient 40-50 K increase in platelet count
Cryoprecipitate (Cryo): Approximately 30 minutes to prepare	10 packs typically raises Fibrinogen 80-100 mg/dL

Postpartum Unit Care

1. All patients are to have all blood loss quantified by weighing for 24 H post-delivery and the patient is stable.
2. PPH Risk assessment is done at patient transfer and every shift for 24 hours following delivery
3. Any patient who has been identified as high risk for Postpartum Hemorrhage or has had a Postpartum Hemorrhage requires increased surveillance for 24H post-delivery. This includes Q2 hour fundal/lochia checks and maintaining IV access for 24 hours (if IV infiltrates, no need to restart)
4. If a patient's fundus is assessed to be not firm do the following:
    - Vigorous crede
    - Have the patient empty her bladder
    - Consider giving the ordered Methergine/Hemabate (must notify the OB Resident if this is given*)

If the patient has a Stage 1 Bleeding Concern and has not responded to treatment within 10 minutes she is to be transferred immediately to L&D

- ◊ Notify L&D of transfer

If this is a CHC, UUHN, UFP, BCHC or private provider patient please notify them as well

J Fisher RNC/ Jan 2019

(b)(4)

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

Exhibit 20: Clean copy of revised Jada System Quick Reference Guide

Quick Reference Guide

Caution: Please refer to the Jada System Instructions for Use (IFU) for complete information. The Jada System IFU can be found at www.alydiahealth.com/IFU

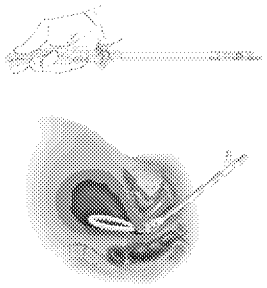
1. Evaluate patient & prepare Jada

- Evaluate patient for lacerations, retained products of conception, or other causes of bleeding before using Jada.
- Connect a vacuum canister and standard vacuum tubing to a regulated vacuum source.
- Connect syringe to Seal Valve to REMOVE AIR from Cervical Seal.

Remove air from Cervical Seal before use

2. Insert Jada

- Grasp and compress Intrauterine Loop and insert transvaginally.
- Use gentle traction on the anterior cervical lip to stabilize the cervical opening, if needed.
- Ensure correct placement: Intrauterine Loop within the uterus and Cervical Seal within the vagina at the external cervical os.

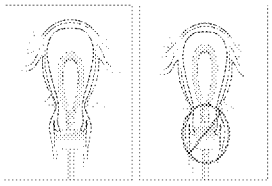


Transvaginal Placement

3. Fill Cervical Seal

- Fill the Cervical Seal with 60 mL of sterile fluid.
- Add up to another 60 mL of fluid, if needed, to achieve full coverage of the external cervical os; do not exceed 120 mL.
- Do NOT advance Cervical Seal into the uterus while filling.

Fill Cervical Seal with 60 mL of sterile fluid (up to 120 mL)



Confirm Cervical Seal is outside cervical os

4. Turn on and set vacuum, then connect tubing

- Turn on vacuum source and set to 80 mm Hg (+/- 10 mm Hg) while occluding the end of the tubing. Maximum vacuum pressure is 90 mm Hg.
  - 80 mm Hg = 1.5 psi = 10.7 kPa = 3.2 in Hg = 106.7 mbar
- Connect Jada to vacuum tubing.

5. Treatment

- Leave Jada in place with vacuum applied, using tape to secure the Tube to the patient's inner thigh.
- Blood flow into the vacuum tubing and/or improvement in uterine tone should be noted after initiation of vacuum.
- After initial evacuation of any pooled blood, presentation may vary during treatment: there may be no further blood evacuation, or additional blood moving into the tubing, or accumulation of blood in the canister.
- Verify bleeding is controlled.
- Leave vacuum on for at least one hour after bleeding is controlled, and verify the uterus is firm and patient is stable before disconnecting vacuum.
- Consider prophylactic antibiotics for prolonged use. Do not leave the Jada in place for >24 hours.

Set vacuum to 80 ±10 mm Hg

6. Verify

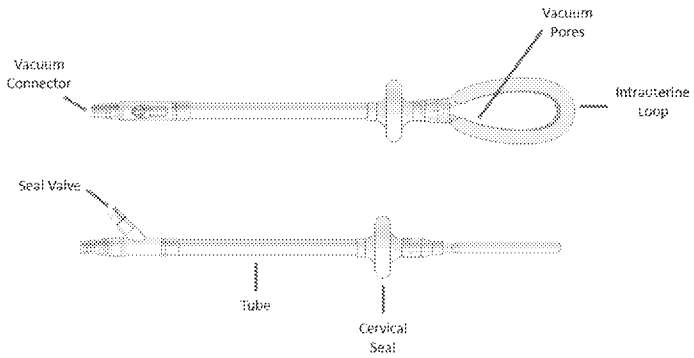
- Ensure Tube remains secured with tape to patient's inner thigh.
- Disconnect vacuum tubing from Jada while vacuum is on.
- Remove all sterile fluid from Cervical Seal.
- Wait at least 30 minutes to verify bleeding is controlled.
- If bleeding recurs, repeat steps 3 – 6, if appropriate.

7. Remove Jada

- If bleeding remains controlled and the uterus remains firm, remove the Jada slowly while supporting the uterine fundus.

TROUBLESHOOTING

SITUATION	RECOMMENDED ACTION
Vacuum is not detected at the end of the vacuum tubing.	a) Check connection on all system components: • Confirm vacuum source is functional, including regulator. • Confirm lid of vacuum canister is fully seated and that canister is not cracked. • Confirm vacuum tubing is securely connected at both ends and any connection in between. b) Confirm desired vacuum level is regulated in the appropriate units (i.e. mm Hg vs. cm Hg).
Vacuum system is connected and working but uterus does not collapse and/or bleeding does not stop.	a) Increase vacuum pressure to maximum (90 mm Hg). b) Disconnect the vacuum tubing from Jada and occlude the end of the tubing to check vacuum. c) Confirm appropriate Jada placement, with ultrasound if needed: • Confirm proper placement of Intrauterine Loop in uterus (vs. misplacement in posterior vaginal fornix). • Confirm proper placement of Cervical Seal outside of the cervical os (vs. misplacement into uterus). • Ensure Cervical Seal is sufficiently filled with sterile fluid to create adequate seal at the cervix. d) Re-evaluate patient for other sources of bleeding.



MATERIALS REQUIRED BUT NOT SUPPLIED

• Sterile Luer Tapered Syringe: 60 mL recommended	• Regulated Vacuum Source
• 60 mL Sterile Fluid (Maximum 120 mL)	• Vacuum Canister
• Sterile Vacuum Tubing: 10'-12'	• Tape

CAUTION: Federal law (USA) restricts the Jada System to sale by or on the order of a physician.

LBL-12 V 2.0

Hello Reginald,

(b)(4) Deficiencies

Thank you for your continued reivew of our file.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

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> Hello,

>

> I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? If possible, please provide a response by noon on Tuesday, August 25, 2020.

(b)(4) Deficiencies

> Do not hesitate to contact me if you have any questions or concerns.

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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> DHT3B: Division of Reproductive, Gynecology and Urology Devices

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(b)(4)

(b)(4) Protocol

(b)(4) Protocol

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(b)(4) Protocol

CMQCC
California Maternal
Quality Care Collaborative

Tranexamic acid (TXA) for Obstetric Hemorrhage
July 2017

Background

Obstetric hemorrhage is most often caused by either uterine atony, retained placental fragments or trauma (perineal, vaginal, cervical or uterine laceration). The initial approach is to address the underlying cause (e.g. uterotonics for atony and surgical correction for lacerations). A low fibrinogen from loss or dilution or evidence of fibrinolysis (on either TEG® or ROTEM® testing) can predict the transition to massive hemorrhage (>1500 ml). The presence of coagulopathy can make obstetric or postpartum hemorrhage (PPH) particularly dangerous, resulting in multiple units of blood transfusion, hysterectomy or death.

Tranexamic acid (TXA) is an inhibitor of fibrinolysis and may reduce bleeding in the setting of coagulation abnormalities. Prior studies have shown minimal, if any, benefit for prophylactic use of TXA at cesarean section. The recent WOMAN international randomized controlled trial showed a 31% reduction in death from hemorrhage when 1g of TXA was administered intravenously within 3 hours after the diagnosis of PPH.[1] This trial included over 20,000 women with PPH in a mix of low and high resource countries.

Should we use TXA for obstetric hemorrhage treatment in high resource settings? First, we need to stress that TXA is NOT an initial treatment—we cannot overemphasize the importance of early diagnosis and management with uterotonics or surgical repair. If the hemorrhage continues, the risk of coagulopathy rises, at which time TXA may have an important role.

TXA Safety

TXA has a reassuring safety profile for the dosage used in the WOMAN trial (1gm intravenous over 10 minutes with a second 1 gm dose administered at 30 minutes if the bleeding persists). Venous thromboembolic events, seizures and renal complications were NOT seen at higher rates than the controls in this study (these complications have been a concern with higher TXA doses). However, there have been reports of medication errors in orthopedic cases with "look-alike" vials of local anesthetics (bupivicaine) where TXA was inadvertently administered intrathecally resulting in deaths or major neurologic injuries.[2,3] These errors were not identiifed in the WOMAN trial but there have been several such errors in obstetric cases reported to SOAP (personal communication, Alex Butwick, MD).

Where should TXA fit in a hemorrhage management protocol?

Again, we consider TXA to be an adjunctive treatment and NOT a primary treatment for PPH. The exact placement in your facility's hemorrhage protocol will depend on local resources; our preliminary recommendations suggest use of TXA if:

- Bleeding continues after higher dose oxytocin and methergine have been administered (end of CMQCC Hemorrhage Stage 1), or
- Additional interventions (e.g. Hemabate® or compression balloons) are being considered (beginning of CMQCC Hemorrhage Stage 2).

- TXA should be considered for inclusion in the unit OB Hemorrhage medication kit for rapid accessibility. Restriction to a hemorrhage medication kit may reduce the risk of look-alike drug error (specifically do not put TXA in same place as local anesthetics). Another approach is to clearly label vials of TXA as "NOT FOR NEURAXIAL ADMINISTRATION" to limit the likelihood of inadvertent wrong site administration.
- Fibrinogen replacement (e.g. cryoprecipitate) in the setting of fibrin breakdown is most effective if given AFTER administration of TXA (but don't delay blood products to administer TXA if the clinical condition calls for transfusion).

Important points of emphasis:

- A serious postpartum hemorrhage requires "many hands" and there is concern for "task saturation" (many things to be done at the same time by a limited number of people), Your hospital protocol should emphasize that 1) usual initial treatment steps need to be undertaken first (and not delayed for TXA administration), 2) as TXA is an additional step, it is important to ensure that enough staff are mobilized, and that 3) TXA should be a formal part of the PPH protocol so the staff is familiar and organized in its use.
- Dosing limits should be respected; the TXA dose that has been shown to be safe and effective for limiting OB hemorrhage is 1gm that may be repeated ONCE at 30 minutes.
- The WOMAN trial clearly demonstrated that TXA is most effective when given within 3 hours of hemorrhage diagnosis, hence the recommendation that it be considered relatively early in the hemorrhage protocol.

Intravenous Administration (from PDR)

- TXA solution for intravenous use contains 100mg per ml. can be used as slow IV injection or diluted within a 50 or 100ml IV piggyback to be given as an intravenous infusion.
- To avoid hypotension, administer at a rate not to exceed 100 mg per minute. (i.e 1gm over 10 minutes)
- Prepare the same day the solution is to be used; discard any remaining solution after single-use.
- May be mixed with most solutions for infusion such as electrolyte, carbohydrate, amino acid, and dextran solutions.
- Do not add heparin to injection or mix with blood; do not mix with solutions containing penicillin.

Renal Failure/Renal Impairment Cautions (from PDR)

Use tranexamic acid cautiously in patients with renal impairment or renal failure; elimination may be significantly delayed in these patients. Tranexamic acid is eliminated primarily via the kidneys by glomerular filtration with >95% excreted unchanged in the urine. Dosage adjustment in patients with renal impairment are required (see Dosage recommendations in the PDR). Patients with renal impairment should be observed carefully for signs and symptoms of toxicity (e.g., thromboembolism) during tranexamic acid therapy.

Note: for the low doses described for PPH (1gm IV infusion with a single repeat does of 1gm) toxicity has not been described even in the setting of renal impairment.

Experience of TXA Usage in France and United Kingdom

TXA has been used for PPH for many years in France and the United Kingdom. Discussions with colleagues leading national obstetric safety programs in those countries (UK-NPEU/MBRRACE and France-INSERM and AUDIPOG)[4] identified similar usage between the two countries and is described below (July 2017, personal communications, Elliott Main, MD):

1. TXA 1gm is usually administered after routine first line PPH drugs have not controlled the bleeding but before the need for blood products and/or additional procedures (similar to the position in the CMQCC hemorrhage treatment protocol recommended above).
2. 1gm TXA diluted into a 50ml or 100ml saline bag is usually administered by an anesthesiologist (if involved) or by a nurse and usually as an intravenous drip over 10-30 minutes. The solution is commonly made up by the anesthesiologist or nurse with a double check of the label.
3. The undiluted solution of 10ml (1 gm) TXA can also be administered by slow IV push over 10 minutes.

July 24, 2017

CMQCC Hemorrhage Update Committee:

Elliott Main, MD , Chair
Alex Butwick , MBBS
Maurice L Druzin, MD
William Gilbert, MD
Jed Gorlin, MD
Neeru Gupta, MD
David Lagrew, MD
Richard Lee, MD
Evelyn Lockhart, MD
Audrey Lyndon, RN PhD
Jennifer McNulty, MD
Mark Rollins, MD PhD
Christa Sakowski, CNM
Larry Shields, MD

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[1] WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet. 2017 May 27;389(10084):2105-2116.

[2] Yeh HM, Lau HP, Lin PL, et al. Convulsion and refractory ventricular fibrillation after intrathecal administration of a massive dose of tranexamic acid. Anaesthesiology 2003;98:270–2.

[3] Garcha PS, Mohan CV, Sharma RM. Death after an inadvertent intrathecal injection of tranexamic acid. Anesth Analg. 2007 Jan;104(1):241-2.

[4] UK NPEU/MBRRACE is the UK National Perinatal Epidemiology Unit and the section that oversees the confidential enquiries into maternal deaths; INSERM is the French equivalent to the NIH; AUDIPOG is a national data-driven OB quality improvement program in France

WHO recommendation on tranexamic acid for the treatment of postpartum haemorrhage

World Health Organization

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Contents

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Therese Dowswell and Anna Cuthbert reviewed the scientific evidence, prepared the GRADE tables and drafted the narrative summary of evidence. Joshua Vogel and Olufemi Oladapo revised the narrative summaries and double-checked the corresponding GRADE tables. Joshua Vogel, Olufemi Oladapo, A. Metin Gülmezoglu and Mercedes Bonet commented on the draft document before it was reviewed by participants at the WHO technical consultation. The External Review Group peer-reviewed the final document.

We acknowledge the various organizations that were represented by observers at the final technical consultation, including Deborah Armbruster (United States Agency for International Development), Kusum Thapa (Maternal and Child Survival Program/Jhpiego), Janna Patterson (Bill & Melinda Gates Foundation), Sally Tracy (International Confederation of Midwives), Gerard Visser (International Federation of Gynecology and Obstetrics) and Beverly Winikoff (Gynuity Health Projects). Haleema Shakur-Still (London School of Hygiene and Tropical Medicine) provided an overview of the conduct and findings of the WOMAN trial but did not participate in the GDG deliberations. We appreciate the contributions of WHO Regional Office staff to this update - Mavjuda Babamuradova, Ramez Khairi Mahaini, Anoma Jayathilaka, Bremen De Mucio, Claudio Sosa, Mari Nagai and Léopold Ouedraogo.

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Acronyms and abbreviations

CI	confidence interval
CRASH-2	Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage trial
DOI	Declaration of Interest
FIGO	International Federation of Gynecology and Obstetrics
FWC	Family, Women's and Children's Health (a WHO cluster)
GDG	Guideline Development Group
GRC	Guideline Review Committee
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
GSG	Executive Guideline Steering Group
ICM	International Confederation of Midwives
IPD	individual participant data meta-analysis
LMIC	low- and middle-income country
LY	life-year
MCA	WHO Department of Maternal, Newborn, Child and Adolescent Health
MPA	Maternal and Perinatal Health & Preventing Unsafe Abortion (a team in WHO's Department of Reproductive Health and Research)
MPH	maternal and perinatal health
NNT	number needed to treat
PICO	population (P), intervention (I), comparison (C), outcome (O)
PPH	postpartum haemorrhage
RHR	[WHO Department of] Reproductive Health and Research
RR	relative risk
SDG	Sustainable Development Goals
TXA	tranexamic acid
UN	United Nations
UNFPA	United Nations Population Fund
USAID	United States Agency for International Development
WHO	World Health Organization
WOMAN	World Maternal Antifibrinolytics trial

Executive Summary

Introduction

Postpartum haemorrhage (PPH) is commonly defined as a blood loss of 500 ml or more within 24 hours after birth, and it affects about 5% of all women giving birth around the world. Globally, nearly one quarter of all maternal deaths are associated with PPH, and in most low-income countries it is the main cause of maternal mortality.

Improving care for women around the time of childbirth to prevent and treat PPH is a necessary step towards achievement of the health targets of the Sustainable Development Goals (SDGs). Efforts to prevent and reduce PPH-associated morbidity and mortality can reduce the profound inequities in maternal health globally. To achieve this, healthcare providers, health managers, policy makers and other stakeholders need up-to-date and evidence-based recommendations to inform clinical policies and practices.

In 2017, the Executive Guideline Steering Group (GSG) on WHO maternal and perinatal health recommendations prioritized the updating of the existing WHO recommendation on the use of tranexamic acid (TXA) for PPH treatment in response to important new evidence on this intervention. This updated recommendation thus supersedes the previous recommendation on TXA for PPH treatment, which was issued in the 2012 WHO recommendations on prevention and treatment of PPH.

Target audience

The primary audience includes health professionals who are responsible for developing national and local health protocols (particularly those related to PPH) and those directly providing care to pregnant women and their newborns, including midwives, nurses, general medical practitioners, obstetricians, managers of maternal and child health programmes, and relevant staff in ministries of health, in all settings.

Guideline development methods

The updating of this recommendation was guided by standardized operating procedures in accordance with the process described in the *WHO handbook for guideline development.* The recommendation was initially developed using this process, namely (i) identification of the priority question and critical outcomes, (ii) retrieval of the evidence, (iii) assessment and synthesis of evidence, (iv) formulation of the recommendation, and (v) planning for the dissemination, implementation, impact evaluation and updating of the recommendation.

The scientific evidence supporting the recommendation was synthesized using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. The systematic review was used to prepare evidence profiles for the prioritized question. WHO convened an online technical consultation on 29 August 2017 where an international group of experts - the Guideline Development Group (GDG) - formulated and approved the recommendation.

Recommendation

The WHO technical consultation adopted one recommendation related to the use of TXA for the treatment of PPH. In formulating the recommendation, the GDG reviewed the balance between desirable and undesirable effects of TXA and overall quality of supporting evidence, values and preferences of stakeholders, resource requirements and cost-effectiveness, acceptability, feasibility and equity. To ensure that the recommendation is correctly understood and applied in practice, the contributing experts provided additional remarks. Guideline users should refer to these remarks, as well as to the evidence summary, if there is any doubt as to the basis for the recommendation and how best to implement it. The WHO recommendation on TXA for treatment of PPH is summarized in Table 1 below.

Table 1: Updated WHO recommendation on tranexamic acid for the treatment of postpartum haemorrhage

Early use of intravenous tranexamic acid (within 3 hours of birth) in addition to standard care is recommended for women with clinically diagnosed postpartum haemorrhage following vaginal birth or caesarean section. *(Strong recommendation, moderate quality of evidence)*
Remarks
• Based on the dosing regimen used in the WOMAN trial, the GDG supports the administration of tranexamic acid (TXA) at a fixed dose of 1 g (100 mg/ml) intravenously (IV) at 1 ml per minute (i.e. administered over 10 minutes), with a second dose of 1 g IV if bleeding continues after 30 minutes, or if bleeding restarts within 24 hours of completing the first dose.
• The WOMAN trial defined "clinically diagnosed postpartum haemorrhage" as clinically estimated blood loss of more than 500 ml after a vaginal birth or 1000 ml after caesarean section, or any blood loss sufficient to compromise haemodynamic stability.
• Based on evidence from the WOMAN trial, the reference point for the start of the 3-hour window for starting TXA administration is time of birth. If time of birth is unknown, the best estimate of time of birth should be used as the reference point. As most deaths due to postpartum haemorrhage (PPH) occur within the first 2 to 3 hours after birth, it is critical that TXA is given as soon as possible to achieve clinical benefits.
• Analysis of the effects of timing of administration in the WOMAN trial, as well as an individual participant data (IPD) meta-analysis of 40 138 bleeding patients (including WOMAN trial participants), indicates that TXA administration beyond 3 hours does not confer any clinical benefit. Furthermore, the point estimates of effect of TXA use beyond 3 hours on death for trauma or after PPH were both in the direction of harm, albeit not statistically significant for women with PPH. In view of this evidence, the GDG does not support the use of TXA more than 3 hours after birth.
• Administration of TXA should be considered as part of the standard PPH treatment package. Standard care in the context of this recommendation includes routine care for PPH treatment, including fluid replacement, medical (uterotonics), monitoring of vital signs, nonsurgical (e.g. bimanual compression, intrauterine balloon tamponade, nonpneumatic antishock garment, aortic compression) and surgical interventions (e.g. brace sutures, arterial ligation, or hysterectomy) in accordance with WHO guidelines or adapted local PPH treatment protocols.
• TXA should be used in all cases of PPH, regardless of whether the bleeding is due to genital tract trauma or other causes.
• The use of TXA should be avoided in women with a clear contraindication to antifibrinolytic therapy (including TXA) (e.g. a known thromboembolic event during pregnancy).
• This recommendation applies only to IV use. The evaluation of benefits and potential harms of other routes of TXA administration is a research priority.
• Regardless of the level of health system resources, TXA should be recognized as a life-saving intervention and be made readily available for the management of PPH in settings where emergency obstetric care is provided.

1. Background

PPH is commonly defined as a blood loss of 500 ml or more within 24 hours after birth, and affects about 5% of all women giving birth around the world.[1,2] Globally, nearly one quarter of all maternal deaths are associated with PPH, and in most low-income countries it is the main cause of maternal mortality.[3]

Severe PPH is generally defined as a blood loss of 1000 ml or more after birth. Severe maternal health conditions, such as organ dysfunction or death, generally occur following substantial blood loss that compromises maternal haemodynamic stability. Uterine atony is the most common cause of PPH and a leading cause of maternal mortality worldwide.[3] Genital tract trauma (that is, vaginal or cervical lacerations), uterine rupture, retained placental tissue, or maternal bleeding disorders are frequently associated with PPH. Although the majority of women presenting with PPH have no identifiable risk factor, grandmultiparity, prolonged labour and multiple gestation are obstetric conditions that are associated with an increased risk of bleeding after birth.[4] In addition, anaemia is a common aggravating factor.

The majority of PPH-associated deaths could be avoided by the use of prophylactic uterotonics during the third stage of labour and appropriate treatment. Thus, improving health care for women during childbirth to prevent and treat PPH is a necessary step towards achievement of the health targets of the Sustainable Development Goals (SDGs). Furthermore, 99% of all maternal deaths occur in low- and middle-income countries (LMICs). Efforts to prevent and reduce PPH-associated morbidity and mortality can thus reduce the profound inequities in maternal health globally. In support of this, health workers at all levels of care (particularly in LMICs) need to have access to appropriate medications and training in relevant procedures. Healthcare providers, health managers, policy-makers and other stakeholders also need up-to-date, evidence-based recommendations to inform clinical policies and practices, in order to enable improved healthcare outcomes.

In 2012, WHO published 32 recommendations for the prevention and treatment of PPH, including a recommendation on the use of TXA for treatment of PPH.[5] These recommendations were developed according to WHO guideline development standards, including synthesis of available research evidence, use of the GRADE methodology, and formulation of recommendations by a guideline panel of international experts.

In 2017, the Executive GSG on WHO maternal and perinatal health recommendations prioritized the updating of the existing WHO recommendation on the use of TXA for PPH treatment in response to important new evidence on this question. This updated recommendation thus supersedes the previous recommendation on TXA for PPH treatment, issued in the 2012 WHO recommendations on prevention and treatment of PPH.

Rationale and objectives

TXA is a competitive inhibitor of plasminogen activation, and it can reduce bleeding by inhibiting the enzymatic breakdown of fibrinogen and fibrin clots.[6] It is in routine clinical use for reduction of blood loss in surgery and trauma, and it is listed on the WHO Essential Medicines List for management of anticoagulation.[7] At the time of

the GDG meeting on prevention and treatment of PPH in March 2012, there was no direct evidence on the effectiveness and safety of TXA when used for treatment of PPH. The GDG conditionally recommended the use of TXA for the treatment of PPH only when uterotonics fail to control the bleeding or when the bleeding is thought to be partly due to trauma. The GDG noted that a large, randomized controlled trial - the World Maternal Antifibrinolytic (WOMAN) trial examining the effect of early administration of TXA on mortality, hysterectomy, and other morbidities in women with clinically diagnosed PPH - was ongoing.[8] The WOMAN trial has now concluded, and the primary findings were published in April 2017.[9] In light of this new evidence, the Executive GSG prioritized the updating of the recommendation on TXA use for PPH treatment.

As part of WHO's normative work on supporting evidence-informed policies and practices, the Department of Reproductive Health and Research (RHR) has now updated the recommendation on the use of TXA for treatment of PPH. This recommendation provides a foundation for the sustainable implementation of the intervention globally.

Target audience

The primary audience includes health professionals who are responsible for developing national and local health guidelines and protocols (particularly those related to PPH) and those directly providing care to women during labour and childbirth, including midwives, nurses, general medical practitioners, obstetricians, managers of maternal and child health programmes and relevant staff in ministries of health, in all settings.

This recommendation will also be of interest to professional societies involved in the care of pregnant women, nongovernmental organizations concerned with promotion of people-centred maternal care, and implementers of maternal and child health programmes.

Scope of the recommendation

The question for this recommendation was: in women with PPH (P), does administration of TXA for PPH treatment (I) compared to placebo, no treatment or other treatments (C), improve outcomes (O)? If so, what is the most appropriate period to administer TXA to improve outcomes? The population affected by this recommendation includes women who experience PPH in low-, middle- or high-income settings.

2. Methods

This recommendation is an update of the existing recommendation relating to TXA use for PPH treatment, published in the *WHO recommendations for prevention and treatment of postpartum haemorrhage* (2012).[5]

The recommendation was first developed using standardized operating procedures in accordance with the process described in the *WHO handbook for guideline development*.[10] In summary, the process included: (i) identification of the priority question and critical outcomes, (ii) retrieval of the evidence, (iii) assessment and

synthesis of evidence, (iv) formulation of the recommendation, and (v) planning for the dissemination, implementation, impact evaluation and updating of the recommendation. The WHO recommendation on TXA use for treatment of PPH was identified by the Executive GSG as a high priority for updating in response to new, important evidence on this question.

The updating of this recommendation involved five main groups to guide the process, with their specific roles as described in the following sections.

Contributors to the guideline

Executive Guideline Steering Group (Executive GSG)

The Executive GSG is an independent panel of external experts and relevant stakeholders from the six WHO regions. This group advises WHO on the prioritization of new and existing questions in maternal and perinatal health for recommendation development or updating.

WHO Steering Group

The WHO Steering Group, comprising WHO staff members from the Departments of Reproductive Health and Research (RHR) and Maternal, Newborn, Child and Adolescent Health (MCA), managed the updating process. The Group drafted the key recommendation question in PICO format, identified the systematic review team and guideline methodologist, as well as the guideline development and external review groups. In addition, the WHO Steering Group supervised the retrieval and syntheses of evidence, organized the Guideline Development Group meeting, drafted and finalized the guideline document, and managed the guideline dissemination, implementation and impact assessment. The members of the Steering Group are presented in Annex 1.

Guideline Development Group

The WHO Steering Group identified a pool of approximately 50 experts and relevant stakeholders from the six WHO regions to constitute the WHO Maternal and Perinatal Health Guideline Development Group (MPH-GDG). This is a diverse group of experts who are skilled in critical appraisal of research evidence; implementation of evidence-based recommendations; guideline development methods; and clinical practice, policy and programmes relating to maternal and perinatal health. Members of the MPH-GDG are identified in a way that ensures geographic representation and gender balance, and there were no significant conflicts of interest. Members' expertise cuts across thematic areas within maternal and perinatal health.

From the MPH-GDG pool, 14 external experts and relevant stakeholders were invited to constitute the Guideline Development Group (GDG) for updating this recommendation. This wasis a diverse group of individuals with expertise in PPH research, guideline development methods, and clinical policy and programmes relating to PPH prevention and treatment.

The GDG members convened for this recommendation were selected in a way that ensured geographic representation and gender balance, and there were no important conflicts of interest. The Group appraised the evidence that was used to inform the recommendation, advised on the interpretation of this evidence,

formulated the final recommendation based on the draft prepared by the Steering Group, and reviewed and approved the final document. The members of this Group are presented in Annex 1.

External Review Group

This Group included five technical experts with sufficient interest in the provision of evidence-based obstetric care. None of its members declared a conflict of interest. The Group reviewed the final document to identify any errors of fact and commented on clarity of the language, contextual issues and implications for implementation. The Group ensured that the decision-making processes have considered and incorporated contextual values and preferences of potential users of the recommendations, healthcare professionals and policy makers. They did not change the recommendation that was formulated by the GDG. The members of the External Review Group are presented in Annex 1.

Systematic review team and guideline methodologists

A Cochrane systematic review on this question was initiated, supported by the Cochrane Pregnancy and Childbirth Group. The WHO Steering Group reviewed and provided input into the protocol, and it worked closely with the Cochrane Pregnancy and Childbirth Group to appraise the evidence using the GRADE methodology. A representative of the Cochrane Pregnancy and Childbirth Group attended the GDG meeting to provide an overview of the available evidence and GRADE tables and to respond to technical queries from the GDG.

External partners and observers

Representatives of the United States Agency for International Development (USAID), the Maternal and Child Survival Programme (MCSP)/Jhpiego, the Bill & Melinda Gates Foundation (BMGF), the International Confederation of Midwives (ICM), the International Federation of Gynecology and Obstetrics (FIGO) and Gynuity Health Projects participated in the GDG meeting as observers. These organizations, with a long history of collaboration with the RHR Department in guideline dissemination and implementation, are implementers of the updated recommendation. In addition, one of the WOMAN trial co-ordinators from the London School of Hygiene and Tropical Medicine (LSHTM) provided an overview of the conduct and findings of the WOMAN trial and responded to questions from the GDG, but did not participate in GDG deliberations nor revision of the recommendation. The list of observers who participated in the final technical consultation is presented in Annex 1.

Identification of critical outcomes

The critical and important outcomes were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of PPH (2012).[5] These outcomes were initially identified through a search of key sources of relevant, published, systematic reviews and a prioritization of outcomes by the 2012 GDG panel. During the updating of this recommendation, a further two outcomes were identified by the WHO Steering Group and the GDG as critical outcomes for this question: namely, maternal death (all causes) and maternal death due to bleeding. Thus, a total of 13 outcomes were rated as ‘critical’ and nine outcomes were rated as ‘important’ for this question. All outcomes were included in the scope of

this document for evidence searching, retrieval, grading and formulation of the recommendation. The list of critical and important outcomes is provided in Annex 2.

Evidence identification and retrieval

A Cochrane systematic review on the efficacy of TXA for PPH treatment was initiated by the Cochrane Pregnancy and Childbirth Group, as an offshoot of the existing Cochrane review of treatment for PPH.[11] This systematic review[12] was the primary source of evidence for this recommendation.

Randomized, controlled trials relevant to the key question were screened by the review authors, and data on relevant outcomes and comparisons were extracted into Review Manager (RevMan) software. The RevMan file was retrieved from the Cochrane Pregnancy and Childbirth Group and customized to reflect the key comparisons and outcomes (those that were not relevant to the recommendation were excluded). Then the RevMan file was exported to GRADE profiler software (GRADEpro) and GRADE criteria were used to critically appraise the retrieved scientific evidence. Finally, evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgements for each outcome, and the estimated risks.

Quality assessment and grading of the evidence

The quality assessment of the body of evidence for each outcome was performed using the GRADE approach.[13] Using this approach, the quality of evidence for each outcome was rated as 'high', 'moderate', 'low' or 'very low' based on a set of established criteria. The final rating of quality of evidence was dependent on the factors briefly described below.

Study design limitations The risk of bias was first examined at the level of individual study and then across studies contributing to the outcome. For randomized trials, quality was first rated as 'high' and then downgraded by one ('moderate') or two ('low') levels, depending on the minimum quality criteria met by the majority of the studies contributing to the outcome.

Inconsistency of the results The similarity in the results for a given outcome was assessed by exploring the magnitude of differences in the direction and size of effects observed from different studies. The quality of evidence was not downgraded when the directions of the findings were similar and confidence limits overlapped, whereas quality was downgraded when the results were in different directions, and confidence limits showed minimal or no overlap.

Indirectness The quality of evidence was downgraded when there were serious or very serious concerns regarding the directness of the evidence, that is, whether there were important differences between the research reported and the context for which the recommendation was being prepared. Such differences were related, for instance, to populations, interventions, comparisons or outcomes of interest.

Imprecision This assessed the degree of uncertainty around the estimate of effect. As this is often a function of sample size and number of events, studies with relatively few participants or events, and thus wide confidence intervals around effect estimates, were downgraded for imprecision.

Publication bias Quality rating could also be affected by perceived or statistical evidence of bias to underestimate or overestimate the effect of an intervention as a result of selective publication based on study results. We considered downgrading evidence by one level for strong suspicion of publication bias.

Formulation of recommendations

The WHO Steering Group used the evidence profiles to summarise evidence on effects of TXA on the prespecified outcomes. The evidence summary and corresponding GRADE tables, other related documents for assessment of values and preferences, resource requirements and cost-effectiveness, acceptability, feasibility and equity were provided in advance to members of the GDG. The GDG members and other participants were then invited to attend an online technical consultation (see Annex 1 for the list of participants) organized by the Steering Group in Geneva, Switzerland, on 29 August 2017. During the technical consultation, the GDG members reviewed and discussed the balance between desirable and undesirable effects of TXA and the overall quality of supporting evidence, values and preferences of stakeholders, resource requirements and cost-effectiveness, acceptability, feasibility and equity, before finalizing the recommendation and remarks.

Declaration of interests by external contributors

According to WHO regulations, all experts must declare their relevant interests prior to participation in WHO guideline development processes and meetings. All GDG members were therefore required to complete a standard WHO Declaration of Interest (DOI) form before engaging in the guideline development process and before participating in the guideline-related meeting. The WHO Steering Group reviewed all declarations before finalizing the experts' invitations to participate. Where any conflict of interest was declared, the Steering Group determined whether such conflicts were serious enough to affect objective judgement of the expert on the guideline development process and recommendation. To ensure consistency, the Steering Group applied the criteria for assessing the severity of conflict of interests in the *WHO Handbook for Guideline Development* for all experts. All findings from the received DOI statements were managed in accordance with the WHO DOI guidelines on a case-by-case basis and communicated to the experts. Where a conflict of interest was not considered significant enough to pose any risk to the guideline development process or reduce its credibility, the experts were only required to openly declare such conflict at the beginning of the GDG meeting, and no further actions were taken.

Annex 3 shows a summary of the DOI statements, and how declared conflicts of interest were managed by the Steering Group.

Decision-making during the technical consultation

During the technical consultation, the GDG reviewed and discussed the evidence summary and sought clarifications. In addition to evaluating the balance between desirable and undesirable effects of TXA and the overall quality of the evidence, the GDG applied additional criteria based on the GRADE evidence-to-decision framework to determine the direction and strength of the recommendation. These criteria

included values of stakeholders, resource implications, acceptability, feasibility and equity. Considerations were based on the experience and opinions of members of the GDG and supported by evidence from a literature search where available. However, specific systematic reviews of evidence (for example, qualitative evidence synthesis or detailed economic evaluation) were not performed to inform discussions on these criteria. Evidence-to-decision tables were used to describe and synthesize these considerations.

The decision was based on consensus defined as the agreement by three quarters or more of the participants. None of the GDG members expressed opposition to the recommendation.

Document preparation

Prior to the online technical consultation, the WHO Steering Group prepared a draft version of the GRADE evidence profiles, evidence summary and other documents relevant to the deliberation of the GDG. The draft documents were made available to the participants of the technical consultation two weeks before the meeting for their comments. During the meeting, these documents were modified in line with the participants' deliberations and remarks. Following the meeting, members of the WHO Steering Group drafted a full guideline document to accurately reflect the deliberations and decisions of the participants. The draft document was sent electronically to GDG members and the External Review Group for final review and approval.

Peer review

The final document was sent to five external independent experts who were not involved in the guideline panel for peer review. The WHO Steering Group evaluated the inputs of the peer reviewers for inclusion in this document. After the technical consultation and peer review, the modifications made by the WHO Steering Group to the document were limited to correction of factual errors and improvement in language to address any lack of clarity.

3. Evidence and recommendation

The following section outlines the recommendation and the corresponding narrative summary of evidence for the prioritized question. The GRADE table is presented in Annex 5. The evidence-to-decision table, summarizing the balance between desirable and undesirable effects and the overall quality of the supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity that were considered in determining the strength and direction of the recommendation, is presented in Annex 4.

The following recommendation was adopted by the GDG. Evidence on the effectiveness of the intervention was derived from one systematic review and was summarized in GRADE tables (Annex 5). The quality of the supporting evidence was rated as 'moderate' for most critical outcomes. To ensure that the recommendation is correctly understood and appropriately implemented in practice, additional 'remarks' reflecting the summary of the discussion by GDG are included under the recommendation.

Early use of intravenous tranexamic acid (within 3 hours of birth) in addition to standard care is recommended for women with clinically diagnosed postpartum haemorrhage following vaginal birth or caesarean section. *(Strong recommendation, moderate quality of evidence)*

Remarks

- Based on the dosing regimen used in the WOMAN trial, the GDG supports the administration of tranexamic acid (TXA) at a fixed dose of 1 g (100 mg/ml) intravenously (IV) at 1 ml per minute (i.e. administered over 10 minutes), with a second dose of 1 g IV if bleeding continues after 30 minutes, or if bleeding restarts within 24 hours of completing the first dose.
- The WOMAN Trial defined "clinically diagnosed postpartum haemorrhage" as clinically estimated blood loss of more than 500 ml after a vaginal birth or 1000 ml after caesarean section, or any blood loss sufficient to compromise haemodynamic stability.
- Based on evidence from the WOMAN trial, the reference point for the start of the 3-hour window for starting TXA administration is time of birth. If time of birth is unknown, the best estimate of time of birth should be used as the reference point. As most deaths due to postpartum haemorrhage occur within the first 2 to 3 hours after birth, it is critical that TXA is given as soon as possible to achieve clinical benefits.
- Analysis of the effects of timing of administration in the WOMAN trial, as well as an individual participant data (IPD) meta-analysis of 40 138 bleeding patients (including WOMAN trial participants), indicates that TXA administration beyond 3 hours does not confer any clinical benefit. Furthermore, the point estimates of effect of TXA use beyond 3 hours on death for trauma or after PPH were both in the direction of harm, albeit not statistically significant for women with PPH. In view of this evidence, the GDG does not support the use of TXA more than 3 hours after birth.
- Administration of TXA should be considered as part of the standard postpartum haemorrhage treatment package. Standard care in the context of this recommendation includes routine care for PPH treatment, including fluid replacement, medical (uterotonics), monitoring of vital signs, nonsurgical (e.g. bimanual compression, intrauterine balloon tamponade, nonpneumatic antishock garment, aortic compression) and surgical interventions (e.g. brace sutures, arterial ligation or hysterectomy) in accordance with WHO guidelines or adapted local PPH treatment protocols.
- TXA should be used in all cases of PPH regardless of whether the bleeding is due to genital tract trauma or other causes.
- The use of TXA should be avoided in women with a clear contraindication to antifibrinolytic therapy (including TXA) (e.g. a known thromboembolic event during pregnancy).
- This recommendation applies only to IV use. The evaluation of benefits and potential harms of other routes of TXA administration is a research priority.
- Regardless of the level of health system resources, TXA should be recognized as a life-saving intervention and be made readily available for the management of postpartum haemorrhage in settings where emergency obstetric care is provided.

A. Review Question

- For women with postpartum haemorrhage (P), does administration of tranexamic acid in addition to standard care (I) compared to standard care alone (C), improve outcomes (O)?
    - If so, when is the most appropriate period to administer tranexamic acid to improve outcomes?

B. Assessment

Effects of the intervention

What are the anticipated effects of administration of TXA in addition to standard care for PPH treatment?

Research evidence

Evidence on the use of TXA for treatment of PPH was extracted from a forthcoming Cochrane systematic review of two trials (20 212 women).[12] This review included trials that compared the use of any fibrinolytic drug with no treatment in women with PPH. However, no evidence was identified for interventions other than TXA.

One multicentre trial was conducted in eight obstetric units in France with recruitment between 2005 and 2008.[14] This trial randomized 152 women with PPH > 800 ml after a vaginal birth. The intervention group received a loading dose of 4 g TXA mixed with 50 ml saline, administered IV over 1 hour, followed by a maintenance dose of 1 g/hour for 6 hours. Women in the control group were given standard care only, as per the routine practice in participating facilities. The primary outcome was blood loss between randomization and 6 hours.

The second (WOMAN trial) was a multicountry, multicentre, placebo-controlled randomised trial of 20 060 women in 193 hospitals, across 21 high-, middle- and low-income countries conducted between March 2010 and April 2016.[9] The trial randomized women with clinically diagnosed PPH, defined as clinically estimated blood loss after a vaginal birth of > 500 ml, or > 1000 ml following a caesarean section, or any blood loss sufficient to compromise haemodynamic stability and where the clinician responsible for care was uncertain as to whether or not to use TXA. In addition to usual care, women in the experimental group were initially given 1 g TXA IV in a 10 ml solution, at an approximate rate of 1 ml/minute, as soon as possible after randomization. A second dose was used if bleeding continued after 30 minutes or if it stopped and restarted within 24 hours after the first dose. The control arm received placebo (normal saline) using the same regimen. When the trial protocol was registered, the primary outcome was a composite of death from all causes or hysterectomy within 42 days. During the course of the study (but before results were available or any unblinding), the primary outcome was revised to maternal death due to bleeding, and the sample size increased.

Evidence regarding this intervention is almost entirely derived from the WOMAN trial.

Comparison: TXA (in addition to standard care) versus standard care alone

The effects of TXA on critical outcomes for all women with PPH, regardless of how PPH was defined, the mode of birth or timing of PPH administration, are described below.

- **Maternal mortality (all causes):** Moderate certainty evidence suggests slightly fewer deaths in the group receiving TXA although this difference was not statistically significant (two studies, 20 172 women; 227/10 113 (2.2%) vs 256/10 059 (2.5%); RR 0.88, 95% CI 0.74 to 1.05).

- **Maternal mortality due to PPH:** In both trials, clinicians were asked to record the primary cause of death. Moderate certainty evidence suggests that deaths that were considered to be due to bleeding were probably reduced in the TXA group (two studies, 20 172 women, 155/10 113 (1.5%) vs 191/10 059 (1.9%), RR 0.81, 95% CI 0.65 to 1.00). The number needed to treat (NNT) to prevent one maternal death due to bleeding is 258 (95% CI 133.2 to 4051.8).
- **Severe maternal morbidity:** The French trial reported multiple organ failure; there were no events in either arm and very few admissions to intensive care (one study, 152 women, 3/77 (3.9%) vs 5/74 (6.8%), RR 0.58 (95% CI 0.14 to 2.33). The number of women suffering any severe morbidity was not reported in the WOMAN trial report, but specific morbidities were reported. Moderate certainty evidence suggested little or no difference between groups for any of morbidity outcomes reported (respiratory failure: RR 0.87, 95% CI 0.67 to 1.12; seizure: two studies; RR 0.76, 95% CI 0.49 to 1.20; hepatic failure RR 0.96, 95% CI 0.58 to 1.60; cardiac failure: RR 0.95, 95% CI 0.73 to 1.23; renal failure: two studies; RR 1.09, 95% CI 0.85 to 1.39).
- **Blood products transfusion (all):** Moderate certainty evidence suggests there is very little or no difference between groups for transfusion of blood products, with more than half of the women in both arms of the WOMAN trial receiving a transfusion (two studies; RR 1.00, 95% CI 0.97 to 1.03).
- **Additional blood loss:** The French trial reported additional blood loss > 500 ml or > 1000 ml. Low-quality evidence suggests TXA probably reduces blood loss > 500 ml (RR 0.50, 95% CI 0.27 to 0.93, 151 women). Although the direction of effect was the same for loss > 1000 ml, the study had insufficient power to demonstrate a difference between groups (4/77 women versus 8/74).
- **Additional uterotonics:** The vast majority of women in the WOMAN trial received uterotonics (99.3% vs 99.1%, two studies; RR 1.00, 95% CI 1.0 to 1.0).
- **Surgical interventions:** High or moderate certainty evidence suggests there is probably little difference between groups for most surgical interventions to control bleeding (hysterectomy (all): two studies; RR 1.01, 95% CI 0.88 to 1.17; ligature: RR 0.88, 95% CI 0.74 to 1.05; embolization: RR 0.82, 95% CI 0.42 to 1.62). High certainty evidence suggests laparotomy to control bleeding is reduced for women in the TXA group (0.8% vs 1.3%) (RR 0.64, 95% CI 0.49 to 0.85) while brace sutures are increased (RR 1.19, 95% CI 1.01 to 1.41).
- **Invasive nonsurgical interventions:** High certainty evidence suggests there is probably little or no difference in intrauterine tamponade (one study; RR 0.96, 95% CI 0.87 to 1.06) or manual removal of placenta: (one study; RR 0.95, 95% CI 0.87 to 1.04).
- **Procedure-related complications:** Moderate certainty evidence suggests there is probably little or no difference between groups for thromboembolic events (any maternal thromboembolic event: RR 0.88, 95% CI 0.54 to 1.43; deep venous thrombosis: two studies; RR 0.62 95% CI 0.20 to 1.88; pulmonary embolism RR 0.85, 95% CI 0.44 to 1.61; myocardial infarction: RR 0.66, 95% CI 0.11 to 3.97; stroke: RR 1.33, 95% CI 0.46 to 3.82).
- **Neonatal adverse effects**: Available neonatal outcome data were limited (data from WOMAN trial only). There were no neonatal thromboembolic events and no clear differences in deaths in breastfed neonates (eight deaths with TXA vs seven deaths with placebo) in the WOMAN trial.
- **Longer-term outcomes:** Available data on longer-term outcomes was limited (data from the WOMAN trial only). Outcomes in the WOMAN trial were measured up to hospital discharge or 42 days if still in hospital. There was no information on longer-term outcomes in women or babies.
- Subgroup analysis examining treatment effect by mode of birth (vaginal or caesarean) suggests no clear difference in effect on maternal death (all causes) and maternal death due to PPH for type of birth (moderate certainty of evidence).

Comparison: TXA (in addition to standard care) versus standard care alone, by timing of TXA administration

Evidence for this subgroup comparison was derived from a pre-planned subgroup analysis of the WOMAN trial.

- **Maternal mortality due to PPH:** There are subgroup differences for the timing of drug administration. Women receiving TXA less than 1 hour after birth had reduced risk of death from bleeding, but the confidence interval crossed the line of no effect (less than 1 hour: RR 0.80, 95% CI 0.55 to 1.16). Women receiving TXA 1 to 3 hours after birth were at reduced risk of death from bleeding (1 to 3 hours: RR 0.60, 95% CI 0.41 to 0.88) compared with women where more than 3 hours had elapsed before TXA was administered (more than 3 hours: RR 1.07, 95% CI 0.76 to 1.51).
- **Maternal mortality (all cause):** Compared to the control group, women receiving TXA less than 1 hour after birth had similar risks of death (any cause) (less than 1 hour: RR 0.98, 95% CI 0.72 to 1.33), as did women receiving TXA more than 3 hours after birth (more than 3 hours: RR 1.00, 95% CI 0.75 to 1.33). However, women receiving TXA 1 to 3 hours after birth were at reduced risk of death from all causes (1 to 3 hours: RR 0.69, 95% CI 0.49 to 0.96).
- **Death or hysterectomy:** Compared to the control group, women receiving TXA less than 1 hour after birth had similar risks of death or hysterectomy (less than 1 hour: RR 1.08, 95% CI 0.91 to 1.28), as did women receiving TXA more than 3 hours after birth (more than 3 hours: RR 1.01, 95% CI 0.82 to 1.25). However, women receiving TXA 1 to 3 hours after birth were at reduced risk of death or hysterectomy (1 to 3 hours: RR 0.80, 95% CI 0.63 to 1.00).
- **Laparotomy for bleeding:** Compared to the control group, women receiving TXA less than 1 hour after birth had reduced risk of laparotomy for bleeding (less than 1 hour: RR 0.48, 95% CI 0.29 to 0.79), as did women receiving TXA at 1 to 3 hours after birth (1 to 3 hours: RR 0.54, 95% CI 0.31 to 0.95). Women receiving TXA more than 3 hours after birth were not at reduced risk of laparotomy for bleeding (more than 3 hours: RR 0.89, 95% CI 0.59 to 1.35).

Desirable effects

How substantial are the desirable anticipated effects of TXA + standard care vs standard care alone?

Judgement					
☐ Don't know	☐ Varies	☐ Trivial	☐ Small	☐ Moderate	☒ Large

Undesirable effects

How substantial are the undesirable anticipated effects TXA + standard care vs standard care alone?

Judgement					
☐ Don't know	☐ Varies	☐ Large	☐ Moderate	☐ Small	☒ Trivial

Certainty of the evidence

What is the overall certainty of the evidence of effects?

Judgement				
☐ No included studies	☐ Very low	☐ Low	☒ Moderate	☐ High

Additional considerations
Additional evidence was obtained from a forthcoming individual patient data (IPD) on the impact of treatment delay on the effectiveness and safety of antifibrinolytics in acute, severe haemorrhage.[15] The IPD meta-analysed 40 138 bleeding patients (with 3 558 deaths recorded) who received TXA or placebo from WOMAN and CRASH-2 trials combined. The authors reported that deaths from PPH peaked at 2 to 3 hours after childbirth, and immediate treatment improved bleeding survival. Treatment delay appears to reduce benefit - the benefit appears to decrease by 10% for every 15 minutes' delay, with no benefit seen after 3 hours. The point estimates of effect of TXA use beyond 3 hours on death for trauma or after PPH were both in the direction of harm, albeit not statistically significant for women with PPH.

Values and preferences

Is there important uncertainty about, or variability in, how much women value the main outcomes?

Typically, women, healthcare providers and policy-makers place a higher value on avoiding a maternal death, even when potentially associated with an increase in invasive surgical interventions, such as brace sutures. Therefore, women, healthcare providers and policy-makers in all settings are likely to place a high value on the reduction in the risk of maternal death due to bleeding. The GDG is confident that women, healthcare providers and policy-makers in any setting will invariably place a higher value on this benefit, compared to any inconvenience (or drawbacks) that TXA use might cause to the woman, her baby or the health system. Stakeholders with different values in different contexts are unlikely to make different decisions when presented with these choices.

Judgement			
☐ Important uncertainty or variability	☐ Possibly important uncertainty or variability	☐ Probably no important uncertainty or variability	☒ No important uncertainty or variability

Balance of effects

Does the balance between desirable and undesirable effects favour use of TXA in addition to standard care (intervention) or standard care alone (comparison)?

There is evidence that TXA is probably beneficial in reducing maternal deaths due to bleeding and reducing the need for laparotomy to stop bleeding. Early treatment appears to optimize benefit. There does not appear to be evidence of maternal or newborn harms, or significant side-effects. While no difference in newborn thromboembolic events were seen, in the WOMAN trial most women and babies were followed until discharge from the health facility, thus this evidence is more likely representative of the first few days after birth.

Judgement						
☐ Don't know	☐ Varies	☐ Favours the standard care alone	☐ Probably favours the standard care alone	☐ Does not favour TXA + standard care or standard care alone	☐ Probably favours TXA + standard care	☒ Favours TXA + standard care

Resources required

What are the resource requirements for administering TXA in addition to standard care for PPH treatment?

Research evidence

None of the studies included in the Cochrane systematic review conducted a formal cost-effectiveness analysis.

Main resource requirements

The use of TXA in addition to standard PPH treatment requires the existence of healthcare providers who have been trained in how to administer intravenous drugs.

Resource	Description
Training	2 to 3 day practice-based training/practice drills for PPH management
Supplies	1 to 2 g of TXA (varies between settings, with an approximate range of $1.00 to $5.70 per g) [16] IV infusion set Syringe/needle/swabs = approximately US$0.08 to $0.10
Equipment	None required.
Time	Average time needed is 10 to 15 minutes for gaining IV access and administration of the drug (depending on other factors such as provider skills). However, sufficient time is needed for monitoring the response of the woman to treatment as required for all cases of PPH.
Supervision and monitoring	Regular supervision and review by labour ward lead, especially when first introduced.

Additional considerations
• TXA is relatively cheap in most contexts, easy to administer, and it is often available in healthcare settings due to its use in trauma and surgery. Research evidence on cost-effectiveness can be extrapolated from cost-effectiveness analysis of TXA for bleeding trauma patients.16 The study found that administering TXA to bleeding trauma patients within 3 hours of injury saved an estimated 372, 315 and 755 life-years (LYs) per 1 000 trauma patients in Tanzania, India and the UK respectively. The cost of giving TXA to 1 000 patients was $17 483 in Tanzania, $19 550 in India and $30 830 in the UK. The incremental cost of giving TXA versus not giving TXA was $18 025 in Tanzania, $20 670 in India and $48 002 in the UK. The estimated incremental cost per LY gained of administering TXA is $48, $66 and $64 in Tanzania, India and the UK respectively. Early administration of TXA to bleeding trauma patients is likely to be highly cost-effective in low-, middle- and high-income settings. • The use of TXA may also reduce subsequent costs related to surgical procedures for PPH treatment (such as laparotomy) as well as any complications associated with surgery. • Out-of-pocket costs to individual women might be higher when TXA is added to standard care for PPH in settings where women incur financial costs for births.

Resource requirements

How large are the resource requirements for administering TXA in addition to standard care for PPH treatment compared to standard care alone?

Judgement						
☐ Don't know	☐ Varies	☐ Large costs	☐ Moderate costs	☒ Negligible costs or savings	☐ Moderate savings	☐ Large savings

Certainty of evidence on required resources

What is the certainty of the evidence on costs?

Judgement				
☒ No included studies	☐ Very low	☐ Low	☐ Moderate	☐ High

Cost-effectiveness

Does cost-effectiveness favour TXA + standard care or standard care alone?

Judgement						
☐ Don't know	☐ Varies	☐ Favours the standard care alone	☐ Probably favours the standard care alone	☐ Does not favour either the TXA + standard care or the standard care alone	☒ Probably favours TXA + standard care	☐ Favours TXA +standard care

Equity

What would be the impact on health equity of TXA administration in addition to standard care for PPH treatment?

Research evidence

- No direct evidence of the impact of the TXA administration in addition to standard care for PPH treatment on equity was found. However, indirect evidence from a review of barriers and facilitators to facility-based birth indicates that poor quality of care, as evident by poor birth outcomes, is probably a significant barrier to the uptake of facility birth by women in LMICs.[17]

Additional considerations

- The 2015 WHO State of Inequality report indicates that women who are poor, least-educated, and reside in rural areas have lower health intervention coverage and worse health outcomes than more advantaged women.[18] Therefore, reducing maternal deaths due to bleeding through scaling up of TXA for PPH treatment could have a positive impact on health equity and improve outcomes among disadvantaged women, especially in LMICs where these women are at significantly higher risk of PPH-related maternal deaths.
- Reducing the need for expensive, life-saving surgical interventions (such as laparotomy to stop bleeding in women with vaginal birth) through an IV medication would probably reduce inequities, especially in contexts where health services are covered through out-of-pocket means.

Judgement

☐ Don't know	☐ Varies	☐ Reduced	☐ Probably reduced	☐ Probably no impact	☒ Probably increased	☐ Increased

Acceptability

Is TXA (in addition to standard care) acceptable to key stakeholders (women and healthcare providers) for PPH treatment?

The intervention is likely to be acceptable to both women and healthcare providers. TXA is administered in adequately equipped health facilities (providing emergency obstetric care) by a skilled healthcare provider via a standard IV infusion over a short period of time. There is no evidence of adverse maternal or neonatal effects. The balance between benefits and harms suggests that TXA will be acceptable to key stakeholders (women, providers and policy makers) across settings. An incremental cost with substantial benefits in terms of saving lives would be generally acceptable.

Judgement

☐ Don't know	☐ Varies	☐ No	☐ Probably No	☒ Probably Yes	☐ Yes

Feasibility

Is TXA feasible to implement in addition to standard care for PPH treatment?

The use of IV TXA for treatment of PPH in healthcare facilities was regarded by the GDG as feasible. Standard IV infusion equipment is required, as well as healthcare providers with sufficient training to safely administer IV bolus infusions (similar to oxytocin infusion). Many hospitals already have access to TXA due to its common use for trauma and surgery. Available preparations are compatible with recommended dosing regimens for PPH treatment. In many healthcare facilities (including in LMICs) no (or minimal) additional resources, infrastructure or training is required to commence using TXA for this indication. Administration of TXA should be relatively easy to integrate into standard PPH treatment packages. It is listed on the WHO Model List of Essential Medicines under medicines affecting coagulation.

The successful implementation of the WOMAN trial in 193 hospitals in 21 countries, which recruited over 20 000 women, in itself can be considered a potential demonstration of the feasibility of implementing this intervention.[9] The pragmatic nature of the trial, coupled with the variations in the capacities of participating institutions (from low to very high) also supports feasibility across low-, middle- and high-income settings. These hospitals are likely to implement a recommendation of TXA easily.

However, given that evidence currently supports IV TXA for treatment, the intervention may not be feasible in settings where IV administrations are restricted to doctors working in high-level or referral facilities.

Judgement					
☐ Don't know	☐ Varies	☐ No	☐ Probably No	☒ Probably Yes	☐ Yes

4. Research implications

- The GDG identified that further research on the use of TXA for PPH is a priority. While the large, multicountry WOMAN trial has assessed the benefits and harms of IV TXA for PPH treatment, other research priorities include:
- What are the effects of TXA by other routes of administration (for example, oral, intramuscular, topical, buccal) when used for PPH treatment?
- What is the cost-effectiveness of TXA when used for PPH treatment?
- What is the optimal dosing regimen of TXA for PPH treatment?
- What are the longer-term effects (on women and breastfed newborns) of TXA when used for PPH treatment?
- What are the effects of oral or intravenous TXA when used for PPH prevention? [19]

5. Dissemination and implementation of the recommendation

Dissemination and implementation of the recommendation is to be considered by all actors involved in the provision of care for pregnant women at the international, national and local levels. There is a vital need to increase access and strengthen the capacity of health centres to provide high quality services for all women giving birth. It is therefore crucial that this recommendation is translated into PPH treatment packages and programmes at country and health-facility levels.

Recommendation dissemination and evaluation

The recommendation will be disseminated through WHO regional and country offices, ministries of health, professional organizations, WHO collaborating centres, other United Nations agencies and nongovernmental organizations, among others. This recommendation will be also available on the WHO website and in the WHO Reproductive Health Library. To increase awareness of the recommendation, a short commentary will be published in a peer-reviewed journal. The recommendation will be also disseminated during meetings or scientific conferences attended by WHO staff. The executive summary will be translated into the six UN languages and disseminated through the WHO regional offices. Technical assistance will be provided to any WHO regional office willing to translate the full recommendation into any of the six UN languages.

Implementation considerations

The successful introduction of evidence-based policies (related to the prevention and management of PPH) into national programmes and healthcare services depends on well planned and participatory, consensus-driven processes of adaptation and implementation. These processes may include the development or revision of existing national guidelines or protocols based on this document. TXA should be included as part of the standard package for PPH treatment. It should therefore be available at all times in the labour room of facilities providing emergency obstetric care.

Due consideration should be given to any specific manufacturer's instructions on precautions and contraindications. TXA for injection may be mixed with most solutions for infusion, such as electrolyte solutions, carbohydrate solutions, amino acid solutions and dextran solutions.[20] TXA should be administered as a bolus IV injection over 10 minutes, as there is a potential risk of transient lowering of blood pressure. TXA should not be mixed with blood for transfusion, solutions containing penicillin or mannitol.[20] It can be administered via the same IV cannula used for IV hydration or uterotonic administration.

An enabling environment should be created for the use of TXA (for example, by widening its availability) in order to support changes in the behaviour of healthcare practitioners to enable the use of evidence-based practice. This includes technical support for local guideline implementers in the development of training manuals, flowcharts and quality indicators as well as their participation in stakeholders' meetings. Local professional societies play important roles in this process, and an inclusive and participatory process should be encouraged.

Health facilities where emergency obstetric care is provided need to have the necessary supplies and equipment, as well as the necessary training for staff attending births, so that TXA can be administered safely by IV infusion. The shelf life of TXA is generally three years, and can be stored at room temperature (15 to 30 degrees Celsius). The opened product must be used immediately. The manufacturer's instructions on storage and use, however, should always be given precedence.

The recommendation should be adapted into locally appropriate documents that are able to meet the specific needs of each country and health service. Modifications to the recommendation should be justified in an explicit and transparent manner.

6. Applicability issues

Anticipated impact on the organization of care and resources

Implementing this evidence-based recommendation can be achieved without substantive additional resources. The GDG noted that updating training curricula and providing training on the updated recommendation would increase the recommendation's impact and facilitate its implementation. Standardizing PPH treatment by including this recommendation into existing packages of care can encourage healthcare provider behaviour change.

Monitoring and evaluating guideline implementation

Implementation should be monitored at the health-service level as part of broader efforts to monitor and improve the quality of maternal and newborn care. For example, interrupted time series, clinical audits or criterion-based clinical audits can be used to obtain relevant data related to the management of PPH. Clearly defined review criteria and indicators are needed and these could be associated with locally agreed targets. These can be aligned with the standards and indicators described in the WHO document *Standards for improving quality of maternal and newborn care in health facilities*.[21]

In 2012, the GDG of the WHO recommendations on prevention and treatment of PPH strongly recommended the use of coverage of prophylactic uterotonics as a process indicator for the monitoring of PPH prevention.[5] This indicator provides an overall assessment of adherence to a key recommendation within all of WHO's recommendations on PPH prevention and treatment. The use of other locally agreed and more specific indicators (for example, the assessment of the use of specific uterotonics or use of TXA for PPH treatment) may be necessary to obtain a more complete assessment of the quality of care related to the prevention and treatment of PPH. WHO has developed specific guidance for evaluating the quality of care for severe maternal complications (including PPH) based on the near-miss and criterion-based clinical audit concepts.[22]

In collaboration with the WHO RHR and MCA Departments' monitoring and evaluation team, data on country and regional level implementation of the recommendation will be collected and evaluated in the short- to medium-term to evaluate the recommendation's impact on the national policy of individual WHO Member States.

Information on recommended indicators can also be obtained at the local level by interrupted time series or clinical audits.

7. Updating the recommendation

The Executive GSG will convene annually to review WHO's current portfolio of maternal and perinatal health recommendations, and to prioritize new and existing questions for recommendation development and updating. Accordingly, the recommendation on TXA use for the treatment of PPH will be reviewed and prioritized by the Executive GSG. In the event that new evidence (that could potentially impact the current evidence base) is identified, the recommendation may be updated. If no new reports or information is identified, the recommendation may be revalidated.

Following publication and dissemination of the updated recommendation, any concern about validity of the recommendation will be promptly communicated to the guideline implementers, in addition to plans to update the recommendation.

WHO welcomes suggestions regarding additional questions for inclusion in the updated recommendation. Please email your suggestions to mpa-info@who.int.

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Annex 1. External experts and WHO staff involved in the preparation of the guideline

A. Participants at the who technical consultation on TXA for the treatment of PPH

Guideline Development Group

Edgardo Abalos (unable to attend)
Centro Rosarino de Estudios Perinatales (CREP)
Rosario, Argentina

Yap-Seng Chong
Department of Obstetrics and Gynaecology
National University Hospital
Singapore

Catherine Deneux-Tharaux
Inserm U1153
Obstetrical, Perinatal and Pediatric Epidemiology Research Team
Centre of Research in Epidemiology and Statistics
Sorbonne Paris Cité
Université Paris Descartes
Paris, France

Bukola Fawole
Department of Obstetrics & Gynaecology
College of Medicine
University of Ibadan
Ibadan, Nigeria

Justus Hofmeyr
Universities of the Witwatersrand
and Walter Sisulu/Eastern Cape Department of Health
East London, South Africa

Caroline Homer (unable to attend)
WHO Collaborating Centre for Nursing, Midwifery and Health Development
Faculty of Health
University of Technology
Sydney, Australia

Pisake Lumbiganon
Department of Obstetrics and Gynaecology
Faculty of Medicine
Khon Kaen University
Khon Kaen, Thailand

Suellen Miller
Department of Obstetrics, Gynecology & Reproductive Sciences
Director, Safe Motherhood Program
Bixby Center for Global Reproductive Health
San Francisco, United States

Ashraf Nabhan
Department of Obstetrics and Gynecology
Faculty of Medicine
Ain Shams University
Abbasia, Cairo, Egypt

James Neilson
Department of Women's and Children's Health
The University of Liverpool
Women's NHS Foundation Trust
Liverpool, United Kingdom

Hiromi Obara
JICA Health Policy Advisor
Lao People's Democratic Republic

Zahida Qureshi
Department of Obstetrics and Gynaecology
School of Medicine
University of Nairobi
Nairobi, Kenya

Rahat Qureshi
Aga Khan University
Department of Obstetrics and Gynecology
Karachi, Pakistan

Helen West
The University of Liverpool
Women's NHS Foundation Trust
Liverpool, United Kingdom

Observers

Deborah Armbruster
United States Agency for International Development (USAID)
Bureau for Global Health
Washington DC, United States

Kusum Thapa
MCSP/Jhpiego
USAID Grantee
1776 Massachusetts Ave
Washington DC, United States

Janna Patterson
Maternal, Neonatal & Child Health
Global Development Program
Bill & Melinda Gates Foundation
Seattle, Washington, United States

Haleema Shakur-Still
London School of Hygiene and Tropical Medicine
London, United Kingdom

Sally Tracy
International Confederation of Midwives (ICM)
Sydney University
Sydney, Australia

Gerard H.A. Visser
International Federation of Gynecology and Obstetrics (FIGO)
London, United Kingdom

Beverley Winikoff
Gynuity Health Projects
New York, United States

Systematic Review Team

Therese Dowswell
Department of Women's and Children's Health
The University of Liverpool
Women's NHS Foundation Trust
Crown Street
Liverpool, United Kingdom

WHO Regional Offices

Mavjuda Babamuradova
Sexual and Reproductive Health
Noncommunicable diseases and life-course
WHO Regional Office for Europe
Copenhagen, Denmark

Anoma Jayathilaka
Family Health, Gender and Life Course
WHO Regional Office for South-East Asia
New Delhi, India

Ramez Khairi Mahaini (unable to attend)
Reproductive and Maternal Health
WHO Regional Office for the Eastern Mediterranean
Cairo, Egypt

Bremen De Mucio
Sexual and Reproductive Health
WHO Regional Office of the Americas
Montevideo, Uruguay

Mari Nagai (unable to attend)
Reproductive, Maternal, Newborn, Child and Adolescent Health Division of NCD and Health through Life-Course
Regional Office for the Western Pacific
Manila, Philippines

Léopold Ouedraogo (unable to attend)
Reproductive Health
Health Promotion Cluster (HPR)
WHO Regional Office for Africa
Brazzaville, Republic of Congo

Claudio Sosa
Sexual and Reproductive Health
WHO Regional Office of the Americas
Montevideo, Uruguay

WHO Secretariat

A. Metin Gülmezoglu
Coordinator, RHR/MPA
Maternal and Perinatal Health & Preventing Unsafe Abortion
Department of Reproductive Health and Research

Mercedes Bonet
Medical Officer, RHR/MPA
Maternal and Perinatal Health & Preventing Unsafe Abortion
Department of Reproductive Health and Research

Olufemi T. Oladapo
Medical Officer, RHR/MPA
Maternal and Perinatal Health & Preventing Unsafe Abortion
Department of Reproductive Health and Research

Joao Paulo Souza (unable to attend)
Medical Officer, RHR/MPA
Maternal and Perinatal Health & Preventing Unsafe Abortion
Department of Reproductive Health and Research

Joshua P. Vogel
Technical Officer, RHR/MPA
Maternal and Perinatal Health & Preventing Unsafe Abortion
Department of Reproductive Health and Research

Maurice Bucagu (unable to attend)
Medical Officer, MCA/PPP
Policy, Planning and Programmes
Department of Maternal, Newborn, Child and Adolescent Health

Fran McConville (unable to attend)
Technical Officer, MCA/PPP
Policy, Planning and Programmes
Department of Maternal, Newborn, Child and Adolescent Health

Anayda Portela
Technical Officer, MCA/MRD
Research and Development
Department of Maternal, Newborn, Child and Adolescent Health

B. WHO Steering Group

A. Metin Gülmezoglu
(WHO Department of Reproductive Health and Research)

Olufemi T. Oladapo
(WHO Department of Reproductive Health and Research)

Anayda Portela
(WHO Department of Maternal, Newborn, Child and Adolescent Health)

Joshua Vogel
(WHO Department of Reproductive Health and Research)

C. External Review Group

Richard M.K. Adanu
School of Public Health
University of Ghana
Accra, Ghana

Fernando Althabe
Department of Maternal and Child Health Research
Institute for Clinical Effectiveness and Health Policy
Buenos Aires, Argentina

Sue Fawcus
Department of Obstetrics and Gynaecology
University of Cape Town
Cape Town, South Africa

Jamilu Tukur
Department of Obstetrics and Gynaecology
Bayero University
Kano, Nigeria

Dilys Walker
Department of Obstetrics, Gynecology & Reproductive Sciences
UCSF School of Medicine
University of California
San Francisco, United States

Annex 2. Critical and important outcomes for decision-making

Key question	Priority Outcomes
For women with postpartum haemorrhage (P), does administration of tranexamic acid in addition to standard care (I) compared to standard care alone (C), improve outcomes (O)?	**Critical outcomes** • Maternal death (all cause)* • Maternal death due to bleeding* • Additional blood loss ≥ 500 ml • Additional blood loss ≥ 1000 ml • Blood transfusion • Additional uterotonics • Invasive nonsurgical interventions • Surgical interventions (including hysterectomy) • Maternal temperature ≥ 40 °C • Procedure-related complications • Infections • Severe morbidity • Maternal transfer • Reduction of time from decision-making to implementation • Availability of drugs and treatment
	Important outcomes • Accuracy in blood loss assessment • Mean blood loss • Postpartum anaemia • Additional nonsurgical interventions (e.g. external aortic compression and compression garments) • Artery embolization • Nausea, vomiting or shivering • Maternal temperature ≥ 38 °C • Delayed initiation of breastfeeding • Prolonged hospitalization

* Maternal death (all cause) and maternal death due to bleeding were added as critical outcomes for the update of this recommendation.

Annex 3: Summary and management of declared interests from GDG members

Name and expertise contributed to the guideline development	Declared interest	Management of conflict of interest
Edgardo Abalos Content expert and end-user	None declared	Not applicable
Yap-Seng Chong Content expert and end-user	None declared	Not applicable
Catherine Deneux-Tharaux Content expert and end-user	None declared	Not applicable
Therese Dowswell Guideline methodologist	None declared	As one of the methodologists for this guideline, Therese Dowswell did not have voting rights at the meeting.
Bukola Fawole Content expert and end-user	Professor Fawole was a country investigator (Nigeria) on the WOMAN trial. He has participated in previous GDGs, including the previous WHO GDG on prevention and treatment of postpartum haemorrhage (2012).	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation. His perspectives on implementation of this intervention (resulting from WOMAN trial) were regarded as important.
Justus Hofmeyr Content expert and end-user	None declared	Not applicable
Caroline Homer Content expert and end-user	Co-Chair of National Antenatal Guidelines Expert Advisory Committee in Australia (2008 onwards)	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation
Pisake Lumbiganon Content expert and end-user	Was a DSMB member of the WOMAN trial	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation
Suellen Miller Content expert and end-user	Prof Miller's employer (University of California, San Francisco) holds the trademark on a nonpneumatic antishock device (NASG) for PPH management	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation
Ashraf Nabhan Content expert and end-user	None declared	Not applicable

Name and expertise contributed to the guideline development	Declared interest	Management of conflict of interest
James Neilson Content expert and end-user	None declared	Not applicable
Hiromi Obara Content expert and implementer	None declared	Not applicable
Zahida Qureshi Content expert and end-user	Professor Qureshi was a country investigator (Kenya) on the WOMAN trial. She has participated in previous GDGs, including the previous WHO GDG on prevention and treatment of postpartum haemorrhage (2012).	The conflict was not considered serious enough to affect GDG membership or participation in the Technical Consultation. Her perspectives on implementation of this intervention (resulting from WOMAN trial) were regarded as important.
Rahat Qureshi Content expert and end-user	None declared	Not applicable
Helen West Consumer representative	None declared	Not applicable

Annex 4. Summary of the considerations related to the strength of the recommendations

Desirable effects	- Don't know	- Varies		- Trivial	- Small	- Moderate	✓ Large
Undesirable effects	- Don't know	- Varies		- Large	- Moderate	- Small	✓ Trivial
Certainty of the evidence	- No included studies			- Very low	- Low	✓ Moderate	- High
Values and preferences				- **Important uncertainty or variability**	- Possibly important uncertainty or variability	- Probably no important uncertainty or variability	✓ No important uncertainty or variability
Balance of effects	- Don't know	- Varies	- Favours the comparison	- Probably favours the comparison	- Does not favour either the intervention or the comparison	- Probably favours the intervention	✓ Favours the intervention
Resources required	- Don't know	- Varies	- Large costs	- Moderate costs	✓ Negligible costs or savings	- Moderate savings	- Large savings
Certainty of evidence of required resources	✓ No included studies			- Very low	- Low	- Moderate	- High
Cost-effectiveness	- Don't know	- Varies	- Favours the comparison	- Probably favours the comparison	- Does not favour either the intervention or the comparison	✓ Probably favours the intervention	- Favours the intervention
Equity	- Don't know	- Varies	- Reduced	- Probably reduced	- Probably no impact	✓ Probably increased	- Increased
Acceptability	- Don't know	- Varies		- No	- Probably No	✓ Probably Yes	- Yes
Feasibility	- Don't know	- Varies		- No	- Probably No	- Probably Yes	✓ Yes

Annex 5. GRADE Tables

Question: Standard care plus tranexamic acid compared to standard care alone for treating primary postpartum haemorrhage

Setting: Data from two studies, one conducted in France (5 tertiary care centres and 3 secondary care obstetric centres: 152 women) and one multicentre RCT with 20 060 women (WOMAN trial).

WOMAN trial: Labour ward settings in high- (United Kingdom: 569 women), and low- and middle-income countries (Nigeria: 5711 women; Pakistan: 5282 women; Uganda: 2235 women; Kenya: 1031 women; Cameroon: 893 women; Sudan: 860 women; Tanzania: 538 women; Nepal: 533 women; Zambia: 496 women; Albania: 485 women; Democratic Republic of Congo: 457 women; Bangladesh: 325 women; Ethiopia: 302 women; Burkina Faso: 142 women; Jamaica: 73 women; Ghana: 41 women; Papua New Guinea: 38 women; Egypt: 33 women; Colombia: 8 women; Côte d'Ivoire: 8 women).

Bibliography: Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Dowswell T, Mousa H. Antifibrinolytic drugs for treating primary postpartum haemorrhage. Cochrane Database Syst Rev. 2017;(unpublished).

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Maternal mortality (all causes)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none	227/10113 (2.2%)	256/10059 (2.5%)	**RR 0.88** (0.74 to 1.05)	**3 fewer per 1000** (from 1 more to 7 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Maternal mortality (due to PPH)												
2	randomised trials	not serious	not serious	not serious	serious [b]	none	155/10113 (1.5%)	191/10059 (1.9%)	**RR 0.81** (0.65 to 1.00)	**4 fewer per 1000** (from 0 fewer to 7 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Severe maternal morbidity (maternal intensive care admission)												
1	randomised trials	serious [c]	not serious	not serious	very serious [d]	none	3/77 (3.9%)	5/74 (6.8%)	**RR 0.58** (0.14 to 2.33)	**28 fewer per 1000** (from 58 fewer to 90 more)	⨁◯◯◯ VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Severe maternal morbidity (maternal respiratory failure)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	108/10033 (1.1%)	124/9985 (1.2%)	**RR 0.87** (0.67 to 1.12)	**2 fewer per 1000** (from 1 more to 4 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Severe maternal morbidity (maternal seizure)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none	33/10110 (0.3%)	43/10059 (0.4%)	**RR 0.76** (0.49 to 1.20)	**1 fewer per 1000** (from 1 more to 2 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Severe maternal morbidity (hepatic failure)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	29/10033 (0.3%)	30/9985 (0.3%)	**RR 0.96** (0.58 to 1.60)	**0 fewer per 1000** (from 1 fewer to 2 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Severe maternal morbidity (cardiac failure)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	110/10033 (1.1%)	115/9985 (1.2%)	**RR 0.95** (0.73 to 1.23)	**1 fewer per 1000** (from 3 fewer to 3 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Severe maternal morbidity (maternal renal failure)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none	129/10110 (1.3%)	118/10059 (1.2%)	**RR 1.09** (0.85 to 1.39)	**1 more per 1000** (from 2 fewer to 5 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Blood Products transfusion (all)												
2	randomised trials	not serious	serious [e]	not serious	not serious	none	5474/10113 (54.1%)	5446/10059 (54.1%)	**RR 1.00** (0.97 to 1.03)	**0 fewer per 1000** (from 16 fewer to 16 more)	⨁⨁⨁◯ MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Additional blood loss > 500 ml												
1	randomised trials	serious [c]	not serious	not serious	serious [f]	none	12/77 (15.6%)	23/74 (31.1%)	**RR 0.50** (0.27 to 0.93)	**155 fewer per 1000** (from 22 fewer to 227 fewer)	⊕⊕◯◯ LOW	CRITICAL
Additional blood loss > 1000 ml												
1	randomised trials	serious [c]	not serious	not serious	very serious [d]	none	4/77 (5.2%)	8/74 (10.8%)	**RR 0.48** (0.15 to 1.53)	**56 fewer per 1000** (from 57 more to 92 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
Additional uterotonics												
2	randomised trials	not serious	not serious	not serious	not serious	none	10032/10106 (99.3%)	9964/10058 (99.1%)	**RR 1** (1 to 1)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Surgical intervention (hysterectomy)												
2	randomised trials	not serious	not serious	not serious	not serious	none	358/10109 (3.5%)	352/10059 (3.5%)	**RR 1.01** (0.88 to 1.17)	**0 fewer per 1000** (from 4 fewer to 6 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Surgical intervention (ligature)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none	225/10109 (2.2%)	255/10059 (2.5%)	**RR 0.88** (0.74 to 1.05)	**3 fewer per 1000** (from 1 more to 7 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Surgical intervention (embolization)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none	15/10109 (0.1%)	18/10059 (0.2%)	**RR 0.82** (0.42 to 1.62)	**0 fewer per 1000** (from 1 fewer to 1 more)	⊕⊕⊕◯ MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Surgical intervention (laparotomy)												
1	randomised trials	not serious	not serious	not serious	not serious	none	82/10032 (0.8%)	127/9985 (1.3%)	**RR 0.64** (0.49 to 0.85)	**5 fewer per 1000** (from 2 fewer to 6 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Surgical intervention (brace sutures)												
1	randomised trials	not serious	not serious	not serious	not serious	none	300/10032 (3.0%)	250/9985 (2.5%)	**RR 1.19** (1.01 to 1.41)	**5 more per 1000** (from 0 fewer to 10 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Invasive non-surgical intervention (intrauterine tamponade)												
1	randomised trials	not serious	not serious	not serious	not serious	none	705/10032 (7.0%)	729/9985 (7.3%)	**RR 0.96** (0.87 to 1.06)	**3 fewer per 1000** (from 4 more to 9 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Invasive non-surgical intervention (manual removal of placenta)												
1	randomised trials	not serious	not serious	not serious	not serious	none	918/10032 (9.2%)	961/9985 (9.6%)	**RR 0.95** (0.87 to 1.04)	**5 fewer per 1000** (from 4 more to 13 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Procedure-related complication (any maternal thromboembolic event)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	30/10033 (0.3%)	34/9985 (0.3%)	**RR 0.88** (0.54 to 1.43)	**0 fewer per 1000** (from 1 more to 2 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Procedure-related complication (deep venous thrombosis)												
2	randomised trials	not serious	not serious	not serious	serious [a]	none	5/10110 (0.0%)	8/10059 (0.1%)	**RR 0.62** (0.20 to 1.88)	**0 fewer per 1000** (from 1 fewer to 1 more)	⊕⊕⊕◯ MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Procedure-related complication (pulmonary embolism)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	17/10033 (0.2%)	20/9985 (0.2%)	**RR 0.85** (0.44 to 1.61)	**0 fewer per 1000** (from 1 fewer to 1 more)	⊕⊕⊕○ MODERATE	CRITICAL
Procedure-related complication (myocardial infarction)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	2/10033 (0.0%)	3/9985 (0.0%)	**RR 0.66** (0.11 to 3.97)	**0 fewer per 1000** (from 0 fewer to 1 more)	⊕⊕⊕○ MODERATE	CRITICAL
Procedure-related complication (stroke)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	8/10033 (0.1%)	6/9985 (0.1%)	**RR 1.33** (0.46 to 3.82)	**0 fewer per 1000** (from 0 fewer to 2 more)	⊕⊕⊕○ MODERATE	CRITICAL
Procedure-related complication (neonatal thromboembolic event)												
1	randomised trials	not serious	not serious	not serious	very serious [g]	none	0/10033	0/9985	No events	No events	⊕⊕○○ LOW	CRITICAL
Procedure-related complication (death of breastfed baby)												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	8/10033 (0.1%)	7/9985 (0.1%)	**RR 1.14** (0.41 to 3.14)	**0 fewer per 1000** (from 0 fewer to 2 more)	⊕⊕⊕○ MODERATE	No baby outcomes in WHO but this could be seen as a procedure related complica-tion

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. Wide confidence interval crossing the line of no effect

b. Wide confidence interval that includes the line of no effect

c. Single study with design limitations (no blinding)

d. Few events, small sample size, and wide confidence interval crossing the line of no effect

e. Moderate statistical heterogeneity and may be clinical heterogeneity

f. Single study with small sample size

g. No events

Question: Standard care plus tranexamic acid compared to placebo or standard care alone for treating primary postpartum haemorrhage (subgroup time from birth)

Setting: Data from one multicentre RCT with 20 060 women (WOMAN trial). Labour ward settings in high- (United Kingdom: 569 women), and low- and middle-income countries (Nigeria: 5711 women; Pakistan: 5282 women; Uganda: 2235 women; Kenya: 1031 women; Cameroon: 893 women; Sudan: 860 women; Tanzania: 538 women; Nepal: 533 women; Zambia: 496 women; Albania: 485 women; Democratic Republic of Congo: 457 women; Bangladesh: 325 women; Ethiopia: 302 women; Burkina Faso: 142 women; Jamaica: 73 women; Ghana: 41 women; Papua New Guinea: 38 women; Egypt: 33 women; Colombia: 8 women; Côte d'Ivoire: 8 women).

Bibliography: Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Dowswell T, Mousa H. Antifibrinolytic drugs for treating primary postpartum haemorrhage. Cochrane Database Syst Rev. 2017;(unpublished).

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Maternal mortality due to bleeding (subgroup time from birth) – less than 1 hour												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	49/4846 (1.0%)	60/4726 (1.3%)	**RR 0.80** (0.55 to 1.16)	**3 fewer per 1000** (from 2 more to 6 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Maternal mortality due to bleeding (subgroup time from birth) – 1 to 3 hours												
1	randomised trials	not serious	not serious	not serious	not serious	none	40/2674 (1.5%)	67/2682 (2.5%)	**RR 0.60** (0.41 to 0.88)	**10 fewer per 1000** (from 3 fewer to 15 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
Maternal mortality due to bleeding (subgroup time from birth) – more than 3 hours												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	66/2514 (2.6%)	63/2569 (2.5%)	**RR 1.07** (0.76 to 1.51)	**2 more per 1000** (from 6 fewer to 13 more)	⨁⨁⨁◯ MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Maternal mortality (all cause) (subgroup time from birth) – less than 1 hour												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	80/4846 (1.7%)	80/4726 (1.7%)	**RR 0.98** (0.72 to 1.33)	**0 fewer per 1000** (from 5 fewer to 6 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Maternal mortality (all cause) (subgroup time from birth) – 1 to 3 hours												
1	randomised trials	not serious	not serious	not serious	not serious	none	57/2674 (2.1%)	83/2682 (3.1%)	**RR 0.69** (0.49 to 0.96)	**10 fewer per 1000** (from 1 fewer to 16 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
Maternal mortality (all cause) (subgroup time from birth) – more than 3 hours												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	90/2514 (3.6%)	92/2569 (3.6%)	**RR 1.00** (0.75 to 1.33)	**0 fewer per 1000** (from 9 fewer to 12 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Composite outcome: death or hysterectomy by subgroups (timing) – less than 1 hour												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	253/4844 (5.2%)	229/4726 (4.8%)	**RR 1.08** (0.91 to 1.28)	**4 more per 1000** (from 4 fewer to 14 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Composite outcome: death or hysterectomy by subgroups (timing) – 1 to 3 hours												
1	randomised trials	not serious	not serious	not serious	serious [b]	none	122/2672 (4.6%)	154/2682 (5.7%)	**RR 0.80** (0.63 to 1.00)	**11 fewer per 1000** (from 0 fewer to 21 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Composite outcome: death or hysterectomy by subgroups (timing) – more than 3 hours												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	159/2514 (6.3%)	161/2569 (6.3%)	**RR 1.01** (0.82 to 1.25)	**1 more per 1000** (from 11 fewer to 16 more)	⨁⨁⨁◯ MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Standard care plus tranexamic acid	Placebo or standard care alone	Relative (95% CI)	Absolute (95% CI)		
Laparotomy for bleeding (subgroups by timing) – less than 1 hour												
1	randomised trials	not serious	not serious	not serious	not serious	none	22/4844 (0.5%)	45/4726 (1.0%)	**RR 0.48** (0.29 to 0.79)	**5 fewer per 1000** (from 2 fewer to 7 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
Laparotomy for bleeding (subgroups by timing) – 1 to 3 hours												
1	randomised trials	not serious	not serious	not serious	not serious	none	19/2672 (0.7%)	35/2682 (1.3%)	**RR 0.54** (0.31 to 0.95)	**6 fewer per 1000** (from 1 fewer to 9 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
Laparotomy for bleeding (subgroups by timing) – more than 3 hours												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	41/2514 (1.6%)	47/2569 (1.8%)	**RR 0.89** (0.59 to 1.35)	**2 fewer per 1000** (from 6 more to 8 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Wide 95% CI crossing the line of no effect

b. Wide 95% CI including the line of no effect

For more information, please contact:

Department of Reproductive Health and Research
E-mail: reproductivehealth@who.int
www.who.int/reproductivehealth

Maternal, Newborn, Child and Adolescent Health
E-mail: mncah@who.int
www.who.int/maternal_child_adolescent

World Health Organization
Avenue Appia 20, CH-1211 Geneva 27
Switzerland

ISBN 978 92 4 159015 4

Alydia HEALTH

3495 Edison Way
Menlo Park, CA 94025 USA

Premarket Notification: Traditional 510(k)

Jada® System

May 1, 2020

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Statistical Data Folder

File	Location
Raw data files in .sas7bdat format	Statistical Data folder
Data dictionary	Statistical Data folder

[1] Exhibit numbers are based on corresponding section within 510(k), so not consecutive within the Exhibit list

(b)(4) SAS FILEPROCEDURE4

DATA (b)(4)

(b)(4)

(b)(4) Clinical Studies

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. NAME OF SPONSOR/APPLICANT/SUBMITTER
Alydia Health

2. DATE OF THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
May 1, 2020

3. ADDRESS *(Number, Street, State, and ZIP Code)*
3495 Edison Way
Menlo Park, CA 94025
USA

4. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 415-990-4104
(Fax) 415-354-3473

PRODUCT INFORMATION

5. **FOR DRUGS/BIOLOGICS:** Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s)
FOR DEVICES: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)
(Attach extra pages as necessary)

Current name: Jada System

Prior name: InPress Device

Common name: Intraunterine Tamponade Balloon

Classification name: Obstetric-Gynecologic Specialized Manual Instrument

APPLICATION / SUBMISSION INFORMATION

6. TYPE OF APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES

☐ IND ☐ NDA ☐ ANDA ☐ BLA ☐ PMA ☐ HDE ☒ 510(k) ☐ PDP ☐ Other

7. INCLUDE IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/OTHER NUMBER *(If number previously assigned)*

8. SERIAL NUMBER ASSIGNED TO APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES

CERTIFICATION STATEMENT / INFORMATION

9. CHECK ONLY ONE OF THE FOLLOWING BOXES *(See instructions for additional information and explanation)*

☐ A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

☐ B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

☒ C. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that those requirements have been met.

10. IF YOU CHECKED BOX C, IN NUMBER 9, PROVIDE THE NATIONAL CLINICAL TRIAL (NCT) NUMBER(S) FOR ANY "APPLICABLE CLINICAL TRIAL(S)," UNDER 42 U.S.C. § 282(j)(1)(A)(i), SECTION 402(j)(1)(A)(i) OF THE PUBLIC HEALTH SERVICE ACT, REFERENCED IN THE APPLICATION/ SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES *(Attach extra pages as necessary)*

NCT Number(s): 02883673 04364386

The undersigned declares, to the best of her/his knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 331, section 301 of the Federal Food, Drug, and Cosmetic Act.
Warning: A willfully and knowingly false statement is a criminal offense, U.S. Code, title 18, section 1001.

11. SIGNATURE OF SPONSOR/APPLICANT/SUBMITTER OR AN AUTHORIZED REPRESENTATIVE (Sign)

(b)(6)

12. NAME AND TITLE OF THE PERSON WHO SIGNED IN NO. 11
(Name) Kathryn D. Wine, MPH
(Title) Vice President, Clinical Operations

13. ADDRESS *(Number, Street, State, and ZIP Code) (of person identified in Nos. 11 and 12)*
Alydia Health
3495 Edison Way
Menlo Park, CA 94025

14. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 415-990-4104
(Fax) 415-354-3473

15. DATE OF CERTIFICATION
30APR2020

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Instructions for Completion of Form FDA 3674

Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))
Form 3674 must accompany an application/submission, including amendments, supplements, and resubmissions, submitted under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.

1. **Name of Sponsor/Applicant/Submitter** - This is the name of the sponsor/applicant/submitter of the drug/biologic/device application/ submission which the certification accompanies. The name must be identical to that listed on the application/submission.
2. **Date** - This is the date of the application/submission which the certification accompanies.
3. **& 4.** - Provide complete address, telephone number and fax number of the sponsor/applicant/submitter.
5. **Product Information - For Drugs/Biologics:** Provide the established, proprietary name, and/or chemical/biochemical/blood product/ cellular/gene therapy name(s) for the product covered by the application/submission. Include all available names by which the product is known. **For Devices:** Provide the common or usual name, classification, trade or proprietary or model name(s), and/or model number(s). Include all available names/model numbers by which the product is known.
6. **Type of Application/Submission** - Identify the type of application/submission which the certification accompanies by checking the appropriate box. If the name of the type of application/submission is not identified, check the box labeled "Other."
7. **IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/Other Number** - If FDA has previously assigned a number associated with the application/ submission which this certification accompanies, list that number in this field. For example, if the application/submission accompanied by this certification is an IND protocol amendment and the IND number has already been issued by FDA, that number should be provided in this field.
8. **Serial Number** - In some instances a sequential serial number is assigned to the application. If there is such a serial number, provide it in this field. If there is no such number, leave this field blank.
9. **Certification** - This section contains three different check-off boxes.

   Box A should be checked if the sponsor/applicant/submitter has concluded that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do not apply because no clinical trials are included, relied upon, or otherwise referred to, in the application/ submission which the certification accompanies.

   Box B should be checked if the sponsor/applicant/submitter has concluded that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do not apply at the time of submission of the certification to any clinical trials that are included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. This means that, even though some or all of the clinical trials included, relied upon, or otherwise referred to in the application/submission may be "applicable clinical trials" under 42 U.S.C. § 282(j)(1)(A)(i), section 402(j)(1)(A)(i) of the Public Health Service Act, on the date the certification is signed, 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, does not require that any information be submitted to the ClinicalTrials.gov Data Bank with respect to those clinical trials.

   Box C should be checked if the sponsor/applicant/submitter has concluded that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, do apply, on the date the certification is signed, to some or all of the clinical trials that are included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. This means that, as of the date the certification is signed, the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, apply to one or more of the clinical trials included, relied upon, or otherwise referred to, in the application/submission which this certification accompanies.
10. **National Clinical Trial (NCT) Numbers** - If you have checked Box C in number 9 (Certification), provide the NCT Number obtained from www.ClinicalTrials.gov for each clinical trial that is an "applicable clinical trial" under 42 U.S.C. § 282(j)(1)(A)(i), section 402(j)(1)(A)(i) of the Public Health Service Act, and that is included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. Type only the number, as the term "NCT" will be added automatically before number. Include any and all NCT numbers that, as of the date the certification is signed, have been assigned to the clinical trials included, relied upon, or otherwise referred to, in the application/submission which this certification accompanies. Multiple NCT numbers may be required for a particular certification, depending on the number of "applicable clinical trials" included, relied upon, or otherwise referred to, in the application/submission which the certification accompanies. Leave this field blank if you have checked Box 9.C but, at the time the certification is completed, you have not yet received any NCT numbers for the "applicable clinical trial(s)" included, relied upon, or otherwise referred to in the application/ submission.
11. **Signature of Sponsor/Applicant/Submitter or an Authorized Representative** - The person signing the certification must sign in this field.
12. **Name and Title of Person Who Signed in number 11** - Include the name and title of the person who is signing the certification. If the person signing the certification is not the sponsor/applicant/submitter of the application/submission, he or she must be an authorized representative of the sponsor/applicant/submitter.
13. **& 14.** - Provide the full address, telephone and fax numbers of the person who is identified in number 11 and signs the certification in number 11.
15. Provide the date the certification is signed. This date may be different from the date provided in number 2.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 15 minutes and 45 minutes (depending on the type of application/submission) per response, including time for reviewing instructions. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the address below.

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer (HFA-250)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information, unless it displays a currently valid OMB control number.

August 28, 2020

Alydia Health
% Cindy Domecus, R.A.C.
Principal
Domecus Consulting Services LLC
1171 Barroilhet Drive
Hillsborough, CA 94010

Re: K201199
Trade/Device Name: Jada® System
Regulation Number: 21 CFR§ 884.4530
Regulation Name: Obstetric-gynecologic specialized manual instrument
Regulatory Class: II
Product Code: OQY
Dated: July 27, 2020
Received: July 29, 2020

Dear Cindy Domecus:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Monica D. Garcia, Ph.D.
Acting Assistant Director
DHT3B: Division of Reproductive,
Gynecology and Urology Devices
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

(b)(4)

(b)(4) Clinical Studies

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CLINICAL STUDY REPORT

APPENDIX 9.2

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

(b)(4) Protocol

SECTION 15: STERILIZATION

There is no device-specific guidance document, special controls document or requirements in a device-specific classification regulation regarding sterility and/or reprocessing that is applicable to the subject device.

The Jada System is provided sterile by Alydia Health and is a single-patient use device.

The subject device is not end user sterilized or disinfected or reusable. The Jada System is a single-patient use device.

The sterilization information provided below is specific to the Jada System:

A. Sterilization Method

Gamma Radiation

B. Description of Method to Validate the Sterilization Parameters

The validation was based on the practices recommended by ANSI/AAMI/ISO 11137-2: Sterilization of Health Care Products – Radiation – Establishing the sterilization dose – Method VD_{max}. A protocol for substantiation of (b)(4) was utilized to verify that a minimum sterilization dose of (b)(4) will provide a Sterility Assurance Level (SAL) of 10^{-6}.

The sterilization dose range is (b)(4)

(b)(4)

C. Sterility Assurance Level

SAL = 10^{-6}

D. Description of Packaging

The Jada System is held in position on a die cut (b)(4) (b)(4) backing card with an additional overlaying (b)(4) strap component to protect the Cervical Seal. The single device and card are placed into a (b)(4) and nylon pouch followed by a single pouch (b)(4) The pouch packaging is validated per ISO 11607-2: Packaging For Terminally Sterilized Medical Devices – Part 2: Validation Requirements For Forming, Sealing And Assembly Processes. The sealed pouch is singularly placed into an (b)(4) shelf carton. Three shelf cartons are then placed into a corrugated shipper box.

E. Description of Method to Validate Non-Pyrogenic Labeling

The Jada System is not labeled as non-pyrogenic. However, Material mediated pyrogenicity testing was performed (see **Section 17: Biocompatibility**).

Alydia HEALTH

July 27, 2020

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: K201199/S001; Response to July 2, 2020 Hold Letter
Jada® System

Attn: Poulomi Nandy, Ph.D.
Microbiologist, Obstetrical and Reproductive Health Devices Team
DHT3B: Division of Reproductive and Urology Devices
OHT3: Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors

Dear Dr. Nandy and 510(k) Review Team,

This supplement to the above referenced 510(k) is being submitted to respond to FDA's requests for additional information identified in its Hold Letter of July 2, 2020. We believe that the responses provided herein adequately address all of FDA's requests and we look forward to addressing any further questions FDA may have upon its review of our responses.

A hard copy of the signed cover letter and one eCopy of the entire 510(k) supplement are provided herein. The eCopy was prepared in accordance with FDA's December 16, 2019 guidance titled "eCopy Program for Medical Device Submissions, Guidance for Industry and Food and Drug Administration Staff."

Alydia Health considers the information described in this 510(k) supplement and all related exhibits to be confidential commercial information and therefore exempt from public disclosure. We request that this notification and its contents be treated as confidential in accordance with 21 CFR § 807.95.

Please direct any questions or requests for additional information to me at the below numbers or by electronic mail at: DomecusConsulting@comcast.net. We thank the FDA review team for its continued review of our application.

Sincerely,

(b)(6)

Cindy Domecus, R.A.C. (US & EU)
Principal, Domecus Consulting Services LLC
Regulatory Consultant to Alydia Health
Office: 650-343-4813 I Mobile: (b)(6) I Fax: 650-343-7822

Enclosure: One paper copy of signed cover letter and one eCopy of entire 510(k) supplement

Table of Contents

Exhibits

(b)(4)

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

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Exhibit 21: Redlined copy of revised Jada System Quick Reference Guide

(b)(4) Draft Package Insert

(b)(4) Draft Package Insert

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

>

> Hello,

>

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
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> CDRH | Food and Drug Administration

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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>

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>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E
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<image008.jpg> <image009.jpg> <image010.jpg> <image011.jpg> <image012.jpg>

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

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Exhibit 23: Redlined copy of revised Jada System Product Labels

(b)(4) Draft Labeling

(b)(4) Draft Labeling

SECTION 6: 510(k) SUMMARY (21 CFR § 807.92(a))

The 510(k) Summary is provided in this section. The 510(k) Summary complies with 807.92(a) and has been prepared in accordance with the formatting in Appendix C of FDA's July 28, 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

510(k) Summary

(b)(4) Draft

(b)(4) Draft

(b)(4) Draft

(b)(4) Draft

(b)(4) Draft

From: Mason, Tiffani * [Tiffani.Mason@fda.hhs.gov]
Sent: 5/4/2020 7:46:39 PM
To: domecusconsulting@comcast.net
Subject: K201199 Acknowledgement Notification
Attachments: K201199-Letter.pdf

Tiffani R. Mason
Tiffani.Mason@fda.hhs.gov
Record Management Specialist 1 DCC 510K

Acknowledgment Letter

5/4/2020

Cindy Domecus, Principal
Domecus Consulting Services LLC
1171 Barroilhet Drive
Hillsborough, CA 94010
UNITED STATES

Dear Cindy Domecus:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has received your submission. This submission has been assigned the unique document control number below. All future correspondence regarding this submission should be identified prominently with the number assigned and should be submitted to the Document Control Center at the above letterhead address. Failure to do so may result in processing delays. If you believe the information identified below is incorrect, please notify the Program Operations Staff at (301) 796-5640.

Submission Number: K201199
Received: 5/4/2020
Applicant: Alydia Health
Device: Jada System

We will notify you when the review of this document has been completed or if any additional information is required. If you are submitting new information about a submission for which we have already made a final decision, please note that your submission will not be re-opened. For information about CDRH review regulations and policies, please refer to http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm.

Sincerely yours,

Center for Devices and Radiological Health

CLINICAL STUDY REPORT

APPENDIX 9.7

(b)(4) Clinical Studies

(b)(4) Clinical Studies

(b)(4) Clinical Studies

(b)(4) Clinical Studies

Ah, understood! Thanks for the clarification Reginald. We look forward to working with you as FDA completes its review of our file.

Take care,

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 21, 2020, at 2:21 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:
>
> Hello Cindy,
>
> She has not left FDA. Due to an increased workload during the COVID-19 public health emergency, some files were reassigned.
>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
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>

>

>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Friday, August 21, 2020 5:08 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: Request for information for Jada System (K201199/S001)

>

> Hello Reginald,

>

> Thanks for the update! Did Dr. Nandy leave FDA (just curious)?

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

>

>

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>

>

> On Aug 21, 2020, at 2:04 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov
<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello Cindy,

>

> I am replacing Dr. Nandy as the lead reviewer for this file and will complete the
review for the Jada System. I have discussed the file with Dr. Nandy to ensure our
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>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Friday, August 21, 2020 4:20 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: Request for information for Jada System (K201199/S001)

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>

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>

> Have a nice weekend.

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

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>

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Clinical comments to Team:

(b)(5) FDA drafts

(b)(5) FDA drafts

(b)(5) FDA drafts

CLINICAL STUDY REPORT

APPENDIX 9.4

List of Third Parties

Company Name and Address	Contact
(b)(4)	

(b)(4) SAS FILEDEV_USE_QUESTION

DATA (b)(4)

(b)(4)

(b)(4) Clinical Studies

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(b)(4)

CERTIFICATE OF CALIBRATION

Report No. (b)(4)

CUSTOMER

Alydia Health
3495 Edison Way
Menlo Park, CA
94025

Cal Date: 07/22/2020
Due Date: 07/22/2021
Cal Int: (b)(4)

(b)(4)

(b)(4) Testing

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 10:41 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)
Principal
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(650) 343-4813 (office)

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Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
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DFA022A0

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Hello Reginald,

Thanks for the update! Did Dr. Nandy leave FDA (just curious)?

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 2:04 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

I am replacing Dr. Nandy as the lead reviewer for this file and will complete the review for the Jada System. I have discussed the file with Dr. Nandy to ensure our review is consistent. Please let me know if you have any questions.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

OHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 21, 2020 4:20 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thank you for your reivew of our file. I am writing to confirm receipt of your below request and that we will respond by the requested date. We stand ready to respond to any further questions FDA may have as the review team completes its review of our file.

Can you please clarify if you are replacing Poulomi as the lead reviewer for this file or is she just on vacation at this time? Thanks.

Have a nice weekend.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? **If possible, please provide a response by noon on Tuesday, August 25, 2020.**

(b)(4) Deficiencies

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

Exhibit 8: Clean copy of revised Jada System Instructions for Use

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: June 30, 2020
See PRA Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
May 1, 2020	(b)(4)	

SECTION A TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Request for Feedback
☐ Original Submission	☐ Regular (180 day)	☐ Original PDP	☒ Original Submission:	☐ Pre-Submission
☐ Premarket Report	☐ Special	☐ Notice of Completion	☒ Traditional	☐ Informational Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Submision Issue Meeting
☐ Amendment	☐ 30-day Supplement		☐ Abbreviated (Complete section I, Page 5)	☐ Day 100 Meeting
☐ Report	☐ 30-day Notice		☐ Additional Information	☐ Agreement Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Determination Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Study Risk Determination
	☐ Amendment to PMA & HDE Supplement			☐ Other *(specify):*
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☒ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
☐ Amendment	☐ Amendment	☐ Additional Information	☐ Additional Information	☐ Other *(describe submission):*
☐ Supplement	☐ Supplement			
	☐ Report			
	☐ Report Amendment			

Have you used or cited Standards in your submission? ☒ Yes ☐ No *(If Yes, please complete Section I, Page 5)*

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Alydia Health	N/A		
Division Name *(if applicable)*	**Phone Number** *(including area code)*		
	650-275-3772		
Street Address	**FAX Number** *(including area code)*		
3495 Edison Way			
City	**State / Province**	**ZIP/Postal Code**	**Country**
Menlo Park	CA	94025	U.S.
Contact Name			
Colby Holtshouse			
Contact Title	**Contact E-mail Address**		
Interim CEO	colby@alydiahealth.com		

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Domecus Consulting Services LLC			
Division Name *(if applicable)*	**Phone Number** *(including area code)*		
	650-343-4813		
Street Address	**FAX Number** *(including area code)*		
1171 Barroilhet Drive	650-343-7822		
City	**State / Province**	**ZIP Code**	**Country**
Hillsborough	CA	94010	U.S.
Contact Name			
Cindy Domecus, R.A.C.			
Contact Title	**Contact E-mail Address**		
Principal	DomecusConsulting@comcast.net		

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ New Device
- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Process change:
  - ☐ Manufacturing ☐ Packaging
  - ☐ Sterilization
  - ☐ Other *(specify below)*

- ☐ Response to FDA correspondence:

- ☐ Change in design, component, or specification:
  - ☐ Software / Hardware
  - ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
  - ☐ Other *(specify below)*

- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
  - ☐ Shelf Life
  - ☐ Trade Name
  - ☐ Other *(specify below)*

- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager

- ☐ Report Submission:
  - ☐ Annual or Periodic
  - ☐ Post-approval Study
  - ☐ Adverse Reaction
  - ☐ Device Defect
  - ☐ Amendment

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify)*:

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - ☐ Correspondent / Applicant
  - ☐ Design / Device
  - ☐ Informed Consent
  - ☐ Manufacturer
  - ☐ Manufacturing Process
  - ☐ Protocol - Feasibility
  - ☐ Protocol - Other
  - ☐ Sponsor

- ☐ Report submission:
  - ☐ Current Investigator
  - ☐ Annual Progress Report
  - ☐ Site Waiver Report
  - ☐ Final

- ☐ Response to FDA Letter Concerning:
  - ☐ Conditional Approval
  - ☐ Deemed Approved
  - ☐ Deficient Final Report
  - ☐ Deficient Progress Report
  - ☐ Deficient Investigator Report
  - ☐ Disapproval
  - ☐ Request Extension of Time to Respond to FDA
  - ☐ Request Meeting
  - ☐ Request Hearing

- ☐ Other Reason *(specify)*:

SECTION D3 REASON FOR SUBMISSION - 510(k)

- ☒ New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☐ Other Reason *(specify)*:

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	OQY	2		3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☐ 510 (k) summary attached

☐ 510 (k) statement

Information on devices to which substantial equivalence is claimed *(if known)*

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K170622	1	Bakri® Postpartum Balloon	1	Cook Inc.
2		2		2	
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Intrauterine tamponade balloon

	Trade or Proprietary or Model Name for This Device		Model Number
1	Jada System	1	
2		2	
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions *(regardless of outcome)*

1	(b)(4)	4	5	6	
7	8	9	10	11	12

Data Included in Submission

☒ Laboratory Testing ☒ Animal Trials ☒ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
OQY	884.4530	☐ Class I ☒ Class II
Classification Panel		☐ Class III ☐ Unclassified
Obstetrics/Gynecology		

Indications *(from labeling)*

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

Note: Submission of the information entered in Section H does not affect the need to submit device establishment registration.	FDA Document Number *(if known)*

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

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☐ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Manufacturer	☐ Contract Sterilizer ☐ Repackager / Relabeler
Company / Institution Name		Establishment Registration Number	
Division Name *(if applicable)*		Phone Number *(including area code)*	
Street Address		FAX Number *(including area code)*	
City		State / Province	ZIP Code / Country
Contact Name	Contact Title	Contact E-mail Address	

SECTION I — UTILIZATION OF STANDARDS

Note: Complete this section if your application or submission cites standards or includes a *"Declaration of Conformity to a Recognized Standard"* statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	11137-2	ISO	Sterilization of Health Care Products -- Radiation -- Part 2: Establishing the Sterilization Dose	Third Edition 2013-06-01	04/04/2016
2	10993-1	ISO	Biological Evaluation Of Medical Devices - Part 1: Evaluation And Testing Within A Risk Management Process	Fifth Edition, 2018-08	01/14/2019
3	11607-1	ANSI/AAMI/ ISO	Packaging For Terminally Sterilized Medical Devices – Part 1: Requirements For Materials, Sterile Barrier Systems And Packaging [Including Amendment 1 (2014)]	2006/R2010	01/27/2015
4	F-1980	ASTM	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices	2016	12/23/2016
5	D4169	ASTM	Standard Practice for Performance Testing of Shipping Containers and Systems	2016	12/23/2016
6	14971	ISO	Medical Devices—Application of Risk Management to Medical Devices	Third Edition 2019-12	12/23/2019
7	111607-2	ISO	Packaging For Terminally Sterilized Medical Devices – Part 2: Validation Requirements For Forming, Sealing And Assembly Processes [Including Amendment 1 (2014)]	First Edition 2006-04-15	01/27/2015

Please include any additional standards to be cited on a separate page.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Department of Health and Human Services
Food and Drug Administration
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Paperwork Reduction Act (PRA) Staff
1350 Piccard Drive, Room 400
Rockville, MD 20850

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U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
OFFICE OF PRODUCT EVALUATION AND QUALITY
OFFICE OF CLINICAL EVIDENCE AND ANALYSIS
DIVISION OF CLINICAL EVIDENCE AND ANALYSIS 2

MEMORANDUM FOR STATISTICAL CONSULT

Date: June 23, 2020

From: Yanping Qu, Ph.D., CDRH/OCEA/DCEA2/TCEA2A

Subject: Statistical Review of 510(k) K201199
Jada® System
Alydia Health, Inc.

To: Poulomi Nandy, CDRH/OHT3/DHT3B/THT3B1

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To: Poulomi Nandy
Cc: Monica Garcia
From: Kelly Colden
Subject: Clinical review of the premarket notification for the Jada System, Alydia Health (K201199)
Date: June 26, 2020

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(b)(5) FDA Reviewer Notes

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Uterine balloon tamponade for the treatment of postpartum hemorrhage: a systematic review and meta-analysis

Sebastian Suarez, MD, MPH; Agustin Conde-Agudelo, MD, MPH, PhD; Anderson Borovac-Pinheiro, MD, PhD; Daniela Suarez-Rebling, BS; Melody Eckardt, MD, MPH; Gerhard Theron, MD; Thomas F. Burke, MD

OBJECTIVE: To assess the efficacy, effectiveness, and safety of uterine balloon tamponade for treating postpartum hemorrhage.

STUDY DESIGN: We searched electronic databases (from their inception to August 2019) and bibliographies. We included randomized controlled trials, nonrandomized studies, and case series that reported on the efficacy, effectiveness, and/or safety of uterine balloon tamponade in women with postpartum hemorrhage. The primary outcome was the success rate of uterine balloon tamponade for treating postpartum hemorrhage (number of uterine balloon tamponade success cases/total number of women treated with uterine balloon tamponade). For meta-analyses, we calculated pooled success rate for all studies, and relative risk with 95% confidence intervals for studies that included a comparative arm.

RESULTS: Ninety-one studies, including 4729 women, met inclusion criteria (6 randomized trials, 1 cluster randomized trial, 15 nonrandomized studies, and 69 case series). The overall pooled uterine balloon tamponade success rate was 85.9% (95% confidence interval, 83.9–87.9%). The highest success rates corresponded to uterine atony (87.1%) and placenta previa (86.8%), and the lowest to placenta accreta spectrum (66.7%) and retained products of conception (76.8%). The uterine balloon tamponade success rate was lower in cesarean deliveries (81.7%) than in vaginal deliveries (87.0%). A meta-analysis of 2 randomized trials that compared uterine balloon tamponade vs no uterine balloon tamponade in postpartum hemorrhage due to uterine atony after vaginal delivery showed no significant differences between the study groups in the risk of surgical interventions or maternal death (relative risk, 0.59; 95% confidence interval, 0.02–16.69). A meta-analysis of 2 nonrandomized before-and-after studies showed that introduction of uterine balloon tamponade in protocols for managing severe postpartum hemorrhage significantly decreased the use of arterial embolization (relative risk, 0.29; 95% confidence interval, 0.14–0.63). A nonrandomized cluster study reported that use of invasive procedures was significantly lower in the perinatal network that routinely used uterine balloon tamponade than that which did not use uterine balloon tamponade (3.0/1000 vs 5.1/1000; $P < .01$). A cluster randomized trial reported that the frequency of postpartum hemorrhage–related invasive procedures and/or maternal death was significantly higher after uterine balloon tamponade introduction than before uterine balloon tamponade introduction (11.6/10,000 vs 6.7/10,000; $P = .04$). Overall, the frequency of complications attributed to uterine balloon tamponade use was low (≤6.5%).

CONCLUSION: Uterine balloon tamponade has a high success rate for treating severe postpartum hemorrhage and appears to be safe. The evidence on uterine balloon tamponade efficacy and effectiveness from randomized and nonrandomized studies is conflicting, with experimental studies suggesting no beneficial effect, in contrast with observational studies. Further research is needed to determine the most effective programmatic and healthcare delivery strategies on uterine balloon tamponade introduction and use.

Key words: Bakri balloon, cesarean delivery, condom UBT, hysterectomy, maternal mortality, placenta previa, uterine atony, uterine bleeding, uterotonics, vaginal delivery

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality and morbidity around the world.[1] In 2017, maternal hemorrhage was responsible for more than 38,000 deaths, of which more than 90% occurred in low- and middle-income countries (LMICs).[1,2] More than 1.5 million women annually have complications related to hemorrhage during pregnancy and the postpartum period.[3] While the prevalence of PPH ranges from 7% to 12% in high-income countries (HICs), it is as high as 25.7% in sub-Saharan Africa.[4,5] The prevalence of PPH has progressively increased in HICs. A Canadian population-based study reported a 27% increase in the rate of PPH from 2000 to 2009,[5] whereas a US nationwide study showed that incidence of severe PPH doubled from 1998 to 2008.[6]

Predisposing factors and etiologies for PPH include multiple pregnancy, fetal macrosomia, abnormal placentation, grand multiparity, older age, obesity, rapid or prolonged labor, labor induction, cesarean delivery, chorioamnionitis, uterine atony, retained placenta, genital tract lacerations, retained products of conception, and coagulation disorders, among others.[7–25] Appropriate treatment of PPH includes uterine massage, uterotonics, tranexamic acid, and, in cases of refractory bleeding, uterine balloon tamponade (UBT), uterine arterial embolization, and other surgical procedures.[26–28] Access to these critical interventions is often lacking in low-resource settings and therefore contributes to the high morbidity and mortality rates attributed to PPH.

Compared to other interventions used to treat refractory PPH, UBT requires

Cite this article as: Suarez S, Conde-Agudelo A, Borovac-Pinheiro A, et al. Uterine balloon tamponade for the treatment of postpartum hemorrhage: a systematic review and meta-analysis. Am J Obstet Gynecol 2020;222:293.e1-52.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2019.11.1287

Related editorial, page 291.

Click Video under article title in Contents at ajog.org

AJOG at a Glance

Why was this study conducted?

This study was conducted to evaluate the efficacy, effectiveness, and safety of uterine balloon tamponade for the management of postpartum hemorrhage.

Key findings

The overall pooled success rate of uterine balloon tamponade in the treatment of postpartum hemorrhage was 85.9%. The success rate was higher in women with postpartum hemorrhage due to uterine atony and placenta previa than in women with postpartum hemorrhage due to placenta accreta spectrum or retained products of conception. The frequency of complications associated with the use of uterine balloon tamponade was low. To date, uterine balloon tamponade appears to have no adverse consequences on subsequent reproductive function.

What does this add to what is known?

Findings from this study indicate that uterine balloon tamponade has a high success rate for treating severe postpartum hemorrhage with a low complication rate. The evidence on uterine balloon tamponade efficacy and effectiveness from randomized and nonrandomized studies is conflicting, with experimental studies suggesting no beneficial effect, in contrast with observational studies.

minimal local resources and does not entail extensive training or complex equipment. UBTs can be used by a variety of healthcare providers and are recently becoming more affordable.[29] However, uncertainty still exists regarding the evidence on the efficacy of UBT for the management of PPH.

A systematic review published in 2013, including 13 observational studies with a total of 241 women, concluded that UBT is effective for the treatment of PPH in low-resource settings.[30] Other systematic reviews have been limited only to the use of the Bakri balloon (Cook Medical, Bloomington, IN) for the treatment of PPH.[31,32] Since then, considerable additional research on UBT has been published, including individual and cluster randomized trials and before-and-after studies of effectiveness. Therefore, examination of the current evidence on the efficacy of this intervention is justified. We conducted a systematic review and meta-analysis to determine the efficacy, effectiveness, and safety of UBT for the treatment of PPH.

Materials and Methods

This systematic review and meta-analysis was performed and reported according to the PRISMA statement.[33] The protocol was registered with PROSPERO in July 2018 (CRD42018102643; available at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=102643). At least 2 of the authors (S.S., D.S.R., and A.B.P.) independently retrieved and reviewed studies for eligibility, assessed their risk of bias, and extracted data. Any disagreements encountered in the review process were resolved through discussion between the reviewers.

Literature search

A literature search was conducted by Harvard library services. PubMed, Ovid MEDLINE, EMBASE, POPLINE, Web of Science, African Index Medicus, LILACS/BIREME, Cochrane Library, and Google Scholar were searched from their inception to August 31, 2019, using a combination of terms related to PPH and UBT (Appendix 1. Search Strategy), without language restrictions. Reference lists of identified studies were also searched.

Eligibility criteria

Randomized controlled trials (RCTs), nonrandomized studies of interventions, and case series that reported on efficacy, effectiveness, and/or safety of UBT device placement in women with PPH after vaginal and/or cesarean delivery were included. Studies were excluded if they (1) reported on surgical techniques simultaneous with UBT use (eg, B-Lynch suture plus UBT); (2) were case reports, editorials, letters to the editors, or reviews without original data; or (3) reported on use of UBT for hemorrhage associated with pregnancy loss before 20 weeks of gestation. Studies with cases of UBT placement after failure of a surgical procedure for PPH were included. In cases of duplicate publications, only the most recent or complete version was included.

Outcome measures

The primary outcome was the success rate of UBT for the treatment of all causes of PPH. UBT success rate was defined as the number of "UBT success" cases divided by the total number of women treated with UBT, regardless of the definition of UBT success in each individual study. Cases of PPH where bleeding was arrested without maternal death and additional surgical or radiological interventions after UBT placement were defined as "UBT success." Cases of PPH where maternal death occurred or where additional surgical or radiological interventions were performed were defined as "UBT failures." For randomized trials and nonrandomized studies, the primary outcome was a composite of maternal death and/or surgical (artery ligation, uterine compression sutures, or hysterectomy) or radiological (arterial embolization) interventions. Secondary outcomes included success rate of UBT for the treatment of individual causes of PPH, frequency of hysterectomy and other invasive procedures (artery ligation, uterine compressive sutures, and arterial embolization), maternal death, mean blood loss, blood loss >1000 mL, blood transfusion, mean change in hemoglobin and hematocrit, admission to the intensive care unit, length of hospital and intensive care unit stay, and complication rates. Complications were defined as undesirable and unintended

events that were likely a direct result of UBT placement, such as infection, trauma, or reproductive consequences.

Risk of bias assessment

The risk of bias of included RCTs, nonrandomized studies, and case series was assessed according to the Cochrane Handbook for Systematic Reviews of Interventions,[34] the ROBINS-I tool (Risk Of Bias In Non-randomized Studies of Interventions),[35] and a modified version of the tool proposed by Murad et al,[36] respectively. Detailed description of these tools are included in the Appendix (II. Tools Used for Assessing the Risk of Bias).

Data extraction and synthesis

A data extraction form was used to collect information on study characteristics (authors, year of publication, design, prospective or retrospective data collection, definition of PPH, risk of bias, and method of assessment of blood loss); setting (country, income level, urban vs rural, number of facilities, and facility type); patient characteristics (inclusion and exclusion criteria, type of delivery, cause of PPH, baseline characteristics, and date of recruitment); details of intervention (type of UBT device, indication for UBT use, time of UBT placement, volume of fluid placed in UBT device, duration of placement, time to UBT device removal, and co-interventions); and outcomes (definitions used, number of outcome events/total number, and mean ± standard deviation for each outcome). Results from different studies were combined to produce a pooled success rate with 95% confidence interval (CI) using random-effects models. For RCTs and nonrandomized studies, estimates of success rate were obtained from the UBT intervention group only. Results were stratified according to study design, mode of delivery, and cause of PPH. Subgroup analyses were performed according to UBT device (Bakri balloon vs condom UBT) and stratified by cause of PPH (all causes of PPH vs uterine atony) and income (HICs vs LMICs). Sensitivity analyses were performed based on risk of bias and inclusion of data from abstracts of studies published only in abstract form or unobtainable articles.

Estimates of treatment effect were obtained from meta-analyses of RCTs and nonrandomized studies. These analyses compared the results of patients who were treated with UBT devices with those of a control group that was not treated with UBT devices. We calculated the pooled relative risk (RR) for dichotomous data and mean difference (MD) for continuous data with an associated 95% CI. If means were not reported in individual studies, we estimated them using the sample size, median, and interquartile ranges.[37] Heterogeneity of the results among studies was tested with the quantity I^2.[38] We pooled results from individual studies using a fixed-effects model if substantial statistical heterogeneity was not present ($I^2 < 30\%$). If I^2 values were $\geq 30\%$, a random-effects model was used to pool data across studies.

We assessed the overall quality of the evidence using the GRADE approach[39] for the following outcomes: composite of maternal death and/or surgical or radiological interventions, maternal death, surgical interventions, hysterectomy, artery ligation, uterine compressive sutures, and arterial embolization. GRADE has 4 levels of evidence: high, moderate, low, and very low (Appendix: III. Quality of Evidence).

Descriptive statistical analyses were performed using RStudio version 1.0.153 (RStudio, Inc, Boston, MA). Meta-analyses were conducted using MedCalc version 19.03 (MedCalc Software, Ostend, Belgium) and Review Manager 5.3.5 (The Nordic Cochrane Centre, Copenhagen, Denmark).

Results

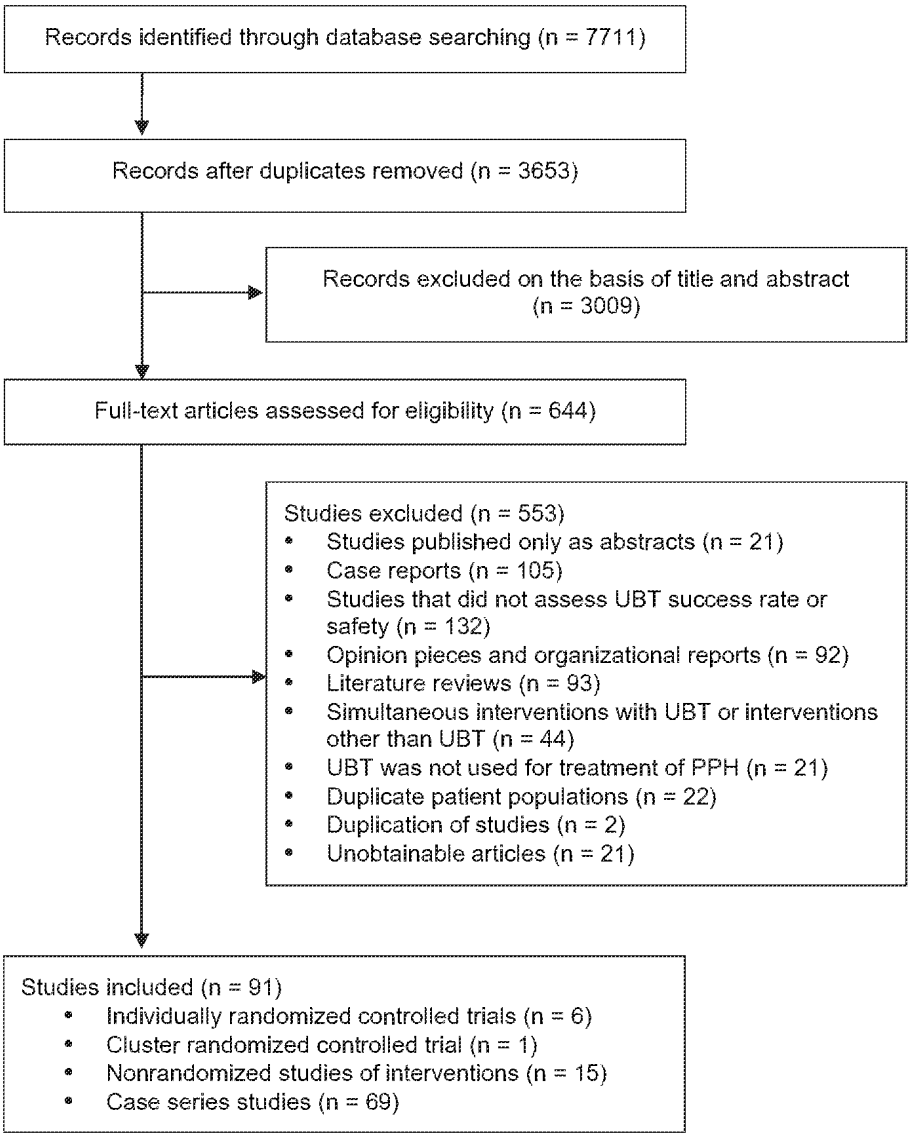
Study selection and characteristics

We identified 3653 studies in our literature search, of which 644 met initial screening criteria and were further assessed for eligibility (Figure 1). Ninety-one studies including a total of 4729 women met inclusion criteria, of which 6 were RCTs,[40–45] 1 was a cluster RCT,[46] 15 were nonrandomized studies of interventions,[47–61] and 69 were case series.[62–130] Three nonrandomized studies of interventions[123,126,129] had control groups that precluded their analysis as nonrandomized studies, but these studies provided data as case series. The corresponding authors of 2 studies were contacted to obtain additional information on relevant unpublished data.[57,120] A nonrandomized study[54] that used the same patient population as a case series[115] was included to evaluate the effectiveness of UBT, so data from the nonrandomized study[54] were excluded from meta-analyses of UBT success rate (for a total of 90 studies included in meta-analyses).

The main characteristics of the studies included in the systematic review are presented in Supplementary Table 1 (Appendix). Forty-six studies (52%) were conducted in 12 Asian countries,[41,42,45,48,49,52,53,55,58–60,63,72,74–76,79,81,87,89–91,94–96,100,101,103–105,107,109,110,112,114,117–119,122,124–129] 22 studies (25%) in 8 European countries,[47,51,64,65,68–71,73,77,78,80,82,85,86,88,92,97,99,102,115,123] 9 studies (10%) in 4 African countries,[40,44,56,61,67,106,109,111,130] 4 studies (4%) in 2 Latin American countries,[83,98,113,121] and 5 studies (6%) in the United States[50,66,84,93,116]; the remaining 4 were multicenter studies conducted in 10 countries.[43,46,62,120] Forty-eight (53%) studies were conducted in LMICs and 42 (47%) were conducted in HICs. Of the studies conducted in LMICs, 5 (10%) were RCTs,[40,42–45] 1 (2%) was a cluster RCT,[46] 9 (19%) were nonrandomized studies,[48,52,55–61] and 33 (69%) were case series.[63,67,72,74–76,81,83,89,91,94–96,98,100,101,104–106,108–111,113,114,117,118,120,121,126–128,130] Of the studies conducted in HICs, 1 (2%) was an RCT,[41] 5 (12%) were nonrandomized studies,[47,49–51,53] and 36 (86%) were case series.[62,64–66,68–71,73,77–80,82,84–88,90,92,93,97,99,102,103,107,112,115,116,119,122–125,129]

The median number of women treated with a UBT device for PPH was 64 (range, 7–120), 40 (range, 13–142), and 29 (range, 4–407) for RCTs, nonrandomized studies, and case series, respectively. The most-used UBT devices were Bakri balloon and condom catheter (Figure 2), which were used in 44 (49%) studies,[41,42,47–53,55,59,61,70,

FIGURE 1
Summary of evidence search and selection



PPH, postpartum hemorrhage; *UBT*, uterine balloon tamponade.

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[73,80,82–84,86,88–90,94,97–104,107,111,112,114,116,118,119,121,123–126,129] and 18 (20%) studies,[43,45,46,58,63,67,72,74,81,91,105,106,108–110,113,117,120,127] respectively. Sengstaken–Blakemore balloons (C.R. Bard Inc., Covington, GA) were used in 6 (7%) studies,[62,64,68,69,79,87] Foley UBTs in 4 (4%),[56,75,76,128] and Rusch balloons (Teleflex Medical, Wayne, PA) in 4 (4%).[65,71,78,92] Belfort-Dildy ("ebb") Complete Tamponade Systems (Glenveigh Medical, LLC, Chattanooga, TN, currently marketed by Clinical Innovation, Salt Lake City, UT),[93] double-balloon cervical ripening catheters,[95] ESM-UBTs (Ujenzi Charitable Trust, Medford, MA),[120] El-Menia,[40] BT-Caths (Utah Medical Products, Inc., Midvale, UT),[96] Ellavi (Sinapi Biomedical, Stellenbosch, South Africa),[130] Linton-Nachlas (Coloplast, Rosny-sous-Bois cedex, France),[85] Metreurynters (Fuji-Metro; Fuji Latex Co., Ltd., Tochigi, Japan and Mini-Metro; Soft Medical Co., Ltd., Tokyo, Japan),[122] and Zhukovsky balloons (Ginamed, Moscow, Russia)[57] were used in 1 study each. Four studies reported a combination of UBT devices.[44,60,66,115] One study did not report the type of UBT device(s) used.[77]

Twelve (13%) studies included only women who delivered vaginally,[40,43–46,58,67,85,105,117,123] and 15 (17%) included only women who delivered by cesarean section.[41,42,48,49,53,56,59,61,76,79,89,103,104,126,128] The remaining studies included vaginal and cesarean deliveries.[47,50–52,55,60,62–66,68–75,77,78,80–84,86–88,90–102,106–116,118–122,124,125,127,129,130]

The indications for using a UBT device for the treatment of PPH included uterine atony in 22 (25%) studies,[40,41,43,44,47,48,50,58,59,67,72,73,83,97,100,105,111,113,117,126,127,130] placenta previa in 8 (9%),[42,49,53,61,79,89,96,103] and placenta accreta spectrum (PAS) in 2 (2%).[56,126] Eleven (12%) studies did not report the causes of PPH for which a UBT device was used.[45,51,70,75,77,91,104,110,114,118,129] The remaining 47 (52%) studies reported the use of UBT for the management of multiple causes of PPH, such as uterine atony, placenta previa, PAS, retained products of conception, coagulopathy, and trauma, among others.

Risk of bias

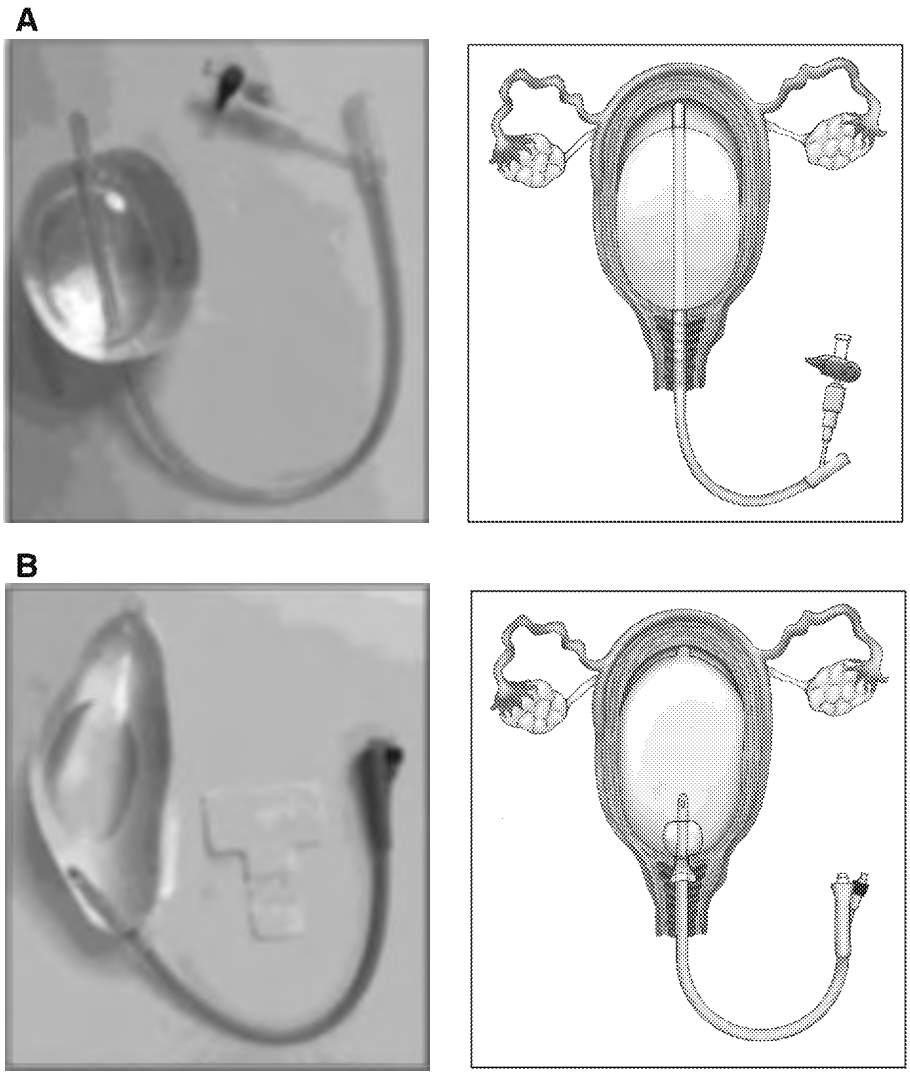
Randomized controlled trials

The risk of bias in each included RCT is shown in Supplementary Table 2 (Appendix). Only 1 RCT fulfilled at least 6 of the 7 criteria for "low" risk of bias.[44] All but 1 RCT[42] had an adequate generation of allocation sequence. Concealment of allocation was adequate in 3 studies and unclear in the remaining 3. Blinding healthcare providers and women in whom UBT devices were placed was not possible. However, because most outcomes were objectively measured, the included RCTs were considered at "low" risk of bias despite lack of outcomes assessment blinding. Among the 4 RCTs that reported estimated blood loss,[41–43,45] 1 assessed it visually,[43] 2 used objective methods,[42,45] and the 1 remaining[41] did not report the method used. One RCT[40] was at "high" risk of performance bias because UBTs were placed

in 19 (16%) women in the control group due to persistent hemorrhage. Movement of participants from the control group to the intervention group (UBT) may have reduced the observed difference between groups, leading to the estimated effect of being biased toward the null. In a study[41] that was stopped early, the treatment effect may have been overestimated and the data on safety and subgroup treatment effects less robust than reported.

The study by Dumont et al[43] had multiple methodological concerns that were likely to favor the control group, implying a decrease in the effect estimate of the UBT device. First, PPH was not measured objectively, as stated in the protocol, but instead was measured through visual estimation of blood loss and patient status. Second, training on UBT use was potentially suboptimal. Despite "frequent turnover of the staff," training sessions occurred every 11–16 months in each participating center with a duration of only half a day. Third, at randomization, there was imbalance between the treatment groups in estimated blood loss ≥1000 mL (42% in the UBT group vs 26% in the control group). This baseline variable is strongly related with the outcome measures and its imbalance likely caused bias in the intervention effect estimate. In addition, women in the UBT group had a higher frequency of manual removal of placenta than women in the control group (19% and 10%, respectively). Overall, women in the UBT group had more severe PPH before randomization than women in the control group. Fourth, misoprostol was not administered within 30 minutes of PPH diagnosis in 54% of women in the UBT group vs 37% in the control group. This implies that second-line uterotonics were administered late more frequently in the UBT group than in the control group. Finally, UBT devices were inserted within 30 minutes of PPH diagnosis in only 58% of women, and 4 of the 57 women allocated to the UBT group did not receive the intervention. Overall, there were significant problems in adherence to the intervention in the UBT group as prespecified in the trial protocol, which could have affected the outcomes.

FIGURE 2
Most-used uterine balloon tamponade devices: A, Bakri balloon; B, condom catheter



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Nonrandomized studies

Of 15 nonrandomized studies, 12 were rated as "critical" risk of bias, 2 as "serious" risk of bias, and 1 as "moderate" risk of bias (Appendix: Supplementary Table 3). The bias was mainly caused by lack of identification of and adjustment for confounding variables at baseline and during intervention. Five studies had "serious" risk of bias in classification of interventions, whereas the risk of bias in selection of participants into the study was "serious" in 3 studies. All studies were at "low" risk of bias due to missing data and in measurement of outcomes. Most studies were at "moderate" risk of bias in selection of reported results.

Case series

Among case series, 34 (49%) fulfilled ≥5 "low" risk criteria for bias, whereas the remaining 35 (51%) fulfilled ≤4 "low" risk criteria (Appendix: Supplementary Table 4). The most common shortcomings were related to patient selection, reporting, and

TABLE 1
Meta-analysis of success rate for uterine balloon tamponade according to study design, mode of delivery, and cause of postpartum hemorrhage

Cause of postpartum hemorrhage	Randomized controlled trials			Nonrandomized studies			Case series			Overall		
	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)
Vaginal birth												
Uterine atony	3	243	92.8 (75.4–99.9)	3	96	85.5 (77.9–91.7)	9	337	86.8 (78.1–93.5)	15	676	88.1 (81.7–93.3)
Undifferentiated	2	170	81.8 (71.2–90.4)	1	48	97.9 (93.9–100.0)	41	974	86.2 (82.7–89.3)	44	1192	86.3 (83.0–89.3)
Total[a]	5	413	89.0 (75.7–97.5)	4	144	89.6 (81.1–95.7)	48	1311	86.6 (83.4–89.4)	57	1868	87.1 (84.1–89.8)
Cesarean delivery												
Uterine atony	1	25	80.0 (64.3–95.7)	3	72	77.1 (66.9–85.8)	4	18	70.0 (32.1–95.5)	8	115	75.2 (63.4–85.4)
Placenta previa	1	7	100.0 (56.1–100.0)	3	121	88.7 (67.7–99.4)	5	159	86.2 (76.6–93.6)	9	287	88.3 (80.2–94.5)
Placenta accreta spectrum	-	-	-	2	46	52.5 (4.0–97.7)	2	26	88.7 (70.3–98.8)	4	72	74.8 (49.0–93.6)
Undifferentiated	-	-	-	1	12	100.0 (69.9–100.0)	39	1077	80.3 (75.4–84.8)	40	1089	80.9 (76.1–85.3)
Total[a]	2	32	87.2 (63.6–99.3)	8	251	83.6 (75.2–90.5)	49	1280	81.0 (76.7–84.9)	59	1563	81.7 (78.0–85.1)
Unknown mode of delivery												
Uterine atony	-	-	-	3	133	87.3 (80.4–93.0)	8	725	92.4 (85.5–97.2)	11	858	90.9 (85.4–95.2)
Placenta previa	-	-	-	2	44	89.8 (48.1–97.7)	4	99	84.6 (66.7–96.4)	6	143	87.0 (71.0–97.2)
Undifferentiated	-	-	-	2	88	83.0 (62.7–96.3)	10	209	80.8 (73.6–87.1)	12	297	81.3 (74.9–86.9)
Total[a]	-	-	-	4	265	86.0 (81.7–89.9)	14	1033	87.1 (81.9–91.5)	18	1298	86.7 (82.8–90.2)
Overall[b]												
Uterine atony	4	268	90.2 (74.1–98.9)	8	301	84.5 (79.9-88.6)	43	1942	87.3 (83.9–90.3)	55	2511	87.1 (84.1–89.9)
Placenta previa	1	7	100.0 (56.1–100.0)	5	165	89.3 (73.8-98.4)	32	516	85.6 (81.1–89.9)	38	688	86.8 (82.3–90.6)
Placenta accreta spectrum	-	-	-	3	74	75.1 (32.9-99.3)	10	69	64.1 (48.0–78.7)	13	143	66.7 (49.4–81.9)
Retained placenta	-	-	-	-	-	-	13	82	76.8 (65.3–86.5)	13	82	76.8 (65.3–86.5)
Undifferentiated	2	170	81.8 (71.2–90.4)	3	120	82.1 (46.6-99.7)	41	1015	82.9 (78.5–86.9)	46	1305	82.8 (78.4–86.8)
Total[a]	7	445	88.8 (77.7–96.4)	14	660	85.2 (80.5-89.4)	769	3624	85.7 (83.4–87.9)	90	4729	85.9 (83.9–87.9)

CI, confidence interval; *UBT*, uterine balloon tamponade.

[a] Total number of studies does not represent the sum of individual causes of postpartum hemorrhage given multiple causes of postpartum hemorrhage reported across studies; [b] Total number of studies and women does not represent the sum of individual causes of postpartum hemorrhage. Although some studies reported mode of delivery, they did not report results for cause of postpartum hemorrhage according to mode of delivery.

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exclusion of alternative causes for observed outcomes.

Efficacy of uterine balloon tamponade

Success rate of uterine balloon tamponade

Among the 90 studies that reported efficacy data, the overall pooled UBT success rate was 85.9% (95% CI, 83.9–87.9%) (Table 1). The highest pooled UBT success rates corresponded to cases of PPH due to uterine atony (87.1%; 95% CI, 84.1–89.9%) and placenta previa (86.8%; 95% CI, 82.3–90.6%), whereas the lowest corresponded to PAS (66.7%; 95% CI, 49.4–81.9%) and retained products of conception (76.8%; 95% CI, 65.3–86.5%). The pooled UBT success rate from all causes of PPH was slightly higher in vaginal deliveries (87.1%; 95% CI, 84.1–89.8%) than in cesarean deliveries (81.7%; 95% CI, 78.0–85.1%). The pooled success rates of UBT in PPH due to uterine atony was higher in vaginal deliveries (88.1%; 95% CI, 81.7–93.3%) than in cesarean deliveries (75.2%; 95% CI, 63.4–85.4%). There were no substantial differences among the pooled UBT success rates for all causes of PPH estimated from RCTs (88.8%), nonrandomized studies (85.2%), and case series (85.7%).

Of the 42 unobtainable articles or case series published only in abstract form, data from 36 were available to perform a sensitivity analysis, which showed a similar pooled UBT success rate (85.8%; 95% CI, 84.0–87.5%; n = 6489) to that obtained in the primary analysis (Appendix: Supplementary Table 5). A sensitivity analysis of UBT success rates stratified by risk of bias among case series showed little difference between studies at "low" risk of bias in ≥5 explanatory questions (85.6%; 95% CI, 82.1–88.7%) and those at "low" risk of bias in <5 explanatory questions (86.0%; 95% CI, 82.8–88.9%) (Appendix: Supplementary Table 6). Given the low number of RCTs and the high risk of bias in the nonrandomized studies, a sensitivity analysis according to risk of bias was not performed for these studies.

A subgroup analysis showed that the pooled UBT success rate for treating all causes of PPH was greater among women treated with a condom UBT (90.4%; 95% CI, 87.7–92.8%) than among women treated with a Bakri balloon (83.2%; 95% CI, 80.5–85.8%) (Appendix: Supplementary Table 7). Similar results were obtained in a subgroup analysis that included only women with PPH due to uterine atony (Appendix: Supplementary Table 8). The only RCT[44] that compared Bakri balloon with condom UBT in women with PPH due to uterine atony after vaginal delivery (n = 66) did not show a significant difference in the success rate between study groups (91.0% for Bakri balloon vs 84.8% for condom UBT; $P = .20$). A further subgroup analysis stratified by country income levels showed a pooled success rate of 90.4% (95% CI, 87.7–92.8%) for condom UBT in LMICs (Appendix: Supplementary Table 9). The pooled UBT success rates among women treated with Bakri balloon in HICs and LMICs for all causes of PPH were 80.8% (95% CI, 77.6–83.9%) and 86.4% (95% CI, 82.4–89.9%), respectively.

Uterine balloon tamponade vs no uterine balloon tamponade in postpartum hemorrhage due to uterine atony after vaginal delivery

We identified 1 retrospective nonrandomized study that compared use of UBT plus standard care (n = 35) vs standard care alone (n = 49) in women with PPH due to uterine atony after vaginal delivery.[57] Use of UBT was associated with a significant decrease in mean blood loss (759 ± 29 mL vs 1582 ± 107 mL; MD, -823 mL, 95% CI, -792 to -854 mL), surgical interventions (14% vs 63%; RR, 0.23, 95% CI, 0.10–0.52), and blood transfusions (11% vs 65%; RR, 0.18, 95% CI, 0.07–0.45) (very low-quality evidence for all).

Two RCTs compared UBT vs no UBT for treatment of PPH due to uterine atony after vaginal delivery.[40,43] One RCT,[40] conducted in Egypt, reported that use of UBT was associated with significant reductions in blood transfusions and intensive care unit length of stay, and increased hemoglobin and hematocrit at discharge. Moreover, this RCT reported a nonsignificant decrease in the frequency of surgical interventions associated with use of UBT. The other RCT[43] was conducted in Benin and Mali and reported that use of UBT was associated with a significant increase in the risk of PPH >1000 mL and a nonsignificant increase in the risk of maternal death and/or surgical interventions. Table 2 shows a meta-analysis of the 2 studies. Overall, there were no significant differences between the UBT and no-UBT groups in the risk of maternal death and/or surgical interventions (RR, 0.59; 95% CI, 0.02–16.69), maternal death (RR, 6.21; 95% CI, 0.77–49.98), hysterectomy (RR, 0.90; 95% CI, 0.03–24.76), uterine compressive sutures (RR, 1.02; 95% CI, 0.04–24.71), and artery ligation (RR, 0.84; 95% CI, 0.25–2.83) (very low-quality evidence for all).

Uterine balloon tamponade vs no uterine balloon tamponade in postpartum hemorrhage due to placenta previa during cesarean delivery

Three nonrandomized studies conducted in Saudi Arabia[49,53] and Egypt[56] compared use of UBT vs no UBT in women with PPH secondary to placenta previa during cesarean delivery. A meta-analysis of the 3 studies showed that use of UBT was associated with a significant reduction in surgical interventions (RR, 0.44; 95% CI, 0.28–0.71; low-quality evidence), hysterectomy (RR, 0.34; 95% CI, 0.12–0.96; low-quality evidence), mean blood loss (MD, -321 mL; 95% CI, -188 to -454 mL), and mean length of hospital stay (MD, -0.9 days; 95% CI, -0.6 to -1.2 days) (Table 3).

TABLE 2
Meta-analysis of randomized controlled trials of uterine balloon tamponade vs no uterine balloon tamponade in postpartum hemorrhage due to uterine atony after vaginal delivery

Outcome	No. of trials	UBT	No UBT	RR or MD (95% CI)	*P* value	I^2, %
Primary outcome						
Maternal death and/or surgical[a] or radiological[b] interventions	2[40,43]	9/177 (5.1%)	9/179 (5.0%)	0.59 (0.02−16.69)	.76	79
Secondary outcomes						
Surgical interventions[a]	1[40]	0/120 (0.0%)	5/120 (4.2%)	0.09 (0.01−1.63)	.10	NA
Maternal death	2[40,43]	6/177 (3.4%)	1/179 (0.6%)	6.21 (0.77−49.98)	.09	NA
Hysterectomy	2[40,43]	4/177 (2.3%)	4/179 (2.2%)	0.90 (0.03−24.76)	.95	70
Uterine compressive sutures	2[40,43]	2/177 (1.1%)	2/179 (1.1%)	1.02 (0.04−24.71)	.99	55
Artery ligation	2[40,43]	4/177 (2.3%)	5/179 (2.8%)	0.84 (0.25−2.83)	.78	24
Blood loss >1000 mL	1[43]	43/54 (79.6%)	31/59 (52.5%)	1.52 (1.15−2.00)	.003	NA
Blood transfusion	1[43]	23/57 (40.4%)	16/59 (27.1%)	1.49 (0.88−2.51)	.14	NA
Admission to ICU	1[43]	10/57 (17.5%)	8/59 (13.6%)	1.29 (0.55−3.04)	.56	NA
Mean stay in ICU (days)	1[40]	1.0 (0.5) 120	1.5 (0.5) 120	-0.50 (-0.63, -0.37)	<.00001	NA
Mean hemoglobin at discharge (g/dL)	1[40]	9.7 (0.2) 120	8.78 (1.6) 120	0.92 (0.63, 1.21)	<.00001	NA
Mean hematocrit at discharge (%)	1[40]	29.0 (0.7) 120	26.7 (4.5) 120	2.30 (1.49, 3.11)	<0.00001	NA

Data are n/N or mean (standard deviation) N.

CI, confidence interval; *ICU*, intensive care unit; *MD*, mean difference; *NA*, not applicable; *RR*, relative risk; *UBT*, uterine balloon tamponade.

[a] Artery ligation, uterine compression sutures, or hysterectomy; [b] Arterial embolization.

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Effectiveness of uterine balloon tamponade

Nonrandomized before-and-after studies on the impact of introducing uterine balloon tamponade for managing severe postpartum hemorrhage

Two nonrandomized before-and-after studies assessed the impact of UBT introduction into protocols for management of severe PPH in obstetrics units of 2 French hospitals.[47,51] Both studies compared outcomes of all patients with PPH who were unresponsive to prostaglandins before and after the introduction of a UBT protocol. A meta-analysis of the 2 studies showed that the rate of arterial embolization significantly decreased after introduction of UBT (1.9% after UBT vs 6.3% before UBT; RR, 0.29; 95% CI, 0.14−0.63; low-quality evidence) (Table 4). The introduction of UBT was also associated with a nonsignificant reduction in the use of surgical or radiological interventions (8.0% after UBT vs 16.2% before UBT; RR, 0.41; 95% CI, 0.15−1.10), artery ligation or uterine compressive sutures (6.0% after UBT vs 9.9% before UBT; RR, 0.43; 95% CI, 0.09−2.07), and hysterectomy (1.0% after UBT vs 2.2% before UBT; RR, 0.47; 95% CI, 0.08−2.70) (very low-quality evidence for all). In the largest study,[47] the use of surgical or radiological interventions significantly decreased after introduction of UBT among women who delivered vaginally (4.1% after UBT vs 14.4% before UBT; RR, 0.29; 95% CI, 0.14−10.59) but not among women who delivered by cesarean section (15.8% after UBT vs 13.5% before UBT; RR, 1.17; 95% CI, 0.64−2.15).

Nonrandomized cluster studies comparing use of uterine balloon tamponade vs nonuse of uterine balloon tamponade

One population-based retrospective study conducted in France compared the rates of invasive procedures (artery ligation, arterial embolization, and hysterectomy) for hemorrhage control between a perinatal network (10 maternity units) that routinely used UBT and another perinatal network (9 maternity units) that did not use UBT in the management of PPH.[54] During the study period, 35,133 women delivered in the perinatal network that used UBT and 37,396 in the network that did not use UBT. The rate of women that underwent at least 1 invasive procedure was significantly lower in the perinatal network that routinely used UBT than in the network that did not use UBT (3.0 per 1000 vs 5.1 per 1000; RR, 0.60; 95% CI, 0.47−0.76); $P < .0001$; moderate-quality evidence). After adjustment for potential confounding factors, the risk of an invasive procedure among women with PPH who delivered vaginally remained significantly lower in the network that routinely used UBT (adjusted odds ratio, 0.14; 95%

TABLE 3
Meta-analysis of nonrandomized studies of uterine balloon tamponade vs no uterine balloon tamponade in postpartum hemorrhage due to placenta previa during cesarean delivery

Outcome	No. of trials	UBT	No UBT	RR or MD (95% CI)	*P* value	I^2, %
Primary outcome						
Maternal death and/or surgical[a] or radiological[b] interventions	3[48,53,56]	20/125 (16.0%)	57/229 (24.9%)	0.44 (0.28–0.71)	.0006	0
Secondary outcomes						
Surgical[a] interventions	3[48,53,56]	20/125 (16.0%)	56/229 (24.4%)	0.44 (0.28–0.71)	.0007	0
Maternal death	3[48,53,56]	0/125 (0.0%)	1/229 (0.4%)	3.62 (0.15–84.75)	.42	NA
Hysterectomy	3[48,53,56]	4/125 (3.2%)	25/229 (10.9%)	0.34 (0.12–0.96)	.04	0
Uterine compressive sutures	2[48,53]	8/85 (9.4%)	13/191 (6.8%)	0.74 (0.29–1.88)	.52	0
Artery ligation	2[53,56]	13/112 (11.6%)	20/78 (25.6%)	0.61 (0.21–1.83)	.38	45
Mean blood loss (mL)	2[53,56]	112	78	-321 (-454, -188)	<.00001	0
Blood transfusion	3[48,53,56]	59/125 (47.2%)	199/229 (86.9%)	0.82 (0.51–1.32)	.41	88
Admission to ICU	3[48,53,56]	24/125 (19.2%)	169/229 (73.8%)	0.62 (0.12–3.07)	.55	93
Mean hospital stay (days)	2[53,56]	112	78	-0.90 (-1.23, -0.57)	<.00001	24
Mean postoperative hemoglobin (g/dL)	2[53,56]	112	78	0.13 (-0.11, 0.37)	.30	38

Data are n/N or total number.

CI, confidence interval; *ICU*, intensive care unit; *MD*, mean difference; *NA*, not applicable; *RR*, relative risk; *UBT*, uterine balloon tamponade.

[a] Artery ligation, uterine compression sutures, or hysterectomy; [b] Arterial embolization.

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CI, 0.08–0.27); it did not significantly differ among women who delivered by cesarean section.

Cluster randomized controlled trials on the impact of introducing uterine balloon tamponade for managing severe postpartum hemorrhage

We identified a stepped-wedge cluster RCT that assessed the effectiveness of condom-catheter UBT introduction for treatment of refractory PPH after vaginal delivery in 18 secondary-level hospitals located in Uganda, Egypt, and Senegal.[46] There were 28,183 and 31,928 deliveries in the control (before UBT introduction) and intervention (after UBT introduction) periods, respectively. UBT was used for 9 of 1357 women and 55 of 1037 women diagnosed with PPH in control and intervention periods, respectively. UBT introduction was associated with a significant increase in the composite outcome of PPH-related invasive procedures and/or maternal death (6.7/10,000 deliveries in the control period vs 11.6/10,000 deliveries in the intervention period). The unadjusted and adjusted incident rate ratios were 1.72 (95% CI, 0.99–2.99) and 4.08 (95% CI, 1.07–15.58), respectively (low-quality evidence). However, the increase in the composite endpoint was not statistically significant in sensitivity analyses excluding outlier hospitals, restricting analyses to outcomes associated with PPH due to uterine atony, and adjusting for interaction of temporal trends by site or country. Several reasons could explain the lack of beneficial effects of introducing UBT reported in this study. First, after introduction of UBT, only a small fraction (5.3%) of women diagnosed with PPH received a UBT device for treatment of PPH. Second, 29 of 37 women (78.4%) who had PPH-related surgery or maternal death in the intervention period did not receive UBT. Third, only 50% of UBT devices were inserted within 30 minutes of PPH diagnosis (range, 0–510 minutes). Fourth, providers had a problem with UBT use in 52% of women and reported blood shortage for almost half of PPH-related deaths. Finally, 66.7% of women with PPH-related invasive surgery or death had PPH complicated by causes other than uterine atony for which UBT is less efficacious. According to the study authors, the outcomes observed after UBT introduction may be partly explained by temporal trends and outlier sites.

Safety of uterine balloon tamponade

Short-term follow-up

Thirty-nine of 90 included studies (43%) reported on complications related to use of UBT. Seven studies reported a total of 29 cases of fever or infection after the placement of a UBT device among 445 women (6.5%).[44,79,81,99,106,109,117] Three studies reported a total of 7 cases of endometritis attributed to the use of UBT among 308 women (2.3%).[47,59,115] Other reported complications included cervical tears (2 among 120 women; 1.7%),[49] acute colonic pseudo-obstruction (1 among 49 women;

TABLE 4
Meta-analysis of nonrandomized before-and-after studies on the effect of introducing uterine balloon tamponade in the management of women with severe postpartum hemorrhage who received prostaglandins

Outcome	No. of trials	After introducing UBT	Before introducing UBT	RR (95% CI)	*P* value	I^2, %
Primary outcome						
Maternal death and/or surgical[a] or radiological[b] interventions	2[47,51]	39/486 (8.0%)	59/364 (16.2%)	0.41 (0.15–1.10)	.08	77
Secondary outcomes						
Surgical[a] or radiological[b] interventions	2[47,51]	39/486 (8.0%)	59/364 (16.2%)	0.41 (0.15–1.10)	.08	77
Artery ligation or uterine compressive sutures	2[47,51]	29/486 (6.0%)	36/364 (9.9%)	0.43 (0.09–2.07)	.29	83
Maternal death	2[47,51]	0/486 (0.0%)	0/364 (0.0%)	Not estimable	NA	NA
Hysterectomy	2[47,51]	5/486 (1.0%)	8/364 (2.2%)	0.47 (0.08–2.70)	.40	47
Arterial embolization	2[47,51]	9/486 (1.9%)	23/364 (6.3%)	0.29 (0.14–0.63)	.002	0
Artery ligation	1[51]	4/91 (4.4%)	12/74 (16.2%)	0.27 (0.09–0.81)	.02	NA
Uterine compressive sutures	1[51]	1/91 (1.1%)	7/74 (9.5%)	0.12 (0.01–0.92)	.04	NA
Blood transfusion	2[47,51]	80/486 (16.5%)	50/364 (13.7%)	1.23 (0.90–1.68)	.19	0
Decrease in hemoglobin ≥2 g/dL	1[47]	194/395 (49.1%)	183/290 (63.1%)	0.78 (0.68–0.89)	.0002	NA

Data are n/N.

CI, confidence interval; *ICU*, intensive care unit; *NA*, not applicable; *RR*, relative risk; *UBT*, uterine balloon tamponade.

[a] Artery ligation, uterine compression sutures, or hysterectomy; [b] Arterial embolization.

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2.0%),[99] laceration of the lower segment of the vagina (1 among 21 women; 4.8%),[48] uterine incision rupture (1 among 53 women; 1.9%),[96] and uterine perforation (1 among 49 women; 2.0%).[124] The remaining 25 studies reported no complications attributed to the use of UBT.

Long-term follow-up

Four studies reported on potential long-term consequences associated with use of UBT.[92,99,102,129] A retrospective cohort study followed 200 women with severe PPH, of which 39 received a Bakri balloon and 161 did not.[129] Most women (87%) in the UBT group had normal menstrual patterns in the 12 months after the index delivery as well as in the most recent 12 months. After exclusion of patients using contraception, the subsequent pregnancy rate was 43% (9/21) in the UBT group compared to 46% (28/61) in the control group ($P = .81$). There were no significant differences in subsequent live birth rates, return of menses, cycle regularity, duration of flow, amount of flow, or presence of dysmenorrhea between the study groups.

A second study followed 31 women who had been treated for PPH with a Rusch balloon to evaluate the subsequent fertility and pregnancy rate.[92] Follow-up visits ranged between 4 and 108 months. Seven women (23%) became pregnant again, of which 4 delivered at term without complications, 2 had early abortions, and 1 had an ectopic pregnancy. Among the 24 women who did not get pregnant again, only 1 had difficulty conceiving.

A third study evaluated the impact of using Bakri balloons on subsequent fertility outcomes at 6 or more months follow-up visits.[99] Among 24 women contacted by phone, 2 considered their menses shorter and lighter and 2 became pregnant soon after their previous delivery, giving birth to healthy babies.

A fourth study assessed fertility after Bakri balloon use for treatment of PPH in 38 women.[102] Nine women expressed a desire for pregnancy and became pregnant again after an average of 23 months (standard deviation, 8 months). Three women delivered healthy newborns, 4 remained pregnant at the time of study publication, 1 voluntarily terminated her pregnancy, and 1 had an ectopic pregnancy.

Comment

Main findings

Our study indicates that UBT has a high success rate to treat PPH, with an overall pooled estimate of 85.9%. Subgroup analyses suggest that (1) UBT has a higher success rate in women with PPH due to uterine atony and placenta previa than in women with PPH due to PAS or retained products of conception; (2) UBT has a higher success rate in women with PPH after vaginal delivery than in women with PPH after cesarean delivery; (3) UBT has a higher success rate in women with PPH resulting from uterine atony after vaginal delivery than in women with PPH resulting from uterine atony after cesarean delivery; (4) condom UBT success rates are at least as comparable as Bakri balloon success rates; and (5) the evidence on UBT efficacy and effectiveness from randomized

and nonrandomized studies is conflicting, with experimental studies suggesting no beneficial effect, in contrast with observational studies.

There is some conflicting evidence regarding the efficacy of UBT to reduce surgical interventions or maternal deaths among women with severe PPH due to uterine atony. A small nonrandomized study[37] and 1 RCT[40] showed beneficial effects of UBT, whereas another RCT[43] suggested that UBT could be harmful. Evidence from nonrandomized studies[49,53,56] suggests that UBT is more efficacious than nonuse of UBT in reduction of surgical interventions among women with PPH due to placenta previa after cesarean delivery. Evidence from 2 nonrandomized before-and-after studies[47,51] and 1 large, methodologically sound nonrandomized cluster study[54] strongly suggests that introduction of UBT in protocols for the management of PPH among obstetric units in HICs is effective in reducing PPH-associated surgical interventions and arterial embolization after vaginal delivery. However, a stepped wedge cluster RCT[46] reported that introduction of condom-catheter UBT in secondary-level hospitals in 3 African countries may have increased the risk of PPH-related maternal deaths and invasive procedures. Additionally, UBT appears safe and possesses few adverse effects on subsequent menstrual and reproductive function.

Overall, it appeared that condom UBTs had higher success rates than Bakri balloon in management of PPH. A possible explanation is that in resource-limited settings, birth attendants may invoke use of UBT earlier, as UBT may often be the only available option. In high-resource settings, where there are no studies on condom UBTs, there are more human resources and more treatment options, but PPH may be more complex or severe when a UBT device is used. There is strong evidence suggesting that a prolonged time between onset of hemorrhage and placement of UBT results in worse outcomes.[115,118,120] Another potential explanation for the observed difference in outcomes between condom and Bakri UBTs is that women in HICs may undergo UBT device placement as an interim measure before embolization or other procedures. These cases were considered treatment failures in this systematic review. Regardless of setting, the success rate of UBT was >80%. It is noteworthy that success rates of Bakri balloon and condom UBT were similar in LMICs (86.4% vs 90.4%). This suggests that condom UBTs are at least as efficacious as Bakri balloon and that success rates may be more dependent on setting than on the device.

The findings of this systematic review reveal a discrepancy between nonrandomized studies and RCTs on the efficacy and effectiveness of UBT in the treatment of severe PPH. UBT success rates were consistently high across all study types. However, 2 randomized studies concluded there is no benefit to introduction of UBT in management of refractory PPH, despite reporting high success rates in the intervention arms.[43,46] One of these studies[43] was not truly an efficacy trial but an effectiveness trial of programmatic implementation of UBT for the treatment of PPH. This study[43] had multiple methodological concerns that likely favored the control group, implying a high risk of bias toward erroneous results. However, the weaknesses of this effectiveness trial remind us of the importance of future research on implementation strategies that lead to desired uptake and optimal performance of interventions designed to improve maternal outcomes. Examples of future recommended strategies include more frequent and higher quality training, improved appropriate use of uterotonics, scale of tranexamic acid, earlier identification of PPH, systematization of PPH emergency care, and reduction in the time between diagnosis of PPH and placement of a UBT device. Finally, conclusions about efficacy of UBT devices should not be based on an effectiveness trial that did not use UBT consistently.

Strengths and limitations

The main strengths of this study include the following: (1) use of rigorous methodology for performing the systematic review and meta-analysis; (2) use of a prospective protocol designed to address a specific research question; (3) assessment of UBT's efficacy, safety, and effectiveness; (4) inclusion of RCTs, nonrandomized studies, and case series to estimate pooled success rates for UBT; (5) comprehensive literature search without language restrictions; (6) strict risk of bias assessment; (7) performance of subgroup analyses according to study design, mode of delivery, cause of PPH, and country income level; (8) comparison of success rates between Bakri balloon and condom UBT; and (8) inclusion of a relatively large number of studies, most of which were recently published.

Several potential limitations of our review must be considered. First, it is limited by the quality of the original data. Most RCTs and nonrandomized studies were considered to be at "high" risk of bias, whereas only half of case series met at least 5 methodological criteria for "low" risk of bias. Thus, the findings should be interpreted with some caution. However, a sensitivity analysis among case series showed only slight differences in success rate between studies that fulfilled at least 5 criteria and those that fulfilled fewer than 5 criteria for "low" risk of bias. Second, we excluded 42 studies that were published as abstracts only or unobtainable. Nevertheless, a sensitivity analysis that included data from abstracts of studies published only in abstract form or unobtainable articles showed that pooled UBT success rates were similar to those obtained in the primary analysis. Third, the limited number of RCTs and nonrandomized studies that assessed efficacy of UBT in the treatment of uterine atony did not allow us to provide conclusive evidence on this topic. Nevertheless, evidence from 3 large nonrandomized studies (2 before-and-after studies[47,51] and 1 cluster nonrandomized study[54]) at low risk of bias strongly suggests that introduction of UBT for managing severe PPH due to uterine atony is effective in reducing use of surgical and radiological interventions. Fourth, underlying causes of PPH might have been difficult to identify in the original

studies because distinction among them is not always easy and some underlying disorders can overlap in the same patient. Finally, most studies did not report safety outcomes, which increases the likelihood of reporting bias. However, the best available evidence suggests that UBT appears to be safe in the treatment of PPH.

To date, this is the most comprehensive systematic review and meta-analysis on the efficacy, effectiveness, and safety of UBT for the treatment of severe PPH. The consistency of study results on the use of UBT indicates that these devices have a high success rate for treating PPH and appear safe. It is not surprising that emergency interventions with high success rates, such as UBT for PPH, fall short of improving outcomes when implementation programs do not adequately integrate interventions into systems of emergency care. There is an urgent need for high-quality studies that help identify strategies that optimize provider and health system performance in delivery of all emergency care interventions among women with PPH.

Conclusions

There is persuasive evidence that UBT devices have a high success rate for arresting bleeding among women with severe PPH unresponsive to uterotonics and initial therapies. In addition, most evidence suggests that use of UBT is associated with a significant reduction in the rate of PPH-related invasive procedures such as artery ligation, uterine compression sutures, hysterectomy, and arterial embolization. The evidence on UBT efficacy and effectiveness from randomized and nonrandomized studies is conflicting, with experimental studies suggesting no beneficial effect, in contrast with observational studies. To optimize maternal outcomes, high-quality implementation research is needed to determine the most effective programmatic and healthcare delivery strategies on UBT introduction and use. ▩

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Author and article information

From the Division of Global Health Innovation, Department of Emergency Medicine, Massachusetts General Hospital, Boston, Massachusetts (Drs Suarez, Borovac-Pinheiro, Suarez-Rebling, Eckardt, and Burke); Department of Internal Medicine, Boston Medical Center, Boston, Massachusetts (Dr Suarez); Perinatology Research Branch, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development/National Institutes of Health/Department of Health and Human Services, Bethesda, Maryland, and Detroit, Michigan (Dr Conde-Agudelo); Department of Obstetrics and Gynecology, School of Medical Sciences, University of Campinas, Campinas (SP), Brazil (Dr Borovac-Pinheiro); Department of Obstetrics and Gynecology, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa (Dr Theron); Harvard Medical School, Boston, Massachusetts (Dr Burke); and Harvard T.H. Chan School of Public Health, Boston, Massachusetts (Dr Burke).

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Correspondence: Sebastian Suarez, MD, MPH. ses516@mail.harvard.edu

Appendix

I. Search Strategy

PubMed

Search	Search query
#1	Search "Uterine Balloon Tamponade"[mesh]
#2	Search ("uterus"[mesh] OR "Uterus"[title/abstract] OR "uterine"[title/abstract] OR "intrauterine"[title/abstract] OR "intra uterine"[title/abstract]) AND (Bakri[title/abstract] OR Belfort Dildy[title/abstract] OR BT Cath[title/abstract] OR ebb balloon [title/abstract] OR ebb balloons[title/abstract] OR ebb tamponade[title/abstract] OR el menia[title/abstract] OR Rusch[title/ abstract] OR Sengstaken Blakemore[title/abstract])
#3	Search ("uterus"[mesh] OR "Uterus"[title/abstract] OR "uterine"[title/abstract] OR "intrauterine"[title/abstract] OR "intra uterine"[title/abstract]) AND "Catheters"[Mesh] AND (foley[title/abstract] OR foley's[title/abstract] OR foleys[title/ abstract])
#4	Search ("uterus"[mesh] OR "Uterus"[title/abstract] OR "uterine"[title/abstract] OR "intrauterine"[title/abstract] OR "intra uterine"[title/abstract]) AND ("foley catheter"[title/abstract] OR "foley's catheter"[title/abstract] OR "foleys catheter"[title/abstract] OR "foley catheters"[title/abstract] OR "foley's catheters"[title/abstract] OR foleys catheters [title/abstract])
#5	Search ("uterus"[mesh] OR "Uterus"[title/abstract] OR "uterine"[title/abstract] OR "intrauterine"[title/abstract] OR "intra uterine"[title/abstract]) AND (balloon[title/abstract] OR balloons[title/abstract] OR tamponade[title/abstract] OR tamponades[title/abstract] OR condom[title/abstract] OR condoms[title/abstract] OR condoms[mesh] OR "Balloon Occlusion"[mesh])
#6	Search ("uterus"[mesh] OR "Uterus"[title/abstract] OR "uterine"[title/abstract] OR "intrauterine"[title/abstract] OR "intra uterine"[title/abstract]) AND (dilatation[title/abstract] OR dilation[title/abstract] OR "fluid filled"[title/abstract] OR gauze [title/abstract] OR hydrostatic[title/abstract] OR packing[title/abstract] OR sponge[title/abstract] OR sponges[title/ abstract] OR Dilatation[mesh] OR "Surgical Sponges"[mesh])
#7	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)
#8	Search (Abruptio Placentae[title/abstract] OR "surgical Blood loss"[title/abstract] OR "Blood Transfusion"[title/abstract] OR Placenta Accreta[title/abstract] OR Placenta Previa[title/abstract] OR Shock[title/abstract] OR "Abruptio Placentae"[mesh] OR "Blood Loss, Surgical"[mesh] OR "Blood Transfusion"[mesh] OR "Maternal Death"[mesh] OR "Maternal Mortality"[mesh] OR "Metrorrhagia"[mesh] OR "Placenta Accreta"[mesh] OR "Placenta Previa"[mesh] OR "Postpartum Hemorrhage"[mesh] OR "Shock, Hemorrhagic"[Mesh:NoExp] OR "Uterine Inertia"[mesh] OR "Uterine Hemorrhage"[mesh])
#9	Search (Mothers[mesh] OR mother[title/abstract] OR mothers[title/abstract] OR Maternal[title/abstract] OR postpartum [title/abstract] OR "post partum"[title/abstract]) AND (death[mesh] OR death[title/abstract] OR mortality[mesh] OR mortality[title/abstract] OR mortality[mesh] OR Mortality[MeSH Subheading])
#10	Search postpartum hemorrhag*[title/abstract] OR postpartum haemorrhag*[title/abstract] OR "post partum" hemorrhag* [title/abstract] OR "post partum" haemorrhag*[title/abstract]
#11	Search ("uterus"[mesh] OR "Uterus"[title/abstract] OR "uterine"[title/abstract]) AND (atony[title/abstract] OR atonic[title/ abstract])
#12	Search ("atonic uterus"[title/abstract]) OR "uterine atony"[title/abstract]) OR "uterine inertia"[title/abstract]
#13	Search (#8 OR #9 OR #10 OR #11 OR #12)
#14	Search (#7 AND #13)

OVID MEDLINE

Search	Search query
#1	Search Uterine Balloon Tamponade.ti,ab,de. or ((uterus adj7 balloon* adj7 tamponade*) or (uterine adj7 balloon* adj7 tamponade*) or (intrauterine adj7 balloon* adj7 tamponade*) or ("intra uterine" adj7 balloon* adj7 tamponade*)).ti,ab.
#2	Search uterus/ or (intrauterine or "intra uterine" or uterine or intrauterine).ti,ab.
#3	Search (Bakri or Belfort Dildy or BT Cath or ebb balloon* or ebb tamponade or "el menia" or Rusch or Sengstaken Blakemore).ti,ab. or (catheter* adj7 foley*).ti,ab,de. or exp Balloon Occlusion/ or (balloon* adj7 occlu*).ti,ab. or (condom* or dilatation or dilation or "fluid filled" or gauze or hydrostatic or packing or sponge*).ti,ab,de.
#4	Search 2 and 3
#5	Search 1 or 4
#6	Search (Abruptio Placentae or Blood Loss Surgical or Blood Transfusion or Maternal Mortality or Maternal Death or Metrorrhagia or Placenta Accreta or Placenta Previa or shock or Postpartum Hemorrhage or Shock Hemorrhagic or Uterine Hemorrhage).ti,ab,de.
#7	Search (Mother* or maternal or "postpartum hemorrhage*" or "post partum hemorrhag*" or "postpartum haemorrhag*" or "post partum hemorrhag*").ti,ab,de. and ((death or mortality).ti,ab,de. or mo.fs.)
#8	Search ((uterus or intrauterine or "intra uterine" or uterine) adj7 (atony or atonic or inertia)).ti,ab. or Uterine Inertia/
#9	Search 5 and (6 or 7 or 8)
#10	Search remove duplicates from 9
#11	Search (10 and humans/) or (10 not animals/)

EMBASE

Search	Search query
#1	Search ('uterine atony'/de OR 'atonic uterus':ti,ab,kw OR 'uterine atony':ti,ab,kw OR 'uterine inertia':ti,ab,kw OR (('uterus'/de OR 'uterus':ti,ab,kw OR 'intra uterine':ti,ab,kw OR 'intrauterine':ti,ab,kw OR 'uterine':ti,ab,kw) AND ('atony':ti,ab,kw OR 'atonic':ti,ab,kw OR 'inertia':ti,ab,kw))
#2	Search ('postpartum hemorrhage'/de OR 'postpartum hemorrhag*':ti,ab,kw OR 'postpartum haemorrhag*':ti,ab,kw OR 'post partum hemorrhag*':ti,ab,kw OR 'post partum haemorrhag*':ti,ab,kw)
#3	Search ('mother'/exp OR 'mother' OR 'mother*':ti,ab,kw OR maternal:ti,ab,kw OR 'puerperium'/exp OR 'puerperium' OR 'postpartum':ti,ab,kw OR 'post partum':ti,ab,kw OR 'puerperium':ti,ab,kw) AND ('death'/exp OR 'death':ti,ab,kw OR 'mortality'/exp OR 'mortality':ti,ab,kw)
#4	Search ('blood transfusion'/exp OR 'dystocia'/exp OR 'maternal death'/exp OR 'solutio placentae'/exp OR 'operative blood loss'/exp OR 'hemorrhagic shock'/exp OR 'maternal mortality'/exp OR 'metrorrhagia'/exp OR 'placenta accreta'/exp OR 'placenta previa'/exp OR 'postpartum hemorrhage'/exp OR 'uterus bleeding'/exp OR 'shock'/exp OR 'abruptio placentae':ti,ab,kw OR 'blood transfusion':ti,ab,kw OR 'hemorrhagic shock':ti,ab,kw OR 'haemorrhagic shock':ti,ab,kw OR 'maternal death':ti,ab,kw OR 'maternal mortality':ti,ab,kw OR 'metrorrhagia':ti,ab,kw OR 'placenta accreta':ti,ab,kw OR 'placenta previa':ti,ab,kw) AND ('postpartum hemorrhage':ti,ab,kw OR 'postpartum haemorrhage':ti,ab,kw OR 'shock':ti,ab,kw OR 'surgical blood loss':ti,ab,kw OR 'uterine hemorrhag*':ti,ab,kw OR 'uterine haemorrhag*':ti,ab,kw OR 'uterine inertia':ti,ab,kw)
#5	Search (#1 OR #2 OR #3 OR #4)
#6	Search ('uterus'/de OR 'uterus':ti,ab,kw OR 'intra uterine':ti,ab,kw OR 'intrauterine':ti,ab,kw OR 'uterine':ti,ab,kw) AND ('dilatation'/exp OR 'gauze'/exp OR 'surgical sponge'/de OR 'dilation':ti,ab,kw OR 'dilatation':ti,ab,kw OR 'fluid filled':ti,ab,kw OR 'gauze':ti,ab,kw OR 'hydrostatic':ti,ab,kw OR 'packing':ti,ab,kw OR 'surgical sponge*':ti,ab,kw)
#7	Search ('uterus'/de OR 'uterus':ti,ab,kw OR 'intra uterine':ti,ab,kw OR 'intrauterine':ti,ab,kw OR 'uterine':ti,ab,kw) AND ('occlusion balloon catheter'/de OR 'condom catheter'/de OR 'balloon*':ti,ab,kw OR tamponade*:ti,ab,kw OR 'condom*':ti,ab,kw OR 'balloon occlusion':ti,ab,kw)
#8	Search ('uterus'/de OR 'uterus':ti,ab,kw OR 'intra uterine':ti,ab,kw OR 'intrauterine':ti,ab,kw OR 'uterine':ti,ab,kw) AND ('foley balloon catheter'/exp OR 'foley*':ti,ab,kw)

(continued)

(continued)

Search	Search query
#9	Search ('uterus'/de OR 'uterus':ti,ab,kw OR 'intra uterine':ti,ab,kw OR 'intrauterine':ti,ab,kw OR 'uterine':ti,ab,kw) AND ('b-t cath':dn,ti,ab,kw OR 'bakri':dn,ti,ab,kw OR 'bakri balloon':dn,ti,ab,kw OR 'bakri balloon tamponade':dn,ti,ab,kw OR 'bakri intrauterine balloon':dn,ti,ab,kw OR 'bakri rusch balloon':dn,ti,ab,kw OR 'bakri tamponade':dn,ti,ab,kw OR 'belfort-dildy':dn,ti,ab,kw OR 'belfort-dildy obstetrical tamponade system':dn,ti,ab,kw OR 'bt-cath':dn,ti,ab,kw OR 'condom catheter':dn,ti,ab,kw OR 'ebb':dn,ti,ab,kw OR 'ebb balloon':dn,ti,ab,kw OR 'ebb device':dn,ti,ab,kw OR 'ebbcomplete tamponade system':dn,ti,ab,kw OR 'postpartum balloon':dn,ti,ab,kw OR 'rusch':dn,ti,ab,kw OR 'sengstaken-blakemore tube':dn,ti,ab,kw OR 'sos bakri':dn,ti,ab,kw)
#10	Search ('uterine balloon'/exp OR 'uterine balloon' OR 'intrauterine balloon'/exp OR 'intrauterine balloon' OR 'uterine balloon':ti,ab,kw OR 'intrauterine balloon':ti,ab,kw OR 'intra uterine balloon':ti,ab,kw)
#11	Search (#6 OR #7 OR #8 OR #9 OR #10)
#12	Search (#5 AND #11)

EBM Reviews — Cochrane Database of Systematic Reviews

ID	Search query
#1	Search (uterus or uterine or "intra uterine" or intrauterine or utero*).ti,ab,kw. and (Bakri or balloon* or Belfort Dildy or BT Cath or condom* or ebb or foley* or foley or "el menia" or occlusion or Rusch or Sengstaken Blakemore or tamponade or gauze or sponge* or fluid filled or hydrostatic or packing).tx.
#2	Search ((mother* or maternal) and (death or mortality)).tx.
#3	Search ((postpartum or "post partum") and (hemorrhag* or haemorrhag* or blood or bleed* or shock)).tx.
#4	Search (inertia or atony or dystocia or abruptio placentae or metrorrhagia or solutio placentae or placenta accreta or placenta previa).tx.
#5	Search 1 and (2 or 3 or 4)

LILACS, IBECS, CUMED, BINACIS, MedCarib, BDENF—Nursing, PAHO

Search	Search query
#1	Search (uterus OR uterine OR intrauterine OR "intra uterine") AND (Balloon$ OR Tamponade$ OR bakri OR belfort dildy OR bt cath OR ebb OR "el menia" OR rusch OR sengstaken blakemore OR foley$ OR condom$ OR gauze OR packing OR sponge$ OR dilatation OR dilation OR "fluid filled" OR hydrostatic)

WOS, BCI, BIOSIS, CABI, CCC, DRCI, DIIDW, KJD, MEDLINE, RSCI, SCIELO, ZOOREC

Search	Search query
#1	Search (TS=(uterus NEAR/7 Balloon NEAR/7 Tamponade) OR TS=(uterine NEAR/7 Balloon NEAR/7 Tamponade) OR TS=(intrauterine NEAR/7 Balloon NEAR/7 Tamponade) OR TS=("intra uterine" NEAR/7 Balloon NEAR/7 Tamponade)
#2	Search TS=(uterus NEAR/7 dilatation) OR TS=(uterine NEAR/7 dilatation) OR TS=(intrauterine NEAR/7 dilatation) OR TS=("intra uterine" NEAR/7 dilatation) OR TS=(uterus NEAR/7 dilation) OR TS=(uterine NEAR/7 dilation) OR TS=(intrauterine NEAR/7 dilation) OR TS=("intra uterine" NEAR/7 dilation) OR TS=(uterus NEAR/7 "fluid filled") OR TS=(uterine NEAR/7 "fluid filled") OR TS=(intrauterine NEAR/7 "fluid filled") OR TS=("intra uterine" NEAR/7 "fluid filled") OR TS=(uterus NEAR/7 gauze) OR TS=(uterine NEAR/7 gauze) OR TS=(intrauterine NEAR/7 gauze) OR TS=("intra uterine" NEAR/7 gauze) OR TS=(uterus NEAR/7 hydrostatic) OR TS=(uterine NEAR/7 hydrostatic) OR TS=(intrauterine NEAR/7 hydrostatic) OR TS=("intra uterine" NEAR/7 hydrostatic) OR TS=(uterus NEAR/7 packing) OR TS=(uterine NEAR/7 packing) OR TS=(intrauterine NEAR/7 packing) OR TS=("intra uterine" NEAR/7 packing) OR TS=(uterus NEAR/7 sponge*) OR TS=(uterine NEAR/7 sponge*) OR TS=(intrauterine NEAR/7 sponge*)OR TS=("intra uterine" NEAR/7 sponge*)
#3	Search TS=(uterus NEAR/7 Bakri) OR TS=(uterine NEAR/7 Bakri) OR TS=(intrauterine NEAR/7 Bakri) OR TS=("intra uterine" NEAR/7 Bakri) OR TS=(uterus NEAR/7 "Belfort Dildy") OR TS=(uterine NEAR/7 "Belfort Dildy") OR TS=(intrauterine NEAR/7 "Belfort Dildy") OR TS=("intra uterine" NEAR/7 "Belfort Dildy") OR TS=(uterus NEAR/7 "BT Cath") OR TS=(uterine NEAR/7 "BT Cath") OR TS=(intrauterine NEAR/7 "BT Cath") OR TS=("intra uterine" NEAR/7 "BT Cath") OR TS=(uterus NEAR/7 ebb) OR TS=(uterine NEAR/7 ebb) OR TS=(intrauterine NEAR/7 ebb) OR TS=("intra uterine" NEAR/7 ebb) OR TS=(uterus NEAR/7 "el menia") OR TS=(uterine NEAR/7 "el menia") OR TS=(intrauterine NEAR/7 "el menia") OR TS=("intra uterine" NEAR/7 "el menia") OR TS=(uterus NEAR/7 Rusch) OR TS=(uterine NEAR/7 Rusch) OR TS=(intrauterine NEAR/7 Rusch) OR TS=("intra uterine" NEAR/7 Rusch) OR TS=(uterus NEAR/7 "Sengstaken Blakemore") OR TS=(uterine NEAR/7 "Sengstaken Blakemore") OR TS=(intrauterine NEAR/7 "Sengstaken Blakemore") OR TS=("intra uterine" NEAR/7 "Sengstaken Blakemore") OR TS=(uterus NEAR/7 foley* NEAR/7 catheter*) OR TS=(uterine NEAR/7 foley* NEAR/7 catheter*) OR TS=(intrauterine NEAR/7 foley* NEAR/7 catheter) OR TS=("intra uterine" NEAR/7 foley* NEAR/7 catheter*) OR TS=(uterus NEAR/7 condom* NEAR/7 catheter*) OR TS=(uterine NEAR/7 condom* NEAR/7 catheter*) OR TS=(intrauterine NEAR/7 condom* NEAR/7 catheter*) OR TS=("intra uterine" NEAR/7 condom* NEAR/7 catheter*) OR TS=(uterus NEAR/7 Balloon* NEAR/7 Occlusion) OR TS=(uterine NEAR/7 Balloon* NEAR/7 Occlusion) OR TS=(intrauterine NEAR/7 Balloon* NEAR/7 Occlusion) OR TS=("intra uterine" NEAR/7 Balloon* NEAR/7 Occlusion)
#4	Search TS=("Abruptio Placentae" OR "Surgical Blood Loss" OR "Blood Transfusion*" OR "Maternal Mortality" OR "Maternal Death*" OR Metrorrhagia OR "Placenta Accreta" OR "Placenta Previa" OR shock OR "Uterine Hemorrhage*" OR "Uterine Haemorrhage*" OR "Postpartum Hemorrhage*" OR "post partum hemorrhag*" OR "postpartum haemorrhag*" OR "post partum hemorrhag*" OR " Uterine Inertia" OR "uterine atony" OR "atonic uterus" OR "inert uterus")
#5	Search (#3 OR #2 OR #1)
#6	Search (#5 AND #4)

POPLINE

Search	Search query
#1	Search (bleeding OR hemorrhage OR haemorrhage OR maternal death OR maternal mortality OR atony OR inertia) AND (ubt OR balloon OR tamponade OR bakri)
#2	Search (bleeding OR hemorrhage OR haemorrhage OR Menorrhagia OR maternal death OR maternal mortality OR atony OR inertia) AND (foley OR gauze OR packing OR sponge)

Google Scholar

Search	Search query
#1	Search (site:.org |site:.edu) AND ("uterine balloon" | "el menia balloon" | "uterine tamponade" |"bakri balloon"| "belfort dildy" |"bt cath" |"ebb balloon" |"rusch balloon" | "sengstaken blakemore")
#2	Search (site:.org |site:.edu) AND ("postpartum hemorrhage"|"postpartum haemorrhage"| Menorrhagia "maternal death"|"maternal mortality"| atony) AND ("foley catheter"| gauze|hydrostatic |"fluid filled"|packing)

WHO

Search	Search query
#1	Search (uterus OR uterine) AND (UBT OR balloon OR tamponade OR bakri OR ebb OR rusch OR sengstaken)

PATH

Search	Search query
#1	Search ubt OR tamponade OR balloon OR bakri OR rusch OR sengstaken

National Library of Medicine's Indexcat

Search	Search query
#1	Search (uterus OR uterine)) AND (tamponade OR balloon)
#2	Search (Keyword:(Hæmorrhage (Uterine, Treatment and prevention of) in pregnancy, labor, and puerperal state))

II. Tools Used for Assessing the Risk of Bias

1. Tool for assessing the risk of bias in randomized controlled trials[34]

Random sequence generation

"Low" risk of bias: Investigators described a random component in the sequence generation process, such as random number table, computer random number generator, shuffling of cards or envelopes, drawing of lots, or computerized minimization.

"High" risk of bias: Investigators described a nonrandom component in the sequence generation process, such as odd or even date of birth, based on date or day of admission, based on hospital or clinical record number, or allocated by judgment of the clinician; preference of the participant; availability of the intervention; or results of laboratory tests.

"Unclear" risk of bias: information insufficient to permit judgment of "low risk" or "high risk."

Allocation concealment

"Low" risk of bias: Investigators used an adequate method to conceal allocation, such as central allocation (including telephone or web-based randomization) or sequentially numbered, opaque, sealed envelopes.

"High" risk of bias: Investigators used a nonadequate method to conceal allocation, such as open random allocation schedule (eg, a list of random numbers), assignment envelopes without appropriate safeguards, alternation or rotation, date of birth, or case record number.

"Unclear" risk of bias: information insufficient to permit judgment of "low risk" or "high risk."

Blinding of participants and personnel

"Low" risk of bias: As insertion of uterine balloon tamponade cannot be blinded to healthcare providers and to most participants, we considered adequate blinding of participants and personnel if review authors judged that the outcome was not likely to be influenced by lack of blinding.

"High" risk of bias: the outcome was likely to be influenced by lack of blinding.

"Unclear" risk of bias: information insufficient to permit judgment of "low risk" or "high risk."

Blinding of outcome assessment

"Low" risk of bias: We considered blinding of outcome assessment to be adequate in either of the following: (1) no blinding of outcome assessment, but review authors judged that outcome measurement was not likely to be influenced by lack of blinding; or (2) blinding of outcome assessment ensured, and unlikely that blinding could have been broken.

"High" risk of bias: either of the following: (1) no blinding of outcome assessment, and outcome measurement was likely to be influenced by lack of blinding; or (2) blinding of outcome assessment, but likely that blinding could have been broken, and that outcome measurement was likely to be influenced by lack of blinding.

"Unclear" risk of bias: information insufficient to permit judgment of "low risk" or "high risk."

Incomplete outcome data

"Low" risk of bias: any 1 of the following: (1) no missing outcome data; (2) reasons for missing outcome data unlikely to be related to true outcome; (3) missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; (4) for dichotomous outcome data, proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; (5) for continuous outcome data, plausible effect size among missing outcomes not enough to have a clinically relevant impact on observed effect size; or (6) missing data imputed by appropriate methods.

"High" risk of bias: any 1 of the following: (1) reasons for missing outcome data likely to be related to true outcome, with imbalance in numbers or reasons for missing data across intervention groups; (2) for dichotomous outcome data, proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; (3) for continuous outcome data, plausible effect size among missing outcomes enough to induce clinically relevant bias impact on observed effect size; (4) "as-treated" analysis done with substantial departure of the intervention received from that assigned at randomization; or (5) potentially inappropriate application of simple imputation.

"Unclear" risk of bias: reporting of attrition/exclusions insufficient to permit judgment of "low risk" or "high risk."

Selective reporting

"Low" risk of bias: any 1 of the following: (1) study protocol was available, and all of the study's prespecified outcomes that were of interest in the review were reported in the prespecified way; or (2) the study protocol was not available, but it was clear that published reports included all expected outcomes, including those that were prespecified.

"High" risk of bias: any 1 of the following: (1) not all of the study's prespecified primary outcomes were reported; (2) 1 or more primary outcomes were reported using measurements, analysis methods, or subsets of data that were not prespecified; (3) 1 or more reported primary outcomes were not prespecified; (4) 1 or more outcomes of interest in the review were reported incompletely, so that they could not be entered into a meta-analysis; or (5) the study report failed to include results for a key outcome that would be expected to have been reported for such a study.

"Unclear" risk of bias: information insufficient to permit judgment of "low risk" or "high risk."

Other bias

"Low" risk of bias: Study appeared to be free of other sources of bias.

"High" risk of bias: At least 1 important risk of bias was present. For example, the study (1) had a potential source of bias related to the specific study design used; or (2) has been claimed to have been fraudulent; or (3) had extreme baseline imbalance; or (4) used blocked randomization in unblinded trials; or (5) had differential diagnostic activity; or (6) had some other problem.

"Unclear" risk of bias: information insufficient to assess whether an important risk of bias existed, or rationale or evidence insufficient to suggest that an identified problem will introduce bias.

2. Tool for assessing the risk of bias in nonrandomized studies of interventions (ROBINS-I)[35]

Domain	Explanation
Preintervention	Risk of bias assessment is mainly distinct from assessments of randomized trials
Bias due to confounding	Baseline confounding occurs when 1 or more prognostic variables (factors that predict the outcome of interest) also predicts the intervention received at baseline ROBINS-I can also address time-varying confounding, which occurs when individuals switch between the interventions being compared and when postbaseline prognostic factors affect the intervention received after baseline
Bias in selection of participants into the study	When exclusion of some eligible participants, or the initial follow-up time of some participants, or some outcome events is related to both intervention and outcome, there will be an association between interventions and outcome even if the effects of the interventions are identical This form of selection bias is distinct from confounding: a specific example is bias due to the inclusion of prevalent users, rather than new users, of an intervention
At intervention	Risk of bias assessment is mainly distinct from assessments of randomized trials
Bias in classification of interventions	Bias introduced by either differential or nondifferential misclassification of intervention status Nondifferential misclassification is unrelated to the outcome and will usually bias the estimated effect of intervention towards the null Differential misclassification occurs when misclassification of intervention status is related to the outcome or the risk of the outcome, and is likely to lead to bias
Postintervention	Risk of bias assessment has substantial overlap with assessments of randomized trials
Bias due to deviations from intended interventions	Bias that arises when there are systematic differences between experimental intervention and comparator groups in the care provided, which represent a deviation from the intended intervention(s) Assessment of bias in this domain will depend on the type of effect of interest (either the effect of assignment to intervention or the effect of starting and adhering to intervention).
Bias due to missing data	Bias that arises when later follow-up is missing for individuals initially included and followed (such as differential loss to follow-up that is affected by prognostic factors); bias due to exclusion of individuals with missing information about intervention status or other variables such as confounders
Bias in measurement of outcomes	Bias introduced by either differential or nondifferential errors in measurement of outcome data. Such bias can arise when outcome assessors are aware of intervention status, if different methods are used to assess outcomes in different intervention groups, or if measurement errors are related to intervention status or effects
Bias in selection of the reported result	Selective reporting of results in a way that depends on the findings and prevents the estimate from being included in a meta-analysis (or other synthesis)

Interpretation of domain-level and overall risk of bias judgments in ROBINS-I

Judgment	Within each domain	Across domains	Criterion
"Low" risk of bias	The study is comparable to a well-performed randomized trial with regard to this domain	The study is comparable to a well-performed randomized trial	The study is judged to be at low risk of bias for all domains
"Moderate" risk of bias	The study is sound for a nonrandomized study with regard to this domain but cannot be considered comparable to a well-performed randomized trial	The study provides sound evidence for a nonrandomized study but cannot be considered comparable to a well-performed randomized trial	The study is judged to be at low or moderate risk of bias for all domains
"Serious" risk of bias	The study has some important problems in this domain	The study has some important problems	The study is judged to be at serious risk of bias in at least 1 domain, but not at critical risk of bias in any domain
"Critical" risk of bias	The study is too problematic in this domain to provide any useful evidence on the effects of intervention	The study is too problematic to provide any useful evidence and should not be included in any synthesis	The study is judged to be at critical risk of bias in at least 1 domain
No information	No information on which to base a judgment about risk of bias for this domain	No information on which to base a judgment about risk of bias	There is no clear indication that the study is at serious or critical risk of bias and there is a lack of information in 1 or more key domains of bias (a judgment is required for this)

The following prespecified confounding factors could potentially influence the intervention: primary causes of postpartum hemorrhage, type of delivery, severity of hemorrhage, length of time from onset of hemorrhage to receive either a uterine balloon tamponade or other intervention or no intervention, availability of intensive care unit, and use of surgical and nonsurgical maneuvers to hold the uterine balloon tamponade in place. The following cointerventions were prespecified: use of misoprostol, ergotamine, tranexamic acid, and carbetocin.

3. Tool for assessing the risk of bias in case series studies[36]

Domain	Leading explanatory questions
Selection	Does the patient(s) represent(s) the whole experience of the investigator (center) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported?
Ascertainment	Was the exposure adequately ascertained?
	Was the outcome adequately ascertained?
Causality	Were other alternative causes that may explain the observation ruled out?
	Was follow-up long enough for outcomes to occur?
Reporting	Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice?

"Low" risk of bias: answering "yes" to the explanatory question.

"High" risk of bias: answering "no" to the explanatory question.

"Unclear" risk of bias: insufficient information to answer the explanatory question. If the risk of bias was unclear, the domain was scored as "high" risk of bias.

III. Quality of Evidence

The GRADE approach[35] takes into account 5 domains—risk of bias, inconsistency, indirectness, imprecision, and publication bias—and categorizes the certainty of the evidence into the following 4 levels:

(1) High: We are very confident that the true effect lies close to that of the estimate of the effect, and further research is unlikely to change our confidence in the estimate of the effect.

(2) Moderate: We are moderately confident in the effect estimate, and the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

(3) Low: Our confidence in the effect estimate is limited, and the true effect may be substantially different from the estimate of the effect.

(4) very low: we have very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of effect.

The evidence can be downgraded from "high quality" by 1 level for serious (or by 2 levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates, or potential publication bias.

SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Individually randomized controlled trials						
Soltan,[40] 2007	Egypt	2003–2004	• Inclusion: Women who delivered vaginally either in hospital or at home and were complicated with atonic PPH • Exclusion: Traumatic PPH, retained placental tissues, other cause and after cesarean delivery.	• El-Menia balloon (n = 120) • Control: Uterine massage and uterotonics (n = 120)	No need for surgical operations to control PPH	El-Menia balloon: 100 Control: 84
Khalil,[41] 2011	Saudi Arabia	2004–2009	• Inclusion: Women with severe atonic PPH during emergency CS, following failed attempts at medical treatment • Exclusion: Women who were less than 28 weeks pregnant; traumatic PPH; PP	• Bakri balloon + traction stitch (n = 25) • Bakri balloon (n = 25)	If the bleeding was minimized and if another surgical was not needed to stop the bleeding	Bakri balloon + traction stitch: 96 Bakri balloon: 80
Kavak,[42] 2013	Turkey	2011–2012	• Inclusion: Pregnant women with a preoperative diagnosis of complete PP who had intractable bleeding after delivery • Exclusion: Serious medical, hematological or surgical diseases; placental implantation anomalies; history of thromboembolism; emergency CS; macrosomia; polyhydramnios; preeclampsia; gestational diabetes; intrauterine growth retardation; and presence of multiple gestations.	• Bakri balloon (n = 7) • Endouterine hemostatic square suture (n = 6)	Achievement of complete hemostasis	Bakri balloon: 100 Sutures: 100
Dumont,[43] 2017	Benin, Mali	2013–2015	• Inclusion: Women delivering vaginally who had clinically diagnosed PPH that was suspected to be due to uterine atony, who were resistant to the first-line treatment (oxytocin). • Exclusion: Contraindication to prostaglandins, uterine rupture or placenta accreta.	• Condom UBT + intrarectal or sublingual misoprostol (n = 57) • Control: intrarectal or sublingual misoprostol alone (n = 59)	Women who did not require an invasive surgery (arterial ligatures, uterine compressive sutures, hysterectomy) and who did not die before hospital discharge	Condom UBT: 84 Control: 93

Suarez et al. Uterine balloon tamponade for treating postpartum hemorrhage. Am J Obstet Gynecol 2020. *(continued)*

SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Darwish,[44] 2018	Egypt	2014–2015	• Inclusion: All women who delivered vaginally in the Labor Ward who developed primary atonic PPH and did not respond to the first line of treatment (oxytocin + misoprostol). • Exclusion: CS delivery, traumatic PPH, placental abruption, PP, chorioamnionitis, pregnancy complicated by preeclampsia, diabetes, anemia, rheumatic heart disease or women known to have coagulation defects	• Condom UBT (n = 33) • Bakri balloon (n = 33)	If the bleeding stopped within 15 minutes after proper balloon application without any need for surgical intervention	Condom UBT: 85 Bakri balloon: 91
Ashraf,[45] 2018	Pakistan	Not reported	• Inclusion: PPH after VD with gestational age >37 weeks and did not respond to medical treatment • Exclusion: Previous CS, PPH due to perineal, cervical or vaginal tear, episiotomy, retained placenta, coagulation disorder, secondary PPH	• Condom UBT (n = 106) • Uterovaginal roll gauze packing (n = 106)	If bleeding was stopped within 15 minutes after uterovaginal packing or UBT and patient remained hemodynamically stable, and if no complications occurred after applying or removing balloon tamponade or intrauterine packing.	Condom UBT: 77 Uterovaginal roll gauze packing: 59
Cluster randomized controlled trials						
Anger,[46] 2019	Senegal, Egypt and Uganda	2016-2018	• Inclusion: Secondary-level public hospitals with an approximate weekly average of 160 vaginal deliveries that agreed integrating UBT into standard care. The study population was women with vaginal delivery. The intervention was • Exclusion: Previous CS, PPH due to perineal, cervical or vaginal tear, episiotomy, retained placenta, coagulation disorder, secondary PPH	• Intervention period: training and introduction of UBT into routine practice for refractory PPH. Condom UBT used in 55 women • Control period: use of pre-existing practices for refractory PPH. Condom UBT used in 9 women	Women who did not require an invasive surgery (arterial ligatures, uterine compressive sutures, repair of uterine rupture, hysterectomy) and who did not die before hospital discharge	Condom UBT: 88 Control: not reported

Suarez et al. Uterine balloon tamponade for treating postpartum hemorrhage. Am J Obstet Gynecol 2020. *(continued)*

SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Nonrandomized studies						
Laas,[47] 2012	France	2005–2010	• Inclusion: Women who gave birth (VD or CS) in the maternity unit of the hospital and developed a PPH due to uterine atony that was unresponsive to sulprostone. • Exclusion: PP, placenta accreta, or uterine rupture.	• Local PPH protocol + Bakri balloon (n = 43) • Control: Local PPH protocol	Arrest of bleeding that did not require further interventions	Bakri balloon: 86
Kaya,[43] 2016	Turkey	2009–2013	• Inclusion: Women who underwent the Bakri balloon and the B-Lynch suture due to uterine atony, and who were unresponsive to medical therapy during CS. • Exclusion: Cases managed with concurrent artery ligation; accidental puncture of Bakri, B-Lynch after unsuccessful balloon	• Bakri balloon (n = 21) • B-Lynch procedure (n = 24)	If vaginal bleeding stopped while in lithotomy position and internal iliac artery ligation was not required	Bakri balloon: 76 B-Lynch: 79
Othman,[49] 2016	Saudi Arabia	2012–2015	• Inclusion: Women with PP and PPH of more than 1000 mL who had uncontrolled bleeding despite the use of oxytocin, carboprost, and figure 8 stitches in the bleeding site of the placental bed • Exclusion: Unreported	• Bakri balloon (n = 13) • Control: PPH management without Bakri balloon (n = 151)	Arrest of bleeding that did not require additional interventions to control the bleeding	Bakri balloon: 100 Control: 78
Lo,[50] 2017	USA	2002–2013	• Inclusion: Women who delivered after gestation week 20 and had PPH refractory to uterotonic agents • Exclusion: Patients with placenta accreta	• Local PPH protocol + Bakri balloon (n = 43) • Control: Local PPH protocol	Arrest of bleeding that did not require hysterectomy or B-Lynch procedures	Bakri balloon: 81
Gauchotte,[51] 2017	France	2008–2013	• Inclusion: Women treated with sulprostone for PPH in the obstetrics unit • Exclusion: Unreported	• Local PPH protocol + Bakri balloon (n = 38) • Control: Local PPH protocol	Arrest of bleeding that did not require surgery or interventional radiology	Bakri balloon: 92

Suarez et al. Uterine balloon tamponade for treating postpartum hemorrhage. Am J Obstet Gynecol 2020. *(continued)*

SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Tahaoglu,[52] 2017	Turkey	2010-2015	• Inclusion: Women with PPH due to uterine atony when conservative measures failed and were treated via Bakri balloon placement and bilateral IIAL at a tertiary hospital • Exclusion: Women with PPH due to genital tract lacerations, placental retention, uterine rupture, or uterine inversion	• Bakri balloon (n = 14) • Bilateral IIAL (n = 12)	If the bleeding drainage flow was <50 mL/h	Bakri balloon: 71 IIAL: 67 (for placenta previa group)
Maher,[53] 2017	Saudi Arabia	2013–2015	• Inclusion: Women of any age, parity, carrying single or multiple pregnancies and with a gestational age suitable for neonatal care according to protocols, prepared for CS because of low-lying placenta or PP • Exclusion: Uterine and placental implantation anomalies and refusal to participate in study	• Bakri balloon (n = 72) • Control: Non-Bakri balloon PPH protocol (n = 40)	No bleeding within 10 min and no further surgical intervention was required	Bakri balloon: 88 Control: 80
Revert,[54] 2018	France	2011–2012	• Inclusion: Hospitalizations of women of reproductive age (12–55 years) from the ICD-10 code Z37, called "birth outcome" • Exclusion: Women who gave birth outside either network but transferred into the network delivery and women who gave birth within 1 of the networks and then transferred out	• Pilot network that used UBT in standard practice (n = 35,133) • Control: Network that did not use UBT in standard practice (n = 37,396)	The need of arterial embolization or surgery (pelvic vessel ligation or hysterectomy) for hemorrhage control	Not reported
Guo,[55] 2018	China	2010–2015	• Inclusion: Women who delivered via CS with persistent active PPH or bleeding above 500 mL after uterine massage and use of a uterotonic • Exclusion: Unreported	• Bakri balloon (n = 142) • Bakri balloon + vaginal gauze (n = 163)	Arrest of bleeding and did not require uterine artery embolization or hysterectomy	Bakri balloon: 87 Bakri + gauze: 96

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Thabet,[55] 2018	Egypt	2013–2016	• Inclusion: Women who underwent elective CS with PP diagnosed by color flow Doppler or magnetic resonance imaging in the third trimester of pregnancy, and confirmed intraoperatively (during CS) • Exclusion: Multifetal pregnancy, medical conditions complicating pregnancy, blood diseases or bleeding tendencies, or moderate or severe antepartum hemorrhage	• Foley UBT (n = 40) • Control: Treatment for PP without Foley UBT (n = 38)	Arrest of bleeding without requirement of IIAL	Foley UBT: 80 Control: 53
Osmonova,[57] 2018	Kyrgyz Republic	2015–2016	• Inclusion: At-term pregnant women who had single spontaneous vaginal delivery and PPH due to uterine atony ≥500 mL • Exclusion: Abnormal placenta attachment (PP), premature detachment of normally located placenta (accidental hemorrhage), severe preeclampsia, polyhydramnios, multi-fetal gestation, uterine anomalies	• Zhukovsky UBT + standard therapy (n = 35) • Control: Standard therapy (n = 49)	The need for organ-preserving surgical hemostasis: ligation of uterine and ovarian arteries, uterine hemostatic compression sutures and internal iliac artery ligation; and the need for hysterectomy	Zhukovsky UBT + standard therapy: 86 Standard therapy: 37
Dalia,[58] 2018	India	2017	• Inclusion: All women who delivered vaginally and those who developed nontraumatic PPH not responding to medical management • Exclusion: Women with retained placenta, uterine rupture, chorioamnionitis, and known uterine anomaly	• Condom UBT (n = 10) • Condom UBT with tip cut (n = 10) • CG balloon (n = 10)	If bleeding was successfully controlled and no additional intervention was required	Condom UBT: 80 Condom UBT + tip cut: 90 CG balloon: 100
Cetin,[59] 2018	Turkey	2014–2017	• Inclusion: Women diagnosed with uterine atony during their CS who failed to respond to uterotonic agents and who were treated with either a Hayman suture or Bakri balloon tamponade • Exclusion: Unreported	• Bakri balloon (n = 39) • Hayman suture (n = 43)	If bleeding stopped after the balloon was inflated without ligation of the uterine artery	Bakri balloon: 74 Hayman suture: 77

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Mishra,[60] 2019	India	2014–2016	• Inclusion: Women having PPH (defined as loss of >500 mL after vaginal delivery and >1 L after CS and/or deteriorating hemodynamic changes due to bleeding) refractory to first-line management (uterine massage and uterotonics, if atony) or failed attempt at surgical repair in lower genital tract tears • Exclusion: Allergy to latex, retained placenta, uterine rupture, genital infection suspected (rupture of membranes for >18 h), genital anomaly or malignancy	• Condom UBT (n = 14) • Chhattisgarh condom balloon device (n = 46)	Successful tamponade after balloon insertion	Condom balloon: 100 Chhattisgarh condom: balloon 98
El Gelany,[61] 2019	Egypt	2012–2017	• Inclusion: Women with previous CS and PP with suspect morbidly adherent placenta who underwent elective CS between 35 and 38 weeks and who were keen to preserve their fertility; cases were only included if partial separation occurred at CS, resulting in major bleeding • Exclusion: Women with previous CS with PP/accreta and women who had preoperative diagnosis of placenta percreta who opted to have an elective hysterectomy or in whom placenta percreta was confirmed intraoperatively	• Bakri balloon (n = 42) • Bakri balloon + bilateral uterine artery ligations (n = 40) • Bilateral uterine artery ligations + cervical tamponade using 2 or 3 simple interrupted stitches (n = 43)	If the procedure controlled the bleeding at the placental bed and there was no need for hysterectomy	Bakri balloon: 69 Bakri balloon + bilateral uterine artery ligations: 72 Bilateral uterine artery ligations + cervical tamponade: 90
Case series						
Condous,[62] 2003	United Kingdom Singapore	Not reported	• Inclusion: Women with intractable PPH who were managed by the tamponade test when they were unresponsive to oxytocic agents and prostaglandin analogues • Exclusion: Unreported	Sengstaken–Blakemore (n = 16)	If no or minimal bleeding is observed via the cervix or through the gastric lumen of the catheter and surgical intervention avoided	88

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Akhter,[63] 2003	Bangladesh	2001–2002	• Inclusion: Women with PPH that occurred as a result of atonicity or morbid adhesion (accreta) that could not be controlled by uterotonics or a surgical procedure • Exclusion: Unreported	Condom UBT (n = 23)	Arrest of bleeding	100
Seror,[64] 2005	France	1999–2003	• Inclusion: Women with PPH who underwent treatment by UBT with a Sengstaken–Blakemore tube after failure of conventional medical treatment • Exclusion: Unreported	Sengstaken–Blakemore (n = 17)	If the bleeding stopped with no need for additional interventions	71
Keriakos,[65] 2006	United Kingdom	2001–2004	• Inclusion: All women with PPH who had undergone initial medical management but failed to control the bleeding • Exclusion: Traumatic PPH	Rusch balloon (n = 8)	If hemorrhage stopped after placement of the device	88
Dabelea,[66] 2007	USA	2003–2005	• Inclusion: Women with PPH unresponsive to medical therapy as part of a management protocol for PPH • Exclusion: Unreported	• Bakri balloon (n = 15) • Sengstaken–Blakemore (n = 5)	If bleeding stopped with balloon inflation without the need for additional procedures	Bakri balloon: 87 Sengstaken–Blakemore: 100
Airede,[67] 2008	Nigeria	2004–2006	• Inclusion: Persistent PPH despite massage of the uterus, emptying of uterus, emptying of the bladder, and repeated doses of intravenous ergometrine and oxytocin infusion • Exclusion: Uterine rupture and genital tract laceration	Condom UBT (n = 4)	If hemorrhage ceased after 30 minutes of placement (by direct observation of cervix)	100
Doumouchtsis,[68] 2008	United Kingdom	2002–2006	• Inclusion: Women of at least 20 weeks' gestation with ongoing PPH • Exclusion: Traumatic PPH or retained products	Sengstaken–Blakemore (n = 27)	If no or minimal bleeding is observed via the cervix or through the gastric lumen of the catheter and further intervention avoided	81

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Nicolas,[69] 2009	United Kingdom	2003–2006	• Inclusion: Women with massive primary PPH who had a balloon placed after failure of routine procedures including AMTSL and administration of at least 2 ecobolic drugs • Exclusion: Unreported	Sengstaken–Blakemore (n = 7)	Cessation of bleeding and avoidance of further medical or surgical interventions	86
Vitthala,[70] 2009	United Kingdom	2002–2006	• Inclusion: Women with PPH who underwent Bakri balloon insertion after unsuccessful medical management of PPH • Exclusion: Traumatic PPH requiring surgery	Bakri balloon (n = 15)	If bleeding is stopped after the balloon was inflated and if another surgical procedure was not needed to stop bleeding	80
Majumdar,[71] 2010	United Kingdom	2008	• Inclusion: All women with PPH who had failed medical therapy and in whom the Rusch balloon was used • Exclusion: Unreported	Rusch balloon (n = 18)	Patients that required no further interventions after balloon tamponade	72
Rather,[72] 2010	India	Not reported	• Inclusion: Women who did not respond to conventional medical management to restore the tone of uterus • Exclusion: Traumatic PPH	Condom UBT (n = 26)	If bleeding stopped within 10 minutes of tamponade and did not require any further intervention	96
Rodó Rodriguez,[73] 2010	Spain	2006	• Inclusion: Women with immediate PPH and persistent bleeding from the uterus despite the realization of uterine massage and the administration of uterine drugs • Exclusion: Unreported	Bakri balloon (n = 5)	If mechanical hemostasis was obtained	100
Thapa,[74] 2010	Nepal	2008–2010	• Inclusion: Women with PPH of more than 500 mL or who continued to bleed despite use of pharmacologic measures for at least 30 minutes • Exclusion: Unreported	Condom UBT (n = 10)	If bleeding stopped within 30 minutes of tamponade application and surgical intervention was not sought	100
Yaqub,[75] 2010	Pakistan	2009–2010	• Inclusion: Women who developed PPH after delivering in the hospital • Exclusion: Massive PPH	Foley UBT (n = 40)	If UBT arrested the bleeding and no uterine packing or surgical procedure were necessary	78

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Albayrak,[76] 2011	Turkey	2005–2010	• Inclusion: All women who delivered via CS with PPH from the lower uterine segment secondary to placenta previa/accreta where standard conservative measures failed to control bleeding • Exclusion: PPH from uterine atony and genital laceration	Foley UBT (n = 15)	If intraoperative hemostasis was achieved after balloon placement	100
Varatharajan,[77] 2011	United Kingdom	2008	• Inclusion: All women who experienced massive primary PPH (total blood loss >1500 mL) • Exclusion: Unreported	Unknown (n = 13)	If bleeding was arrested and no further surgical procedure was performed	77
Keriakos,[78] 2012	United Kingdom	2005–2009	• Inclusion: Women with major PPH who had undergone initial medical management, but failed to control the bleeding, and who underwent insertion of Rusch balloon catheter • Exclusion: Traumatic PPH or latex allergy	Rusch Balloon (n = 31)	If bleeding stopped without requiring other surgical interventions, such as B-Lynch and hysterectomy	84
Ishii,[79] 2012	Japan	2007–2009	• Inclusion: Women who underwent CS due to PP/low-lying placenta with PPH resistant to medical therapy • Exclusion: Unreported	Sengstaken–Blakemore (n = 10)	If hemostasis was achieved and no additional procedure was performed	100
Diemert,[80] 2012	Germany	2005–2010	• Inclusion: Women diagnosed to have a severe PPH and unsuccessful medical treatment with uterotonic agents • Exclusion: Unreported	Bakri balloon (n = 20)	If the bleeding stopped within 15 minutes after the balloon was inflated and B-Lynch and hysterectomy were prevented	60
Rathore,[81] 2012	India	2009–2011	• Inclusion: Women with PPH after failure of medical management, defined as failure to control bleeding in spite of maximum dosage of uterotonic drugs or hemodynamic instability that required surgical intervention • Exclusion: Trauma or retained tissue	Condom UBT (n = 18)	Control of hemorrhage within 15 minutes of balloon placement	96

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(continued)

SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Aibar,[32] 2013	Spain	2010–2011	• Inclusion: Women who were treated with a Bakri balloon if they had PPH that did not respond to standard management consisting of uterine massage, volume replacement, and uterotonic medical treatment • Exclusion: Unreported	Bakri balloon (n = 24)	Control of PPH not requiring any further nonpharmacological intervention	88
Rodriguez-Kovacs,[33] 2013	Venezuela	Not reported	• Inclusion: Women who presented vaginal PPH due to uterine atony refractory to medical management after a pregnancy equal to or greater than 28 weeks • Exclusion: Retained tissue, uterine inversion, uterine rupture, uterine scars, uterine malformations, lower genital tract lacerations, placenta accreta, cervical cancer, purulent discharge through the cervix or vagina, and secondary PPH secondary to abdominal trauma	Bakri balloon (n = 15)	If there was minimal bleeding (100 cm^3 or less) through the cervix or the lumen of the balloon within 5 minutes of placement	100
Olsen,[34] 2013	USA	2008–2010	• Inclusion: All women diagnosed with PPH at our 2 facilities who failed treatment with uterotonic agents (American College of Obstetricians and Gynecologists guidelines), and who received a Bakri balloon if bleeding persisted	Bakri balloon (n = 37)	Arrest of hemorrhage without needing to proceed with another form of hemorrhage control	68
Florian,[35] 2013	French Guiana	2008–2011	• Inclusion: Persistence of PPH despite medical treatment with sulprestone and implementation of the hospital protocol • Exclusion: Unreported	Linton–Nachlas balloon (n = 25)	If bleeding stopped, with or without confirmation of balloon positioning by transabdominal ultrasonography	96
Grönvall,[36] 2013	Finland	2008 –2011	• Inclusion: Women who had bleeding >1000 mL before insertion of a Bakri balloon and women with expected high risk of PPH but bleeding <1000 mL before insertion of a Bakri balloon • Exclusion: Unreported	Bakri balloon (n = 50)	If hemostasis was achieved and other procedures were not needed	86

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Chan,[87] 2013	Hong Kong	2006–2011	• Inclusion: Women with a gestational age of at least 24 weeks and massive primary PPH • Exclusion: Unreported	Sengstaken–Blakemore (n = 12)	No requirement for rescue hysterectomy	75
Vrachnis,[88] 2013	Greece	2008–2011	• Inclusion: Women diagnosed with PPH who underwent Bakri balloon tamponade • Exclusion: Unreported	Bakri balloon (n = 18)	If balloon placement arrested the bleeding.	94
Kumru,[89] 2013	Turkey	2009–2012	• Inclusion: Women diagnosed to have severe PPH with PP and failed medical treatment with uterotonic agents who were treated with the Bakri balloon • Exclusion: Unreported	Bakri balloon (n = 25)	If the bleeding was stopped and additional surgical procedures were not needed	88
Kong,[90] 2013	Hong Kong	2011–2012	• Inclusion: Women with severe PPH following delivery who underwent UBT placement • Exclusion: Unreported	Bakri balloon (n = 19)	If bleeding was arrested and hysterectomy prevented with UBT as the only procedure	79
Yan,[91] 2014	China	2008–2009	• Inclusion: Women who experienced primary PPH unresponsive to first-line therapies including uterine massage, administration of uterotonics, and treatment of the presumed cause • Exclusion: Unreported	Self-made balloon (n = 4)	Control of PPH without need for additional management or hysterectomy	75
Ferrazzani,[92] 2014	Italy	2002–2012	• Inclusion: PPH after failure of medical treatment • Exclusion: Traumatic PPH	Rusch balloon (n = 52)	If the "tamponade test" stopped bleeding and other surgical measures were not necessary	75
Dildy,[93] 2014	USA	2010–2012	• Inclusion: Women with a diagnosis of PPH who had the "ebb" device placed • Exclusion: Unreported	Belfort–Dildy ("ebb") Complete Tamponade System (n = 51)	Arrest of bleeding without other surgical interventions	78

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Kaya,[94] 2014	Turkey	2011–2013	• Inclusion: Women who bled more than 1000 mL and unresponsive to standard medical management (including oxytocin) • Exclusion: Traumatic PPH requiring surgery, hemodynamic instability at the time of Bakri balloon insertion, and hereditary coagulation disorders	Bakri balloon (n = 45)	If bleeding stopped within 15 minutes of the balloon's inflation by observing the amount of hemorrhage drained through the catheter, and no further procedure was performed	76
Kavak,[95] 2014	Turkey	2012–2013	• Inclusion: Women who underwent VD with bleeding from cervix and upper parts of vagina and women who underwent CS due to PP and showed intractable bleeding from lower segments of uterus • Exclusion: Unreported	Double-balloon cervical ripening catheter (n = 7)	If bleeding was successfully controlled intraoperatively	100
Uygur,[96] 2014	Turkey	2011–2013	• Inclusion: Women treated with a BT-Cath after unsuccessful medical treatment of PPH due to PP, confirmed by transvaginal ultrasound examination on admission • Exclusion: Unreported	BT Cath (n = 53)	If bleeding ceased and no further surgical procedures were performed to treat PPH or to treat complications from UBT insertion (perforation)	85
Vintejoux,[97] 2015	France	2010–2011	• Inclusion: Women with primary PPH who received the Bakri balloon secondary to uterine atony and subsequent routine drug treatment were identified • Exclusion: Unreported	Bakri balloon (n = 36)	No bleeding within 5–10 minutes and no further surgical interventions were necessary	69
Vargas-Aguilar,[98] 2015	Mexico	2009–2011	• Inclusion: Pregnant women with obstetric hemorrhage that did not stop with uterotonics • Exclusion: Unreported	Bakri balloon (n = 19)	Arrest of bleeding after placement of the Bakri balloon and no further surgical interventions were necessary (hysterectomy)	95

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Martin,[99] 2015	France	2011–2012	• Inclusion: All women who underwent balloon tamponade treatment for persistent primary PPH and if conservative steps had failed • Exclusion: Unreported	Bakri balloon (n = 49)	Arrest of the hemorrhage after balloon tamponade, with no subsequent invasive procedures	65
Cekmez,[100] 2015	Turkey	2010–2013	• Inclusion: Women with PPH due to uterine atony and managed with medical treatment who were subsequently treated with various interventions • Exclusion: Unreported	Bakri balloon (n = 10)	If bleeding stopped and no additional interventions were required	60
Alkis,[101] 2015	Turkey	2011–2013	• Inclusion: Women in whom standard medical treatment failed to stop the PPH and who were managed with intrauterine Bakri balloon tamponade • Exclusion: Women with bleeding due to lacerations in which surgery was needed	Bakri balloon (n = 47)	If the bleeding stopped after the balloon was inflated, and no other surgical intervention was needed	91
Alouini,[102] 2015	France	2009–2013	• Inclusion: Bakri balloon was placed after VD or CS when hemorrhage did not have an identifiable uterine or vascular wound • Exclusion: Unreported	Bakri balloon (n = 61)	If bleeding stopped and no additional surgical interventions were required	90
Cho,[103] 2015	Korea	2009–2014	• Inclusion: Women who underwent elective CS due to PP or low-lying placenta and who underwent Bakri balloon catheter placement for uncontrolled PPH of more than 1000 mL • Exclusion: Chorioamnionitis, retained placenta, trauma of cervix and vagina, inherited coagulopathy and DIC.	Bakri balloon (n = 64)	Arrest of PPH after proper placement and inflation of the balloon catheter, without the need for additional treatments	75
Açar Eser,[104] 2015	Turkey	2009–2014	• Inclusion: Women who gave birth and had been treated for PPH • Exclusion: Unreported	Bakri balloon (n = 12)	Restoring hemostasis without recourse to hysterectomy	100

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Lohano,[105] 2016	Pakistan	2012	• Inclusion: Women aged 18–35 years, parity 1–6, and gestational age 31-41 weeks who developed or were admitted with primary PPH due to uterine atony in whom medical treatment had failed • Exclusion: PPH due to retained products and genital tract trauma	Condom UBT (n = 139)	Ability of the balloon tamponade to arrest bleeding after 24 hours	91
Kandeel,[106] 2016	Egypt	2011–2012	• Inclusion: Women with primary PPH when standard measures failed • Exclusion: Traumatic PPH, retained placenta, coagulopathy, and severe systemic diseases	Condom UBT (n = 50)	Arrest of bleeding after the balloon catheter was properly inflated for 15 minutes, without the need for additional procedures	96
Nagai,[107] 2016	Japan	2013	• Inclusion: Women with massive PPH who were treated with Bakri balloon tamponade • Exclusion: Unreported	Bakri balloon (n = 10)	If hemostasis was achieved without any additional surgical interventions	90
Ahmad,[108] 2016	India	2013–2014	• Inclusion: All women who delivered vaginally or by CS and developed nontraumatic PPH that did not respond to medical management • Exclusion: Traumatic PPH or retained tissue in uterus	Condom UBT (n = 33)	If hemorrhage was successfully controlled after UBT removal, 12–24 hours after insertion, and no hysterectomy was performed	94
Aderoba,[109] 2017	Nigeria	2012–2014	• Inclusion: Women with a singleton pregnancy who delivered at the obstetric unit and had PPH that was not amenable to first-line therapy • Exclusion: Genital tract lacerations, chorioamnionitis, haemoglobinopathies, Hb <11 g/L, and suspicion of uterine rupture	Condom UBT (n = 229)	Cessation of significant bleeding, improved hemodynamic status, and no need for additional intervention	89
Hasabe,[110] 2016	India	2013–2015	• Inclusion: Women who developed intractable PPH in the hospital and did not respond to the conventional medical management • Exclusion: Traumatic PPH	Condom UBT (n = 36)	If blood loss was <50 mL and did not require further intervention	94

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Brown,[111] 2016	Kenya	2013–2015	• Inclusion: Women with PPH unresponsive to standard intervention • Exclusion: age <18 years; arterial bleeding requiring surgical exploration or angiographic embolization; immediate need for hysterectomy; ongoing pregnancy; cervical cancer; infections; uterine anomaly; active DIC; a surgical site that would prevent the Bakri tamponade balloon from effectively controlling bleeding; referral for obstructed labor; and ruptured uterus	Bakri balloon (n = 58)	If UBT controlled the bleeding without further surgical intervention	95
Kwon,[112] 2016	Korea	2010–2015	• Inclusion: Women with massive PPH (>1500 mL after delivery) who failed conservative management with uterotonic agents and were subsequently treated with UBT • Exclusion: Women with bleeding who need surgical procedure after VD due to lower genital tract lacerations	Bakri balloon (n = 57)	If bleeding from drainage catheter arrested or was <100 mL during 10 minutes and no further intervention was needed	82
Sandoval García-Travesí,[113] 2016	Mexico	2015	• Inclusion: Women with PPH due to uterine atony who did not respond to uterine massage or uterotonic drugs after 10–15 minutes • Exclusion: Traumatic PPH, chorioamnionitis, women with a known latex allergy	Condom UBT (n = 40)	If the bleeding stopped, the patient remained hemodynamically stable, and there was no need for surgical intervention	95
Kadioglu,[114] 2016	Turkey	2013–2016	• Inclusion: Women who developed massive PPH following a VD or CS in whom medical treatment had failed • Exclusion: PPH due to uterine and cervical trauma or retained placental tissue	Bakri balloon (n = 50)	If hemostasis was obtained and no further procedure was performed	84
Revert,[115] 2017	France	2010–2013	• Inclusion: Women treated by UBT as an initial second-line treatment for severe PPH unresponsive to prostaglandins • Exclusion: Unreported	• Bakri balloon (n = 198) • Belfort–Dildy ("ebb") Complete Tamponade System (n = 28)	No bleeding through either the cervix or the balloon drainage channel after 15 minutes	Bakri balloon: 83 Ebb tamponade system: 82

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Son,[116] 2017	USA	2007–2014	• Inclusion: All adult women who underwent placement of an intrauterine balloon after delivery, due to uterine atony, placental site/bed bleeding, or abnormal placentation • Exclusion: If catheter placement was unsuccessful due to the inability of the operator to either insert or inflate it	Bakri balloon (n = 306)	Arrest of bleeding that did not require UAE or hysterectomy	78
Parpillewar,[117] 2017	India	2015	• Inclusion: Women with atonic PPH who delivered vaginally after 28 weeks of gestation and who failed to respond to routine medical methods of management • Exclusion: Women who delivered by CS, traumatic PPH, PPH due to coagulation defects, and women with secondary PPH	Condom UBT (n = 23)	Control of bleeding without further intervention	78
Wang,[118] 2018	China	2015	• Inclusion: Women with live deliveries after 28 weeks of gestation with PPH who failed to respond to the first-line conservative management and underwent placement with the Bakri balloon • Exclusion: Women who received the Bakri balloon, but who did not reach the criteria for PPH	Bakri balloon (n = 407)	If PPH was stopped and no further surgical interventions were necessary	92
Ogoyama,[119] 2017	Japan	2013–2016	• Inclusion: All women with PPH when genital tract laceration sutures, uterotonic agents, uterine massage, or bimanual uterine compression failed to achieve hemostasis • Exclusion: Intra-abdominal bleeding, uterine rupture, suspected amniotic fluid embolism, or severe bleeding where hysterectomy or transarterial embolization was considered better to be immediately employed without Balloon application	Bakri balloon (n = 77)	Achieving hemostasis with no requirement of additional invasive procedures	93

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(continued)

SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Burke,[120] 2017	Kenya, Senegal, Sierra Leone, Tanzania	2012–2016	• Inclusion: All women with uncontrolled PPH originating from an atonic uterus who had an ESM-UBT device placed • Exclusion: Traumatic PPH, uterine rupture, or DIC due to sepsis	ESM-UBT (n = 306)	If no additional interventions were required to control bleeding	92
De la Luna y Olsen,[121] 2017	Mexico	2016	• Inclusion: All women in inpatient medical care units with a PPH unresponsive to medical treatment • Exclusion: Unreported	Bakri balloon (n = 20)	If bleeding was <150–200 mL and hypovolemic signs disappeared within 24 hours	95
Yorifuji,[122] 2018	Japan	2009–2014	• Inclusion: Cases of persistent massive hemorrhage (>1000 mL) despite conventional treatments such as bimanual uterine compression and administration of uterotonic agents • Exclusion: Unreported	Metreurynters balloon (n = 66)	The rate of hemostasis after UBT placement.	94
Grange,[123] 2018	France	2011–2015	• Inclusion: Women with persistent PPH after failure of bimanual uterine massage and uterotonics to stop bleeding after vaginal delivery • Exclusion: UBT placement after cesarean delivery	Bakri balloon (n = 108)	If no additional interventions were required to stop bleeding (such as pelvic arterial embolization, vessel ligation, uterine compression, or peripartum hysterectomy)	74
Mathur,[124] 2018	Singapore	2013–2015	• Inclusion: All women who had a Bakri inserted for the management of PPH • Exclusion: Unreported	Bakri balloon (n = 49)	Achievement of definitive hemostasis without the need of hysterectomy	82
Kong,[125] 2018	Hong Kong	2011–2016	• Inclusion: All women with severe PPH (blood loss ≥1000 mL) and had UBT inserted to arrest bleeding • Exclusion: Unreported	Bakri balloon (n = 39)	If UBT arrested bleeding and no further procedures were necessary	75

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SUPPLEMENTARY TABLE 1

Characteristics of studies included in the review *(continued)*

First author, year	Country	Study period	Inclusion and exclusion criteria	Intervention(s) (sample size)	Definition of intervention success	Intervention success rate (%)
Pala,[126] 2018	Turkey	2012–2016	• Inclusion: Women who were diagnosed with placenta accreta or increta preoperatively and intraoperatively and treated with Bakri balloon tamponade or cesarean hysterectomy • Exclusion: Unreported	Bakri balloon (n = 19)	<100 mL of blood from drainage catheter during first 10 minutes after placement of UBT	84
Santhanam,[127] 2018	India	2015–2016	• Inclusion: Women who developed intractable atonic PPH not responsive to conventional medical management (uterotonics) following VD/CS • Exclusion: Obstetric hemorrhage <28 weeks of gestation; traumatic PPH; allergic to latex; acute uterine infection	Condom UBT (n = 69)	Uterine bleeding that stopped or decreased within 30 minutes of balloon inflation that did not require additional procedures	97
Tahir,[128] 2018	Pakistan	2016–2017	• Inclusion: All women who underwent a CS who developed PPH and were treated with UBT • Exclusion: Unreported	Foley UBT (n = 26)	Arrest of bleeding without requiring hysterectomy	96
Kong,[129] 2018	Hong Kong	2012–2017	• Inclusion: Women who had had UBT attempted as the initial second-line procedure after failed medical treatment • Exclusion: Unreported	Bakri balloon (n = 81)	Bleeding that was effectively controlled shortly after inflation of the balloon and no further intervention was required	73
Theron,[130] 2018	South Africa	2016–2017	• Inclusion: All women with PPH where emergency measures were applied, and medical treatment failed • Exclusion: Unreported	Ellavi UBT (n = 17)	If no additional interventions were needed to arrest hemorrhage	82

AMTSL, active management of the third stage of labor; *CS*, cesarean section; *DIC*, disseminated intravascular coagulopathy; *IIAL*, internal iliac artery ligation; *PP*, placenta previa; *PPH*, postpartum hemorrhage; *UAE*, uterine artery embolization; *UBT*, uterine balloon tamponade; *VD*, vaginal delivery.

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SUPPLEMENTARY TABLE 2

Risk of bias in included randomized controlled trials

First author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Soltan,[40] 2007	Low	Low	High	Low	Unclear	Unclear	Unclear
Khalil,[41] 2011	Low	Unclear	Low/high[a]	Low	Unclear	Unclear	High
Kavak,[42] 2013	Unclear	Unclear	Low/high[a]	Low	Low	Low	Unclear
Dumont,[43] 2017	Low	Low	High	Low	Low	Low	High
Darwish,[44] 2018	Low	Low	Low/high[a]	Low	Low	Low	Low
Ashraf,[45] 2018	Low	Unclear	Unclear/high[b]	Low	Unclear	Unclear	Unclear

[a] Participants blinded; personnel unblinded; [b] Insufficient information on blinding of participants; personnel unblinded.

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SUPPLEMENTARY TABLE 3

Risk of bias in included nonrandomized studies

Study	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of the reported result	Overall
Laas,[47] 2012	Critical	Low	Low	Serious	Low	Low	Moderate	Critical
Kaya,[48] 2016	Critical	Serious	Low	Low	Low	Low	Moderate	Critical
Othman,[49] 2016	Critical	Serious	Serious	Low	Low	Low	No information	Critical
Lo,[50] 2017	Critical	No information	Serious	No information	Low	Low	Moderate	Critical
Gauchotte,[51] 2017	Critical	Low	Low	Serious	Low	Low	Moderate	Critical
Tahaoglu,[52] 2017	Critical	Low	Low	Low	Low	Low	Serious	Critical
Maher,[53] 2017	Serious	Low	Low	Low	Low	Low	Moderate	Serious
Revert,[54] 2018	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Guo,[55] 2018	Critical	Low	Serious	Low	Low	Low	Moderate	Critical
Thabet,[56] 2018	Serious	Low	Low	No information	Low	Low	Moderate	Serious
Osmonova,[57] 2018	Critical	Low	No information	No information	Low	Low	Moderate	Critical
Dalia,[58] 2018	Critical	Low	Low	No information	Low	Low	Moderate	Critical
Cetin,[59] 2018	Critical	Serious	Low	Low	Low	Low	Moderate	Critical
Mishra,[60] 2019	Critical	Low	Serious	No information	Low	Low	Moderate	Critical
El Gelany,[61] 2019	Critical	Low	Serious	Low	Low	Low	Low	Critical

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SUPPLEMENTARY TABLE 4

Risk of bias in included case series

Study (first author, year)	Selection	Ascertainment		Causality		Reporting
		Ascertainment of exposure	Ascertainment of outcome	Rule out of alternative causes	Follow-up	Description of cases
Condous,[62] 2003	High	Low	Low	Low	Low	Low
Akhter,[63] 2003	High	Low	Low	High	Low	High
Seror,[64] 2005	Low	Low	Low	Low	Low	Low
Keriakos,[65] 2006	High	Low	High	Low	Low	High
Dabelea,[66] 2007	Low	Low	Low	Low	Low	Low
Airede,[67] 2008	High	Low	Low	Low	Low	Low
Doumouchtsis,[68] 2008	Low	Low	Low	Low	Low	Low
Nicolas,[69] 2009	Low	Low	Low	High	Low	High
Vitthala,[70] 2009	High	Low	Low	Low	Low	Low
Majumdar,[71] 2010	High	Low	High	High	Low	High
Rather,[72] 2010	High	High	Low	High	Low	High
Rodó Rodriguez,[73] 2010	Low	High	High	High	Low	High
Thapa,[74] 2010	Low	Low	Low	High	Low	Low
Yaqub,[75] 2010	High	High	High	Low	Low	High
Albayrak,[76] 2011	Low	Low	Low	Low	Low	Low
Varatharajan,[77] 2011	Low	High	Low	High	Low	High
Keriakos,[78] 2012	High	High	High	High	Low	High
Ishii,[79] 2012	Low	Low	Low	Low	Low	Low
Diemert,[80] 2012	Low	Low	Low	High	Low	Low
Rathore,[81] 2012	Low	Low	Low	High	Low	Low
Aibar,[82] 2013	High	High	Low	High	Low	High
Rodriguez-Kovacs,[83] 2013	High	Low	Low	Low	Low	Low
Olsen,[84] 2013	High	Low	Low	Low	Low	Low
Florian,[85] 2013	Low	Low	Low	Low	Low	Low
Grönvall,[86] 2013	High	Low	Low	Low	Low	High
Chan,[87] 2013	Low	High	High	High	Low	High
Vrachnis,[88] 2013	High	Low	High	Low	Low	High
Kumru,[89] 2013	High	Low	Low	Low	Low	High

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(continued)

SUPPLEMENTARY TABLE 4

Risk of bias in included case series *(continued)*

Study (first author, year)	Selection	Ascertainment		Causality		Reporting
		Ascertainment of exposure	Ascertainment of outcome	Rule out of alternative causes	Follow-up	Description of cases
Kong,[90] 2013	High	Low	Low	High	Low	High
Yan,[91] 2014	High	High	Low	Low	Low	High
Ferrazzani,[92] 2014	High	Low	Low	Low	Low	Low
Dildy,[93] 2014	High	High	High	High	Low	High
Kaya,[94] 2014	Low	Low	Low	Low	Low	Low
Kavak,[95] 2014	High	Low	Low	Low	Low	Low
Uygur,[96] 2014	Low	Low	Low	Low	Low	Low
Vintejoux,[97] 2015	Low	Low	Low	Low	Low	Low
Vargas-Aguilar,[98] 2015	High	High	Low	Low	Low	High
Martin,[99] 2015	Low	High	Low	Low	Low	High
Cekmez,[100] 2015	Low	High	High	High	Low	High
Alkis,[101] 2015	High	Low	Low	Low	Low	Low
Alouini,[102] 2015	Low	High	Low	Low	Low	High
Cho,[103] 2015	Low	Low	Low	Low	Low	Low
Açar Eser,[104] 2015	High	High	High	High	Low	High
Lohano,[105] 2016	High	High	Low	Low	Low	High
Kandeel,[106] 2016	Low	Low	Low	Low	Low	Low
Nagai,[107] 2016	High	High	Low	High	Low	High
Ahmad,[108] 2016	High	Low	Low	Low	Low	High
Aderoba,[109] 2016	Low	Low	Low	Low	Low	Low
Hasabe,[110] 2016	Low	Low	Low	High	Low	High
Brown,[111] 2016	High	Low	Low	Low	Low	Low
Kwon,[112] 2016	High	Low	Low	Low	Low	Low
Sandoval García-Travesí,[113] 2016	Low	Low	Low	High	Low	Low
Kadioglu,[114] 2016	High	Low	High	Low	Low	Low
Revert,[115] 2017	Low	Low	Low	Low	Low	Low
Son,[116] 2017	High	High	Low	High	Low	High
Parpillewar,[117] 2017	High	Low	Low	Low	Low	High

Suarez et al. Uterine balloon tamponade for treating postpartum hemorrhage. Am J Obstet Gynecol 2020.

(continued)

SUPPLEMENTARY TABLE 4

Risk of bias in included case series *(continued)*

Study (first author, year)	Selection	Ascertainment		Causality		Reporting
		Ascertainment of exposure	Ascertainment of outcome	Rule out of alternative causes	Follow-up	Description of cases
Wang,[118] 2018	Low	Low	Low	Low	Low	Low
Ogoyama,[119] 2017	Low	Low	Low	Low	Low	Low
Burke,[120] 2017	High	Low	High	Low	Low	High
De la Luna y Olsen,[121] 2017	High	Low	Low	High	Low	Low
Yorifuji,[122] 2018	High	Low	High	Low	Low	High
Grange,[123] 2018	Low	Low	Low	Low	Low	High
Mathur,[124] 2018	High	Low	Low	Low	Low	High
Kong,[125] 2018	Low	Low	Low	Low	Low	Low
Pala,[126] 2018	High	Low	Low	Low	Low	Low
Santhanam,[127] 2018	Low	Low	Low	Low	Low	Low
Tahir,[128] 2018	High	High	Low	Low	Low	High
Kong,[129] 2018	Low	Low	Low	Low	Low	Low
Theron,[130] 2018	High	High	High	Low	Low	High

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SUPPLEMENTARY TABLE 5

Sensitivity analysis of success rate for uterine balloon tamponade according to study design and cause of postpartum hemorrhage, including data from abstracts of studies published only in abstract form or abstracts of unobtainable articles[a]

Cause of postpartum hemorrhage	Randomized controlled trials			Nonrandomized studies			Case series			Overall		
	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)
Uterine atony	4[40,41,43,44]	268	90.2 (74.1–98.9)	8[47–50,52,55,58,59]	301	84.5 (79.9–88.6)	47	2066	87.5 (84.4–90.4)	57	2549	87.5 (84.6–90.1)
Placenta previa	1[42]	7	100.0 (56.1–100)	5[49,50,53,55,61]	165	89.3 (73.8–98.4)	34	533	86.0 (81.6–89.9)	40	705	87.0 (82.7–90.8)
Placenta accreta spectrum	-	-	-	3[53,55,56]	74	75.1 (32.9–99.3)	11	75	63.0 (48.1–76.7)	14	149	65.6 (49.1–80.4)
Retained placenta	-	-	-	-	-	-	13	82	76.8 (65.3–86.5)	13	82	76.8 (65.3–86.5)
Undifferentiated	2[45,46]	170	81.8 (71.2–90.4)	3[51,58,60]	120	82.1 (46.6–99.7)	75	2736	84.1 (81.2–86.8)	79	2988	83.7 (80.9–86.6)
Total[b]	7[40–46]	445	88.8 (77.7–96.4)	14[47–61]	660	85.2 (80.5–89.4)	108	5508	85.6 (83.7–87.5)	126	6489	85.8 (84.0–87.5)

CI, confidence interval; *UBT*, uterine balloon tamponade.

[a] References of abstracts can be provided on request to the corresponding author; [b] Total number of studies does not represent the sum of individual causes of postpartum hemorrhage, given multiple causes of postpartum hemorrhage reported across studies.

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SUPPLEMENTARY TABLE 6

Sensitivity analysis of uterine balloon tamponade's success rate in case series according to risk of bias

Cause of postpartum hemorrhage	Low risk of bias in ≥5 explanatory questions			Low risk of bias in <5 explanatory questions		
	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)
Vaginal birth						
Uterine atony	4	142	87.4 (68.7–98.2)	5	195	87.6 (79.7–93.7)
Undifferentiated causes	24	705	85.7 (81.2–89.6)	17	269	86.9 (80.9–91.9)
Total	26	847	86.1 (81.6–90.1)	22	464	87.0 (82.5–91.0)
Cesarean delivery						
Uterine atony	2	12	69.8 (10.9–99.5)	2	6	69.1 (11.1–99.7)
Placenta previa	4	134	87.0 (74.5–95.7)	1	25	88.0 (75.3–100.0)
Placenta accreta spectrum	2	26	88.7 (70.3–98.8)	-	-	-
Undifferentiated causes	20	826	79.1 (71.8–85.6)	19	251	81.8 (75.6–87.3)
Total	27	998	80.5 (74.5–85.9)	22	282	81.8 (75.9–87.0)
Unknown mode of delivery						
Uterine atony	3	110	96.5 (92.3–99.1)	5	615	89.3 (79.1–96.4)
Undifferentiated causes	2	63	63.7 (29.4–91.5)	8	245	82.3 (77.3–86.8)
Total	4	173	91.2 (79.3–98.4)	10	860	85.4 (79.2–90.6)
Overall						
Uterine atony	21	942	88.1 (83.1–92.3)	22	1000	86.5 (81.3–90.9)
Placenta previa	18	347	84.1 (79.5–88.2)	14	169	87.2 (77.1–94.6)
Placenta accreta spectrum	8	56	65.6 (46.3–82.6)	2	13	53.5 (28.9–77.2)
Retained placenta	6	40	78.6 (65.7–89.1)	7	42	69.6 (46.9–88.1)
Undifferentiated causes	19	633	78.9 (70.3–86.4)	22	382	85.8 (80.7–90.2)
Total[a]	34	2018	85.6 (82.1–88.7)	35	1606	86.0 (82.8–88.9)

CI, confidence interval; *UBT*, uterine balloon tamponade.

[a] Total number of studies does not represent the sum of individual causes of postpartum hemorrhage, given multiple causes of postpartum hemorrhage reported across studies.

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SUPPLEMENTARY TABLE 7

Comparison of success rates between Bakri balloon and condom uterine balloon tamponade in postpartum hemorrhage (all causes)

	Randomized controlled trials			Nonrandomized studies			Case series			Overall		
Type of UBT	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)
Vaginal birth												
Bakri balloon	1[44]	33	90.9 (81.1–100.0)	1[47]	31	83.9 (70.9–96.8)	20	468	82.6 (77.7–87.1)	23	532	83.2 (78.8–87.2)
Condom UBT	4[43–46]	260	82.0 (77.2–86.4)	1[53]	30	90.0 (79.3–100.0)	9	476	93.2 (89.9–95.9)	14	865	89.5 (85.7–92.7)
Cesarean delivery												
Bakri balloon	2[41,42]	32	87.2 (63.6–99.3)	6[47–48,53,59,61]	199	82.0 (72.0–90.2)	24	871	78.6 (72.0–84.5)	32	1102	80.0 (74.9–84.7)
Condom UBT	-	-	-	-	-	-	6	99	88.4 (75.3–97.0)	6	99	88.4 (75.3–97.0)
Unknown mode of delivery												
Bakri balloon	-	-	-	4[50–52,55]	265	86.0 (81.7–89.9)	9	741	86.1 (80.5–90.9)	13	1006	85.7 (81.6–89.3)
Condom UBT	-	-	-	1[60]	14	100.0 (73.2–100)	6	427	91.8 (89.1–94.2)	7	441	92.1 (89.4–94.4)
Overall												
Bakri balloon	3[43,44,46]	65	87.4 (76.7–95.2)	10[47–53,55,59,61]	495	83.5 (78.5–88.0)	34	2080	82.9 (79.4-86.1)	47	2640	83.2 (80.5-85.8)
Condom UBT	4[43–46]	260	82.0 (77.2–86.4)	2[58,60]	44	93.6 (80.3–99.7)	15	1002	91.9 (89.7-93.9)	21	1306	90.4 (87.7-92.8)

CI, confidence interval; *UBT*, uterine balloon tamponade.

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SUPPLEMENTARY TABLE 8

Comparison of success rates between Bakri balloon and condom uterine balloon tamponade in postpartum hemorrhage due to uterine atony

	Randomized controlled trials			Nonrandomized studies			Case series			Overall		
Type of UBT	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)
Vaginal birth												
Bakri balloon	1[44]	33	90.9 (81.1–100.0)	-	-	-	1	108	74.1 (65.8–82.3)	2	72	79.1 (52.3–96.6)
Condom UBT	2[43,44]	90	83.7 (75.5–90.5)	1[58]	30	90.0 (79.3–100.0)	3	166	87.6 (77.9–94.7)	6	286	87.4 (83.3–90.9)
Cesarean delivery												
Bakri balloon	1[41]	25	80.0 (64.3–95.7)	2[48,59]	60	74.2 (62.7–84.2)	-	-	-	3	85	75.6 (66.2–84.0)
Condom UBT	-	-	-	-	-	-	-	-	-	-	-	-
Unknown mode of delivery												
Bakri balloon	-	-	-	4[47,50,52,55]	176	87.0 (81.7–91.5)	19	649	83.8 (77.5–89.3)	23	825	84.4 (79.4–88.8)
Condom UBT	-	-	-	1[50]	14	100.0 (73.2–100)	8	693	92.5 (90.1–94.7)	9	706	92.8 (90.4–94.9)
Overall												
Bakri balloon	2[41,44]	58	85.2 (73.4–94.1)	6[47,48,50,52,55,59]	236	83.6 (77.4–89.0)	20	688	82.9 (76.7–88.4)	28	982	83.0 (78.6–87.1)
Condom UBT	2[43,44]	90	83.7 (75.5–90.5)	2[56,60]	43	93.3 (80.3–99.6)	11	859	91.9 (89.4–94.1)	15	992	91.2 (88.6–93.4)

CI, confidence interval; *UBT*, uterine balloon tamponade.

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SUPPLEMENTARY TABLE 9

Comparison of success rates between Bakri balloon and condom uterine balloon tamponade according to setting

		Randomized controlled trials			Nonrandomized studies			Case series			Overall		
Type of UBT	Setting	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)	No. of studies	No. of women	Pooled UBT success rate (%, 95% CI)
All causes of postpartum hemorrhage													
Bakri balloon	HICs	1[41]	25	80.0 (64.3–95.7)	5[47,49–51,53]	209	87.5 (82.0–92.2)	21	1329	79.2 (75.4–82.6)	27	1563	80.8 (77.6–83.9)
	LMICs	2[42,44]	40	91.4 (81.1–97.9)	5[46,52,55,59,61]	286	78.9 (70.6–86.2)	13	751	88.8 (84.5–92.5)	20	1077	86.4 (82.4–89.9)
Condom UBT	HICs	-	-	-	-	-	-	-	-	-	-	-	-
	LMICs	4[43–46]	260	82.0 (77.2–86.4)	2[58,60]	44	93.6 (80.3–99.7)	15	1002	91.9 (89.7–93.9)	21	1306	90.4 (87.7–92.8)
Uterine atony alone													
Bakri balloon	HICs	1[41]	25	80.0 (64.3–95.7)	2[47,50]	86	83.0 (74.5–90.1)	13	523	77.6 (70.7–83.8)	16	634	78.4 (73.0–83.4)
	LMICs	1[44]	33	90.9 (81.1–100)	4[46,52,55,59]	150	83.4 (73.1–91.7)	7	165	90.9 (82.0–96.9)	12	348	88.1 (82.1–93.0)
Condom UBT	HICs	-	-	-	-	-	-	-	-	-	-	-	-
	LMICs	2[43,44]	90	83.7 (75.5–90.5)	2[58,60]	43	93.3 (80.3–99.6)	11	859	91.9 (89.4–94.1)	15	992	91.2 (88.6–93.4)

CI, confidence interval; *HICs*, high-income countries; *LMICs*, low- and middle-income countries; *UBT*, uterine balloon tamponade.

Suarez et al. Uterine balloon tamponade for treating postpartum hemorrhage. Am J Obstet Gynecol 2020.

Alydia

Bakri Postpartum Balloon Dimensional Measurements

Device Measured:

(b)(4)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 28, 2020, at 10:16 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

>

(b)(4) Deficiencies

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

> OPEQ: Office of Product Evaluation and Quality

> CDRH | Food and Drug Administration

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

> <image001.png> <http://www.fda.gov/>

>

> <image002.jpg> <https://www.facebook.com/FDA> <image003.jpg>
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>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Friday, August 28, 2020 1:10 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

(b)(4) Deficiencies

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

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>

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>

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> On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov
<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello,

>

(b)(4) Deficiencies

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

> OPEQ: Office of Product Evaluation and Quality

> CDRH | Food and Drug Administration

>

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

> <image001.png> <http://www.fda.gov/>

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> <image002.jpg> <https://www.facebook.com/FDA> <image003.jpg>
<https://twitter.com/US_FDA> <image004.jpg>
<http://www.youtube.com/user/USFoodandDrugAdmin> <image005.jpg>
<http://www.flickr.com/photos/fdaphotos/> <image006.jpg>
<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>

>

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<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

>

> From: Cindy Domecus <domecusconsulting@comcast.net
<mailto:domecusconsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 6:36 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

(b)(4) Deficiencies

(b)(4) Deficiencies

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

>

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>

>

> On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello Cindy,

>

(b)(4) Deficiencies

(b)(4) Deficiencies

>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
> OPEQ: Office of Product Evaluation and Quality
> CDRH | Food and Drug Administration
>
> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 10:41 AM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re [(b)(4) Deficiencies] (K201199/S001)

>

> Hello Reginald,

>

> Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> [(b)(6)] (cell)

>

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>

> On Aug 27, 2020, at 4:47 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov
<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello Cindy,

>

> Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

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> CDRH | Food and Drug Administration

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> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

> <image007.png> <http://www.fda.gov/>

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> <image008.jpg> <https://www.facebook.com/FDA> <image009.jpg>
<https://twitter.com/US_FDA> <image010.jpg>
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<http://www.flickr.com/photos/fdaphotos/> <image012.jpg>
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<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

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> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 12:50 AM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

> Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

>

>

>

>

> On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello,

>

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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> CDRH | Food and Drug Administration

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<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

>

(b)(4) Deficiencies

Hello Reginald,

Thank you for your communication. I am writing to confirm receipt and to let you know that we will provide the requested information by tomorrow morning @11:00 ET. I will reach out with any questions as we prepare our response.

Regards,

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:
>
> Hello,
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(b)(4) Deficiencies

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(b)(4) Deficiencies

> Thanks,
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> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
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> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: March 31, 2019

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable check box.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	(see attached list)	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Kathryn D. Wine, MPH	Vice President, Clinical Operations
FIRM/ORGANIZATION Alydia Health	
SIGNATURE (b)(6)	DATE *(mm/dd/yyyy)* 05/01/2020

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Do NOT send your completed form to the PRA Staff email address below.

Department of Health and Human Services
Food and Drug Administration
Office of Operations
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

List of Investigators for Form 3454

Investigator	Site

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(b)(6)

(b)(6)

(b)(4) SAS FILENARRATIVE

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SECTION 3: COVER LETTER

Included in this section is the cover letter for this 510(k).

May 1, 2020

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: 510(k) Notification: Traditional 510(k)
Jada® System

Attn: Sharon Andrews
Director
Division of Health Technology 3 B (Reproductive and Urology Devices)
Office of Health Technology 3 (OHT 3: Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors)

Dear Ms. Andrews and 510(k) Review Team,

In accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 807.81(a)(2), Alydia Health is submitting the enclosed premarket notification for its Jada System indicated for use as follows:

> The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

This premarket notification was prepared according to the guidelines provided by FDA on its website and its guidance titled "Guidance for Industry and Staff: Format for Traditional and Abbreviated 510(k)s" (Document issued on August 12, 2005). Additionally, this 510(k) was prepared according to the guidance for Traditional 510(k)s in FDA's "Refuse to Accept Policy for 510(k)s, Guidance for Industry and Food and Drug Administration Staff" (Document issued on September 13, 2019). A completed checklist from this Refuse to Accept (RTA) guidance document is included in this submission in **Section 4. Completed Acceptance Checklist** and indicates where in the submission each checklist item can be found. The requested information pursuant to these guidance documents is provided below and within this 510(k), as noted in the checklist.

A hard copy of the signed cover letter and one eCopy of the entire 510(k) are provided herein. The eCopy was prepared in accordance with FDA's December 16,

2019 guidance titled "eCopy Program for Medical Device Submissions, Guidance for Industry and Food and Drug Administration Staff."

The information recommended for inclusion in the cover letter is provided in **Tables 3-1 and 3-2** below.

Table 3-1. Administrative and Regulatory Information

510(k) Owner	Colby Holtshouse Interim CEO Alydia Health 3495 Edison Way Menlo Park, CA 94025 Phone: 650-275-3772 Fax: 415-354-3473 colby@alydiahealth.com
Submission Correspondent	Cindy Domecus, R.A.C. (US & EU) Principal, Domecus Consulting Services LLC Regulatory Consultant to Alydia Health 1171 Barroilhet Drive Hillsborough, CA 94010 Office: 650-343-4813 Mobile: (b)(6) Fax: 650-343-7822 DomecusConsulting@comcast.net
Establishment Registration	Alydia Health will register its establishment within 30 days of marketing the device in the U.S.
Common Name	Intrauterine Tamponade Balloon
Trade Name	Jada System
Classification Name	21 CFR § 884.4530, Obstetric-Gynecologic Specialized Manual Instrument, Product Code OQY, Class II
Review Panel	Obstetrics/Gynecology
Reason for 510(k)	The basis for this submission is the planned commercial distribution of a new medical device.
Predicate Device	The predicate device is the Bakri® Postpartum Balloon, most recently cleared under K170622.
Special Controls	There are no special controls that are applicable to the subject device.
Confidentiality	Alydia Health considers the information described in this 510(k) premarket notification and all related exhibits to be confidential commercial information and therefore exempt from public disclosure. We request that this notification and its contents be treated as confidential in accordance with 21 CFR § 807.95.

Table 3-2. Design and Use of the Device

Question	Yes	No
Is the device intended for prescription use (21 CFR 801 Subpart D)?	X	
Is the device intended for over-the-counter use (21 CFR 807 Subpart C)?		X
Does the device contain components derived from a tissue or other biologic source?		X
Is the device provided sterile?	X	
Is the device intended for single use?	X	
Is the device a reprocessed single use device?		X
If yes, does this device require reprocessed validation data?	N/A	
Does the device contain a drug?		X
Does the device contain a biologic?		X
Does the device use software?		X
Does the submission include clinical information?	X	
Is the device implanted?		X

Contained in this 510(k) is the information needed to support a substantial equivalence finding for the Jada System. The Jada System is substantially equivalent to the predicate device cited herein. As described in this submission, the intended use of the Jada System is the same as the predicate device. Further, the subject and predicate devices have similar technological characteristics. The differences between the subject and the predicate devices do not raise different types of safety or effectiveness questions. We believe that the information contained in this submission is sufficient to enable a finding that the Jada System is substantially equivalent to the predicate device.

Please direct any questions or requests for additional information to me at the below numbers or by electronic mail at: domecusconsulting@comcast.net. We thank the FDA review team for its review of this application.

Sincerely,

Cindy Domecus, R.A.C. (US & EU)
Principal, Domecus Consulting Services LLC
Regulatory Consultant to Alydia Health
Office: 650-343-4813 | Mobile: (b)(6) | Fax: 650-343-7822

Enclosure: One paper copy of signed cover letter and one eCopy of entire 510(k) submission

(b)(4)

(b)(4) Protocol

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Ah, understood! Thanks for the clarification Reginald. We look forward to working with you as FDA completes its review of our file.

Take care,

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 2:21 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

She has not left FDA. Due to an increased workload during the COVID-19 public health emergency, some files were reassigned.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 21, 2020 5:08 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thanks for the update! Did Dr. Nandy leave FDA (just curious)?

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 2:04 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

I am replacing Dr. Nandy as the lead reviewer for this file and will complete the review for the Jada System. I have discussed the file with Dr. Nandy to ensure our review is consistent. Please let me know if you have any questions.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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CDRH | Food and Drug Administration

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Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 21, 2020 4:20 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thank you for your reivew of our file. I am writing to confirm receipt of your below request and that we will respond by the requested date. We stand ready to respond to any further questions FDA may have as the review team completes its review of our file.

Can you please clarify if you are replacing Poulomi as the lead reviewer for this file or is she just on vacation at this time? Thanks.

Have a nice weekend.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Clinical Investigation Report

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EXHIBIT 14.A: Jada System Instructions for Use

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Hello Reginald,

Thank you for your communication. I am writing to confirm receipt and to let you know that we will provide the requested information by tomorrow morning @11:00 ET. I will reach out with any questions as we prepare our response.

Regards,

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4843 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

As I mentioned during our phone call on Monday, we have some labeling and clarification requests for you to address for the Jada System file. **If possible, please provide a response by 11 am EDT on Thursday, August 27, 2020.** Please do not hesitate to call me if you have any questions or I can clarify any of our requests.

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

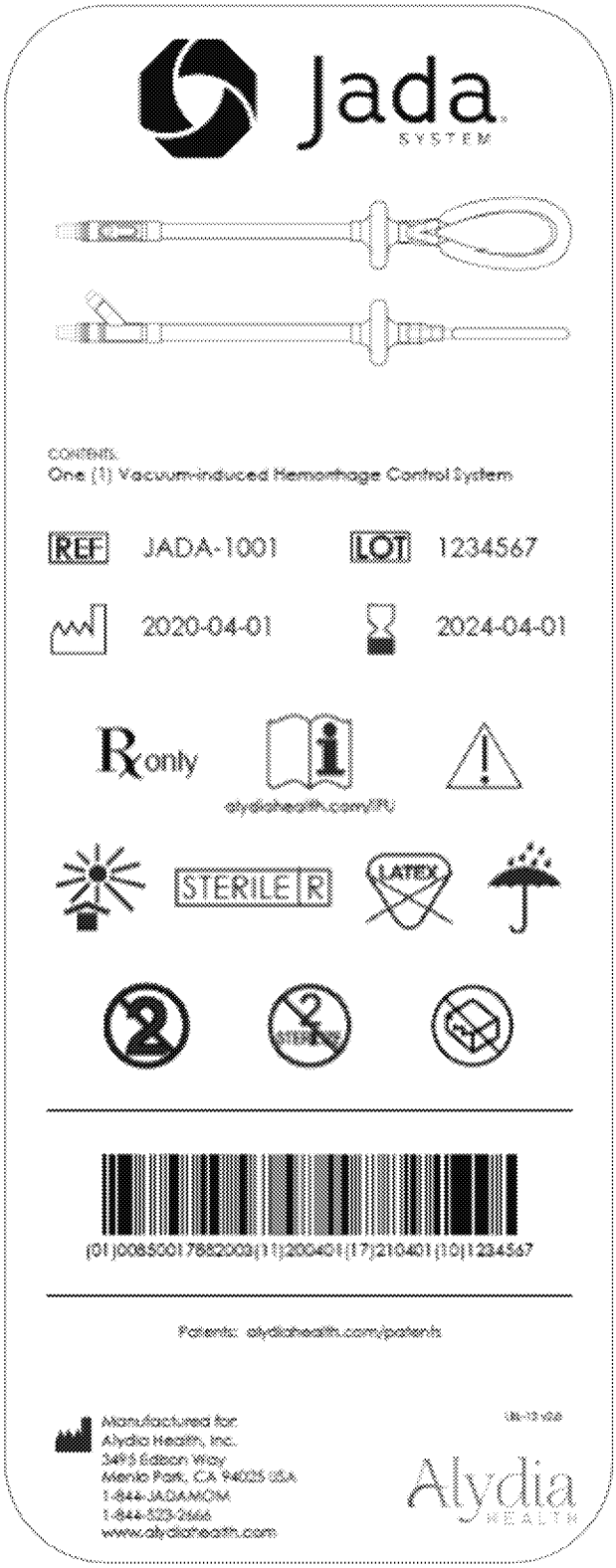
White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

<image001.png>

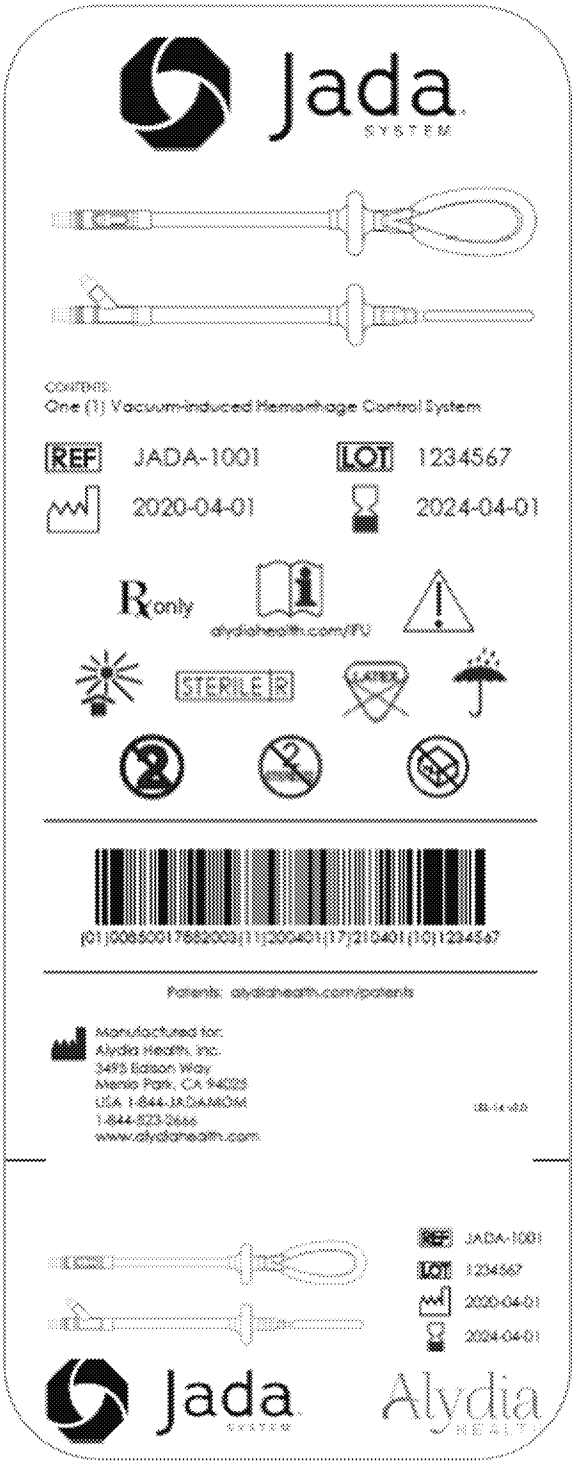
<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

Exhibit 22: Clean copy of revised Jada System Product Labels

Jada System Pouch Label



Jada System Carton Label



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On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

As I mentioned during our phone call on Monday, we have some labeling and clarification requests for you to address for the Jada System file. **If possible, please provide a response by 11 am EDT on Thursday, August 27, 2020.** Please do not hesitate to call me if you have any questions or I can clarify any of our requests.

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

Hello Reginald,

Would you mind confirming receipt of my below email sent on Saturday? I have received a temporary delivery failure notice for the K number email address, but not yours. Nevertheless, I wanted to make sure you received it. Since the beginning of COVID, I have noticed that emails to FDA donâ€™t always get through on first attempt. I imagine that your servers are overloaded with pandemic-related communications.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> Begin forwarded message:

>

> From: Cindy Domecus <domecusconsulting@comcast.net>

> Subject: Re: Request for information for Jada System (K201199/S001)

> Date: August 22, 2020 at 7:06:42 PM PDT

> To: "Avery, Reginald" <Reginald.Avery@fda.hhs.gov>

> Cc: "K201199@docs.fda.gov" <K201199@docs.fda.gov>

>

> Hello Reginald,

(b)(4) Deficiencies

>

> Thank you for your continued reivew of our file.

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (650) 773-3445 (cell)

>

>

>

>

>

>

>> On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>>

>> Hello,

>>

>> I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? If possible, please provide a response by noon on Tuesday, August 25, 2020.

>>

(b)(4) Deficiencies

>>

>> Do not hesitate to contact me if you have any questions or concerns.

>>

>> Thanks,

>> Reginald

>>

>> Reginald Avery, Ph.D.

>> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>>

>> DHT3B: Division of Reproductive, Gynecology and Urology Devices

>> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

>> OPEQ: Office of Product Evaluation and Quality

>> CDRH | Food and Drug Administration

>>

>> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

>> Ph: 240-402-6152

>> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

>> <image013.png> <http://www.fda.gov/>

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>> <image014.jpg> <https://www.facebook.com/FDA> <image015.jpg>
<https://twitter.com/US_FDA> <image016.jpg>
<http://www.youtube.com/user/USFoodandDrugAdmin> <image017.jpg>
<http://www.flickr.com/photos/fdaphotos/> <image018.jpg>
<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>

>>

>> Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received:
https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E
<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

K201199

Alydia HEALTH

May 1, 2020

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: 510(k) Notification: Traditional 510(k)
Jada® System

Attn: Sharon Andrews
Director
Division of Health Technology 3 B (Reproductive and Urology Devices)
Office of Health Technology 3 (OHT 3: Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors)

Dear Ms. Andrews and 510(k) Review Team,

In accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 807.81(a)(2), Alydia Health is submitting the enclosed premarket notification for its Jada System indicated for use as follows:

> The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

This premarket notification was prepared according to the guidelines provided by FDA on its website and its guidance titled "Guidance for Industry and Staff: Format for Traditional and Abbreviated 510(k)s" (Document issued on August 12, 2005). Additionally, this 510(k) was prepared according to the guidance for Traditional 510(k)s in FDA's "Refuse to Accept Policy for 510(k)s, Guidance for Industry and Food and Drug Administration Staff" (Document issued on September 13, 2019). A completed checklist from this Refuse to Accept (RTA) guidance document is included in this submission in **Section 4. Completed Acceptance Checklist** and indicates where in the submission each checklist item can be found. The requested information pursuant to these guidance documents is provided below and within this 510(k), as noted in the checklist.

A hard copy of the signed cover letter and one eCopy of the entire 510(k) are provided herein. The eCopy was prepared in accordance with FDA's December 16,

2019 guidance titled "eCopy Program for Medical Device Submissions, Guidance for Industry and Food and Drug Administration Staff."

The information recommended for inclusion in the cover letter is provided in **Tables 3-1 and 3-2** below.

Table 3-1. Administrative and Regulatory Information

510(k) Owner	Colby Holtshouse Interim CEO Alydia Health 3495 Edison Way Menlo Park, CA 94025 Phone: 650-275-3772 Fax: 415-354-3473 colby@alydiahealth.com
Submission Correspondent	Cindy Domecus, R.A.C. (US & EU) Principal, Domecus Consulting Services LLC Regulatory Consultant to Alydia Health 1171 Barroilhet Drive Hillsborough, CA 94010 Office: 650-343-4813 Mobile: (b)(6) Fax: 650-343-7822 DomecusConsulting@comcast.net
Establishment Registration	Alydia Health will register its establishment within 30 days of marketing the device in the U.S.
Common Name	Intrauterine Tamponade Balloon
Trade Name	Jada System
Classification Name	21 CFR § 884.4530, Obstetric-Gynecologic Specialized Manual Instrument, Product Code OQY, Class II
Review Panel	Obstetrics/Gynecology
Reason for 510(k)	The basis for this submission is the planned commercial distribution of a new medical device.
Predicate Device	The predicate device is the Bakri® Postpartum Balloon, most recently cleared under K170622.
Special Controls	There are no special controls that are applicable to the subject device.
Confidentiality	Alydia Health considers the information described in this 510(k) premarket notification and all related exhibits to be confidential commercial information and therefore exempt from public disclosure. We request that this notification and its contents be treated as confidential in accordance with 21 CFR § 807.95.

Table 3-2. Design and Use of the Device

Question	Yes	No
Is the device intended for prescription use (21 CFR 801 Subpart D)?	X	
Is the device intended for over-the-counter use (21 CFR 807 Subpart C)?		X
Does the device contain components derived from a tissue or other biologic source?		X
Is the device provided sterile?	X	
Is the device intended for single use?	X	
Is the device a reprocessed single use device?		X
If yes, does this device require reprocessed validation data?	N/A	
Does the device contain a drug?		X
Does the device contain a biologic?		X
Does the device use software?		X
Does the submission include clinical information?	X	
Is the device implanted?		X

Contained in this 510(k) is the information needed to support a substantial equivalence finding for the Jada System. The Jada System is substantially equivalent to the predicate device cited herein. As described in this submission, the intended use of the Jada System is the same as the predicate device. Further, the subject and predicate devices have similar technological characteristics. The differences between the subject and the predicate devices do not raise different types of safety or effectiveness questions. We believe that the information contained in this submission is sufficient to enable a finding that the Jada System is substantially equivalent to the predicate device.

Please direct any questions or requests for additional information to me at the below numbers or by electronic mail at: domecusconsulting@comcast.net. We thank the FDA review team for its review of this application.

Sincerely,

(b)(6)

Cindy Domecus, R.A.C. (US & EU)
Principal, Domecus Consulting Services LLC
Regulatory Consultant to Alydia Health
Office: 650-343-4813 | Mobile: (b)(6) | Fax: 650-343-7822

Enclosure: One paper copy of signed cover letter and one eCopy of entire 510(k) submission

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SECTION 17: BIOCOMPATIBILITY

The Jada System is a direct patient contact device. Provided below in **Table 17-1** is a list identifying each patient-contacting device component and associated materials of construction for each component, as well as the contact classification per ISO 10993-1 Fifth Edition 2018-08: Biological Evaluation of Medical Devices – Part 1 Evaluation and Testing Within a Risk Management Process.

Table 17-1. Patient-Contacting Components

Device Component	Material	Contact Classification
Tube (Main Shaft)	Medical grade silicone	Surface device, Breached or compromised surface
Cervical Seal (Occlusion Balloon)	Medical grade silicone + Colorant (b)(4)	Surface device, Breached or compromised surface
Tubing Connector	Medical grade silicone	Surface device, Breached or compromised surface
Loop Tube (Drain Tube)	Medical grade silicone	Surface device, Breached or compromised surface
Shield (Drain Tube Shield)	Medical grade silicone + Colorant (b)(4)	Surface device, Breached or compromised surface

The Jada System was subjected to the following biocompatibility tests based on ISO 10993-1 Fifth Edition 2018-08: Biological Evaluation of Medical Devices – Part 1 Evaluation and Testing Within a Risk Management Process and FDA's guidance document issued June 16, 2016 Use of International Standard ISO 10993-1 "Biological Evaluation of Medical Devices – Part 1 Evaluation and Testing Within a Risk Management Process".:

- Maximization Sensitization (polar and non-polar)
- Vaginal Irritation (polar and non-polar)
- Systemic Toxicity (polar and non-polar)
- Cytotoxicity
- Material Mediated Pyrogenicity
- Hemocompatibility[1]

The results of this testing are summarized below in **Table 17-2** and the full test reports including 1) identification and description of test article, 2) methods, 3) pass/fail criteria, and 4) results are provided in **Exhibits 17.A-17.F**, as noted below.

Table 17-2. Summary of Biocompatibility Testing

Test	Test Method	Result
ISO Guinea Pig Maximization Sensitization Test (b)(4) (**Exhibit 17.A**)	ISO 10993-10 Biological Evaluation of Medical Devices – Part 10: Test of Irritation and Skin Sensitization. (b)(4)	(b)(4)
ISO Vaginal Irritation Study in Rabbits (b)(4) (**Exhibit 17.B**)	ISO 10993-10 Biological Evaluation of Medical Devices – Part 10: Test of Irritation and Skin Sensitization. (b)(4)	
ISO Systemic Toxicity Study in Mice (b)(4) (**Exhibit 17.C**)	ISO 10993-11, Biological Evaluation of Medical Devices – Part 11: Test for Systemic Toxicity. (b)(4)	
Cytotoxicity – Minimal Essential Media (MEM) Elution (b)(4) (**Exhibit 17.D**)	ISO 10993-5, Biological Evaluation of Medical Devices – Part 5: Tests for In-Vitro Cytotoxicity	
Material Mediated Rabbit Pyrogen Test (b)(4) (**Exhibit 17.E**)	ISO 10993-11 Biological Evaluation of Medical Devices – Part 11: Tests for Systemic Toxicity ISO 10993-12, 2012,	The test article is considered non-

	Biological Evaluation of Medical Devices – Part 12: Sample Preparation and Reference Materials	(b)(4)
ASTM Hemolysis (Extract Method)[1]	ASTM F756-17, 2017, Standard Practice for Assessment of Hemolytic Properties of Materials	
(b)(4)		
(**Exhibit 17.F**)	ISO 10993-4:2017 Biological Evaluation of Medical Devices – Part 4: Selection of tests for the interaction with blood	

[1] This test is not required for the contact classification of the subject device, but was conducted in advance of FDA's clarification of the appropriate contact classification for the subject device (email dated April 27, 2020), so is included here for the sake of completeness since the testing was performed.

510(k) Summary – K201199

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Hello Reginald,

Will reply by 2:30 ET as requested!

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:
>
> Hello,
>

(b)(4) Deficiencies

>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
> OPEQ: Office of Product Evaluation and Quality
> CDRH | Food and Drug Administration
>
> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
> Ph: 240-402-6152
> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>
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<https://twitter.com/US_FDA> <image004.jpg>
<http://www.youtube.com/user/USFoodandDrugAdmin> <image005.jpg>
<http://www.flickr.com/photos/fdaphotos/> <image006.jpg>
<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>
>
> Excellent customer service is important to us. Please take a moment to provide

feedback regarding the customer service you have received:
https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E
<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

>

> From: Cindy Domecus <domecusconsulting@comcast.net
<mailto:domecusconsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 6:36 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies K201199/S001)

>

> Hello Reginald,

>

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

>

>

>

>

> On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello Cindy,

>

(b)(4) Deficiencies

(b)(4) Deficiencies

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

> OPEQ: Office of Product Evaluation and Quality

> CDRH | Food and Drug Administration

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

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> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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<https://twitter.com/US_FDA> <image004.jpg>
<http://www.youtube.com/user/USFoodandDrugAdmin> <image005.jpg>
<http://www.flickr.com/photos/fdaphotos/> <image006.jpg>
<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>

>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E
<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 10:41 AM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

> Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

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>

>

> On Aug 27, 2020, at 4:47 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>> wrote:

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> Hello Cindy,

>

> Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

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> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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> DHT3B: Division of Reproductive, Gynecology and Urology Devices

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> CDRH | Food and Drug Administration

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

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>

>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 12:50 AM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

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> Principal

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(b)(6) (cell)

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(b)(4) Deficiencies

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? **If possible, please provide a response by noon on Tuesday, August 25, 2020.**

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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(b)(4)

Sponsor:
(b)(4)
Alydia Health, Inc.
3495 Edison Wy
Menlo Park, CA 94025

ASTM Hemolysis (Extract Method) GLP Report

Test Article:
Purchase Order:
Study Number:
Study Received Date:
Testing Facility:

(b)(4)

Test Procedure(s):
Deviation(s):

(b)(4)

(b)(4)

(b)(4)

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

(b)(4) Testing

Hello Cindy,

She has not left FDA. Due to an increased workload during the COVID-19 public health emergency, some files were reassigned.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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* * * * *

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 21, 2020 5:08 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thanks for the update! Did Dr. Nandy leave FDA (just curious)?

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 2:04 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

I am replacing Dr. Nandy as the lead reviewer for this file and will complete the review for the Jada System. I have discussed the file with Dr. Nandy to ensure our review is consistent. Please let me know if you have any questions.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 21, 2020 4:20 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thank you for your reivew of our file. I am writing to confirm receipt of your below request and that we will respond by the requested date. We stand ready to respond to any further questions FDA may have as the review team completes its review of our file.

Can you please clarify if you are replacing Poulomi as the lead reviewer for this file or is she just on vacation at this time? Thanks.

Have a nice weekend.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

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Reginald

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

Hello Reginald,

Will reply by 2:30 ET as requested!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4313 (office)
(b)(6) (cell)

On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Ph: 240-402-6152
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From: Cindy Domecus <domecusconsulting@comcast.net>
Sent: Thursday, August 27, 2020 6:36 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R (b)(4) Deficiencies K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

(b)(4) Deficiencies

Thanks,
Reginald

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 10:41 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R **(b)(4) Deficiencies** (K201199/S001)

Hello Reginald,

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> Subject: Re: (b)(4) Deficiencies (K201199/S001)

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<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 12:50 AM

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> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies (K201199/S001)

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> Principal

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<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

SECTION 18: SOFTWARE & CYBERSECURITY

The subject device does not include software or contain any external wired and/or wireless communication interfaces, so these elements of FDA's 510(k) Acceptance Checklist are not applicable.

(b)(4)

(b)(4) Draft Manual

Exhibit 9: Redlined copy of revised Jada System Instructions for Use

(b)(4) Draft Manual

(b)(4) Draft Manual

(b)(4) Draft Manual

(b)(4) Draft Manual

(b)(4) Draft Manual

(b)(4) Draft Manual

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DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION **MEDICAL DEVICE USER FEE COVER SHEET**	PAYMENT IDENTIFICATION NUMBER: (b)(4) Write the Payment Identification number on your check.

A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ucm370879.htm

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)	2. CONTACT NAME
Alydia Health, Inc. 3495 Edison Way Menlo Park California CA 94025 US 1.1 EMPLOYER IDENTIFICATION NUMBER (EIN) *****6173	Claudia Orellana 2.1 E-MAIL ADDRESS claudia@alydiahealth.com 2.2 TELEPHONE NUMBER (include Area code) 408-4065916 2.3 FACSIMILE (FAX) NUMBER (Include Area code)

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm345263.htm

Select an application type:	3.1 Select a center
[X] Premarket notification(510(k)); except for third party	[X] CDRH
[ ] 513(g) Request for Information	[ ] CBER
[ ] Biologics License Application (BLA)	3.2 Select one of the types below
[ ] Premarket Approval Application (PMA)	[X] Original Application
[ ] Modular PMA	Supplement Types:
[ ] Product Development Protocol (PDP)	[ ] Efficacy (BLA)
[ ] Premarket Report (PMR)	[ ] Panel Track (PMA, PMR, PDP)
[ ] 30-Day Notice	[ ] Real-Time (PMA, PMR, PDP)
[ ] De Novo Request	[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)

[X] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA

NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number: (b)(4)

5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?

[X] YES (All of your establishments have registered and paid the fee, or this is your first device and you will register and pay the fee within 30 days after entering into an operation that requires you to register and submit device listing information.)

[ ] NO (If you currently market a medical device and your establishment is required to register and submit device listing information, FDA will not accept your submission until you have paid all fees due to FDA. See http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/ucm053165.htm for additional information)

6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.

[ ] This application is the first PMA submitted by a qualified small business, including any affiliates	[ ] The sole purpose of the application is to support conditions of use for a pediatric population
[ ] This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only	[ ] The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).

[ ] YES [X] NO

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8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

(b)(4) 26-Feb-2020

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

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Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 27, 2020, at 4:47 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

>

> Hello Cindy,

>

> Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

> OPEQ: Office of Product Evaluation and Quality

> CDRH | Food and Drug Administration

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 12:50 AM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

> Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

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>

>

>

> On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov
<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello,

>

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

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> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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CLINICAL STUDY REPORT

APPENDIX 9.1

CLINICAL INVESTIGATION PLAN (PROTOCOL)

PEARLE: Prospective, Single Arm, Pivotal Clinical Trial Designed to Assess the Safety and Effectiveness of the Jada™ System In Treating Primary Postpartum Hemorrhage

PEARLE

Short title:	PEARLE Study		
Test device:	Jada System		
Clinical study phase:	Pivotal	Version Date:	25FEB2019
Study no.:	PPH-02	Version No.:	CIP-01 v2.6
Sponsor:	Alydia Health 3475 Edison Way, Suite J Menlo Park, California 94025 USA		
Study Principal Investigator:	Mary D'Alton, MD Columbia University		
Sponsor Contact:	Kathryn Wine, MPH Vice President of Clinical Operations kathryn@alydiahealth.com 415.990.4104		
Independent Medical Monitor:	Christopher Grover, MD Clinical Professor of Medicine, UC Davis cgrover@sbcglobal.net 650.960.5159		

This study shall be conducted under Institutional Review Board approval and in compliance with United States (U.S.) Food and Drug Administration (FDA) regulations, ISO 14155 (2011), the ethical principles that have their origin in the Declaration of Helsinki and all applicable privacy requirements.

Investigator Certification

Prior to participation in the PEARLE Study as an Investigator, I understand that I must obtain written approval from my Institutional Review Board (IRB).

As an Investigator, I must also:

1. Conduct the study in accordance with the study protocol, United States (U.S.) Food and Drug Administration (FDA) regulations (21 Code of Federal Regulations (CFR) Parts 812, 50, 54, & 56), ISO 14155, the ethical principles that have their origin in the Declaration of Helsinki and all applicable privacy requirements.
2. Complete required study training prior to study participation.
3. Ensure that the study is not commenced until IRB approval has been obtained.
4. Ensure that written informed consent is obtained from each subject prior to enrollment into the study, using the most recently IRB-approved subject Informed Consent Form.
5. Provide all required data and reports and agree to allow source document verification of study data with subject's medical records.
6. Allow Sponsor personnel and its designees, as well as U.S. FDA representatives and representatives from other public health agencies, to inspect and copy any documents pertaining to this clinical investigation.

Investigator Signature
I have read and understand the contents of the PEARLE Study protocol (CIP-01 v2.6) and agree to abide by the requirements set forth in this document.

_____	_____
Signature	Date
_____	_____
Printed name	Institution

Revision History

Version Number	Description of Change	Effective Date
Version 1	Initial release. Note: Initial protocol numbered CIV-PIVOTAL-1.0. Version 030716/S2.	7 April 2016
Version 1.1	Change to informed consent section to allow informed consent to be obtained after the onset of labor. Note: Protocol revision numbered CIV-PIVOTAL-1.1.	20 December 2016
Version 2	Protocol rewrite to change the primary endpoint and statistical analysis plan. Editorial and administrative changes also made. Note: Protocol revision numbering changed to PPH-02 version 2.	24 February 2017
Version 2.1	Minor edits to protocol to clarify primary effectiveness endpoint, add a secondary endpoint for maternal morbidity, clarify the definition of time to hemorrhage cessation, and clarify the statistics section. Edits made in response to FDA Study Design Considerations identified in February 24, 2017 approval letter for S006.	11 April 2017
Version 2.2	Minor edits to protocol to clarify statistical analysis in section 5.3.1. Edits made in response to FDA Study Design Considerations identified in the IDE Approval Letter dated April 11, 2017 for S007.	7 July 2017
Version 2.3	Minor edits to protocol to clarify statistical analysis and sample size in Section 5.3. Edits made in response to FDA Study Design Considerations identified in the IDE Approval Letter dated July 7, 2017 for S008. Additional minor edits made to cover sheet and Section 9 for study consistency.	6 November 2017
Version 2.4	Minor edits to protocol to clarify statistical analysis and sample size in Section 5.3. Edits made in response to FDA Study Design Considerations identified in the IDE Approval Letter dated November 6, 2017 for S010.	19 December 2017
Version 2.5	Edits to clarify inclusion and exclusion criteria and the schedule of assessments. Added the consent bracelet as an identifier for consented subjects. Eliminated OUS sites and increased number of sites to 12. Edits to the risk	17 July 2018

	and potential benefits sections and to the name of the Device. Updated the contact information and other minor corrections. A section on training was included. The secondary endpoint of time to PPH control was refined and the steps of Device use were clarified.	
Version 2.6	Updated name of Sponsor to Alydia Health and name of product to Jada System. Updated picture of consent bracelet. Updated maximum number of sites to 20 in the U.S. or O.U.S. Revised secondary endpoints. Revised one inclusion and one exclusion criterion. Revised poolability section. Added study poster as optional recruitment tool.	25FEB2019

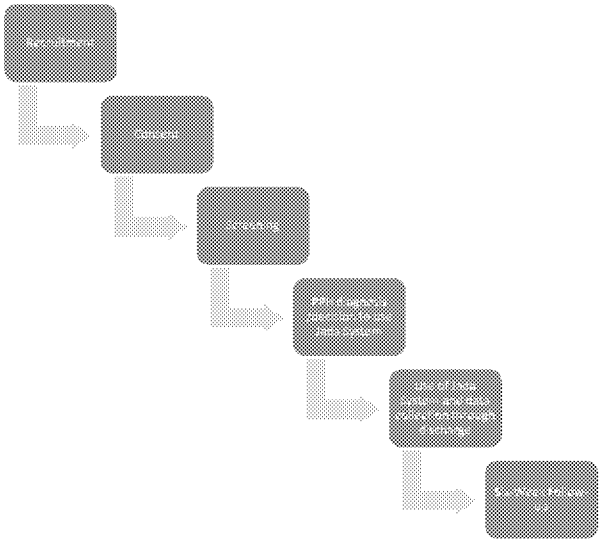
List of abbreviations

Abbreviation	Definition
ADE	Adverse device effect
AE	Adverse event
AMTSL	Active Management of the Third Stage of Labor
CBC	Complete blood count
CRF	Case report form
FDA	Food and Drug Administration
FIH	First-in-Human
GCP	Good clinical practices
GMP	Good manufacturing practices
ICF	Informed consent form
ICU	Intensive care unit
IDE	Investigational device exception
IFU	Instructions for use
IRB	Institutional review board
ISO	International Standards Organization
IV	Intravenous
ITT	Intent to Treat
O.U.S.	Outside the United States
PPH	Postpartum hemorrhage
SADE	Serious adverse device event
SAE	Serious adverse event
SAS	Statistical Analysis System
UADE	Unanticipated adverse device effect
U.S.	United States
WHO	World Health Organization

Table of Contents

1.0 Study Summary

Title:	Prospective, Single Arm, Pivotal Clinical Trial Designed to Assess the Safety and Effectiveness of the Jada System In Treating Primary Postpartum Hemorrhage ("PPH")
Short Title:	PEARLE Study
Design:	Prospective, single-arm, literature-controlled, multi-center study
Purpose:	Evaluate the safety and effectiveness of the Jada System in the control and reduction of primary postpartum hemorrhage.
Inclusion Criteria:	1. Adult Female, 18 years of age or older at time of consent. 2. Able to understand and provide informed consent to participate in the study. 3. Diagnosis of PPH with suspected atony within 24 hours after vaginal or c-section delivery. 4. EBL, to be determined when investigator is ready to have the Jada peel pack opened: Vaginal delivery: 500 – 1500 ml EBL or C-section delivery: 1000 – 1500 ml EBL 5. Failed first-line intervention of uterotonics and uterine massage/bimanual uterine massage to stop bleeding. *Note: Uterotonic administration may continue concomitant with and post Jada use, as long as such use does not exceed the maximum dose of the drug.*
Exclusion Criteria:	1. EBL >1500ml, to be determined when investigator is ready to have the Jada peel pack opened. 2. Delivery at a gestational age < 34 weeks. 3. For C-sections: Cervix < 3 cm dilated before use of Jada. 4. PPH that the investigator determines to require more aggressive treatment, including any of the following: a) hysterectomy; b) b-lynch suture; c) uterine artery embolization or ligation; d) hypogastric ligation. 5. Known uterine anomaly. 6. Ongoing intrauterine pregnancy. 7. Placenta abnormality including any of the following: a) known placenta accreta; b) retained placenta with known risk factors for placenta accreta (e.g. history of prior uterine surgery, including prior c-section and placenta previa); c) retained placenta without easy manual removal. 8. Known uterine rupture. 9. Unresolved uterine inversion. 10. Subject has undergone intrauterine balloon therapy or uterine packing for tamponade treatment of this PPH prior to use of the Jada System. 11. Current cervical cancer. 12. Current purulent infection of vagina, cervix, uterus. 13. Diagnosis of coagulopathy.

Duration of Study:	It is expected to take approximately 12-18 months to enroll, treat, and follow-up all 107 subjects.
Primary Safety Endpoint:	Incidence, severity and seriousness of device-related Adverse Events (AEs).
Primary Effectiveness Endpoint:	Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use. Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy. Note: Continuation of the administration of uterotonics concomitant with and post Jada System use is standard of care and does not constitute failure of the primary effectiveness endpoint.
Statistical Analysis Plan Summary:	The primary effectiveness objective of this Pivotal Study is to show that the observed Treatment Success Rate is not worse than the rate reported in the literature. The study is considered a success when the lower bound of the two-sided Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success is greater than or equal to 73.4%.
Study Flowchart:	

2.0 Postpartum Hemorrhage Background

2.1 Definition and Prevalence of Postpartum Hemorrhage

Postpartum hemorrhage (PPH), or excessive blood loss after childbirth, is the leading cause of maternal mortality. PPH is responsible for over a quarter of maternal deaths worldwide.[1] In Africa and Asia, where most maternal deaths occur, PPH accounts for more than 30% of all maternal deaths.[3] It is estimated that PPH afflicts 6% of women giving birth.[2] Africa has the highest rate of PPH, with a

prevalence of 10.5% of women giving birth.[2] Even developed countries are challenged by this life-threatening complication of childbirth, causing 10.6% of maternal deaths in the United Kingdom, and 12% of maternal deaths in the United States.[4]

Although death is the most tragic event reported in obstetrics, severe maternal morbidity related to PPH such as surgical interventions including hysterectomy, disseminated intravascular coagulopathy, transfusions, and Intensive Care Unit (ICU) admissions, are more common than death.[4-6] PPH can also be a cause of long-term severe morbidity, and approximately 12% of women who survive PPH will have severe anemia.[12] Additionally, women who survive an event of severe PPH are significantly more likely to die in the year following the event.[34]

Primary PPH, which is PPH that occurs within 24 hours after the birth of the baby, is the most common form of major obstetric hemorrhage. The most commonly accepted definition for primary PPH is the loss of 500 ml or more of blood from the genital tract within 24 hours after the birth of a baby. Severe primary PPH is commonly defined as loss of more than 1500 ml of blood within 24 hours after the birth of a baby. Alternative standards for defining and diagnosing PPH include changes in hematocrit, rapidity of blood loss and changes in vital signs.[4,7-10]

It is difficult to predict who will develop PPH because most women who have PPH have no risk factors. Many deaths due to PPH could be prevented with timely diagnosis and intervention. A blood loss of more than 1500 ml is usually considered life threatening and triggers a full complement of emergency measures to achieve resuscitation and hemostasis. It would seem appropriate that PPH protocols activate at much lower thresholds to prevent blood loss that requires drastic measures or becomes life threatening.

2.2 Causes of Postpartum Hemorrhage

PPH may be caused by uterine atony, injury to the birth canal, retained placenta, and coagulopathy, among other etiologies.

Uterine atony, or suboptimal uterine contractions after childbirth, is the most prevalent cause, involved in 75% of primary PPH cases.[8] Normally after delivery, the smooth muscle fibers of the uterus contract and constrict the blood vessels that serve the placental bed. If the uterus does not properly contract after delivery, these blood vessels are exposed to the cavity of the uterus, leading to uterine PPH. Atony may result from prolonged labor, prolonged use of uterotonic stimulants, over-distention of the uterus, infection, placental abnormalities, or bladder distention, but the majority (80%) of women with PPH due to uterine atony will have no risk factors.[11]

2.3 Currently Available Treatment and Prevention Strategies

Organizations and associations including the World Health Organization (WHO), International Confederation of Midwives, International Federation of Gynecologists and Obstetricians, American College of Obstetricians and Gynecologists, and Royal College of Obstetricians and Gynaecologists have released guidelines for PPH prevention and management.[13,14,15-18]

The WHO guideline for the Active Management of the Third Stage of Labor (AMTSL) is recommended for all patients in order to prevent PPH. The AMTSL guideline recommends the use of oxytocin, a uterotonic, for the prevention of PPH during the third stage of labor for all births. In settings where skilled birth attendants are available, controlled cord traction may be used in vaginal births. Postpartum abdominal uterine tone assessment is recommended to identify uterine atony prior to the occurrence of PPH.

If AMTSL does not prevent the occurrence of PPH, initial management guidelines include identifying the source of the PPH and implementing appropriate interventions based on the etiology. Manual removal of the placenta is indicated for a retained placenta; vaginal and vulvar lacerations need to be repaired in parallel to treating uterine bleeding. Interventions to treat PPH due to atony generally proceed from less to more invasive. Most guidelines first recommend the use of additional uterotonic agents, which cause the uterus to contract. These medications include oxytocin (Pitocin®), prostaglandin E1/misoprostol (Cytotec®), methylergonovine (Methergine®), prostaglandin 15-methyl F2α/carboprost tromethamine (Hemabate®), and prostaglandin E2/dinoprostone (Cervidil® or Prepidil®).[13-16,24] All of these medications are available in the United States. Only oxytocin, methylergonovine, and carboprost tromethamine are approved by the US FDA specifically for PPH management.

External uterine massage and bimanual uterine massage may also be used as first-line conservative treatments in conjunction with uterotonics. These techniques encourage uterine contractions that counteract atony and assist with expulsion of retained placenta or clots. Initial PPH management also includes intravenous (IV) fluid therapy to expand volume and give access for parenteral medication.

Some institutions use tamponade methods as a second line therapy if the uterotonics fail to take effect. These methods include uterine packing, the use of multiple Foley catheters or condom catheters (not FDA cleared for the treatment of PPH), or the use of a balloon tamponade device cleared specifically for PPH. These methods create tamponade through compression of blood vessels, leading to the control of hemorrhage. Although tamponade may occur, the expansion caused by the packing materials or balloon may interfere with the normal physiologic uterine retraction and constriction of placental bed vasculature that normally follows childbirth. Thus, the uterine musculature can move back to its atonic state, causing blood loss to recur.

If initial conservative management for PPH of uterine origin fails or is slow to take effect, invasive surgical procedures are indicated. Surgical options include uterine curettage to ensure the removal of any residual products of conception, uterine de-vascularization procedures, uterine compression sutures, and, as a last resort, hysterectomy.[13-16] Surgeries can increase the risk of infection, maternal morbidity and other complications, and they may eliminate or adversely affect future fertility and pregnancy.

3.0 Device Description

3.1 Intended Use

The Jada System is intended to provide control or reduction of postpartum uterine bleeding when conservative management is warranted.

3.2 Jada System Description

The Jada System is a 40 cm long intrauterine device made of silicone. The device consists of an elliptical intrauterine loop collared by a donut shaped vacuum seal and a connecting tube that terminates in a male tubing slip vacuum port attachment (see Figure 1). The loop has twenty pores directed towards the interior of the loop that are partially covered by a shield, which creates a channel to prevent plugging with tissue or clots. The connecting tube has a seal port valve that can be attached to a syringe, allowing the vacuum seal to be filled with sterile IV fluid. The various portions of the device are soft enough to reduce the chance of injury or perforation, but firm enough for easy insertion and smooth function without kinking. The Jada is designed to attach to sterile tubing and a regulated vacuum source with an in-line graduated vacuum collection canister.

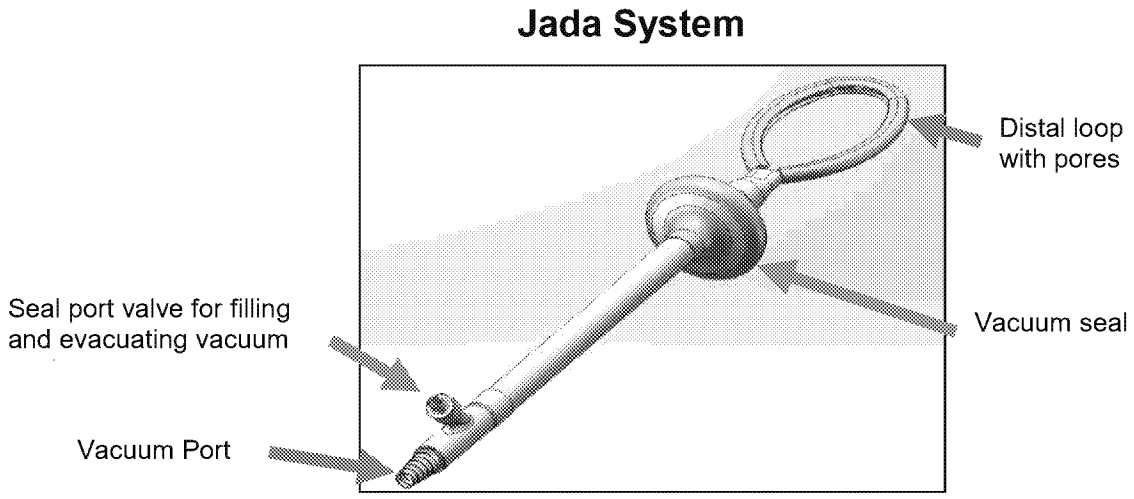


Figure 1: Jada System

3.3 Jada Overview

The Jada System is inserted into a woman's uterus transvaginally in women who have vaginal deliveries and trans-abdominally or transvaginally in women who have Cesarean sections (depending on whether PPH is diagnosed before or after the hysterotomy is closed). The shielded loop of perforated tubing is introduced in the uterine cavity. The vacuum seal is positioned in the upper vagina, against the external cervical os. The male tubing slip vacuum port attachment can then be connected to sterile tubing, regulated vacuum source, and graduated vacuum collection canister. See Figure 2.

When the vacuum seal is filled with sterile IV fluid and the vacuum is turned on, the vacuum seal ensures that a vacuum can be created in the uterine cavity.

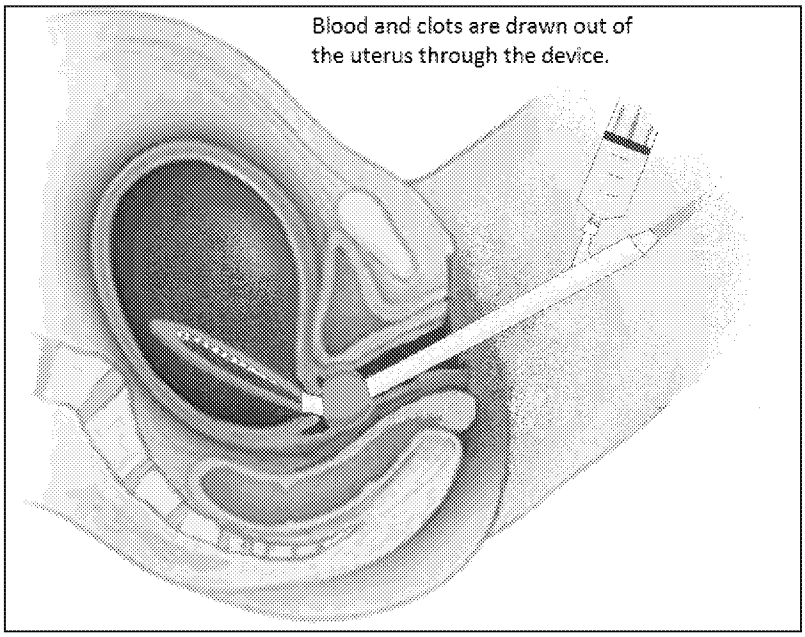


Figure 2: Jada, properly positioned, prior to turning the vacuum on.

Once the vacuum is turned on, residual blood and clots from the PPH are suctioned through the vacuum tube. After the residual materials are suctioned, the continued application of this vacuum force within the uterine cavity will cause the uterus to collapse upon itself, Figure 3. See Section 6.5 for additional detail on the use of the Jada System. See the Instructions for Use for additional instruction on the use of the device.

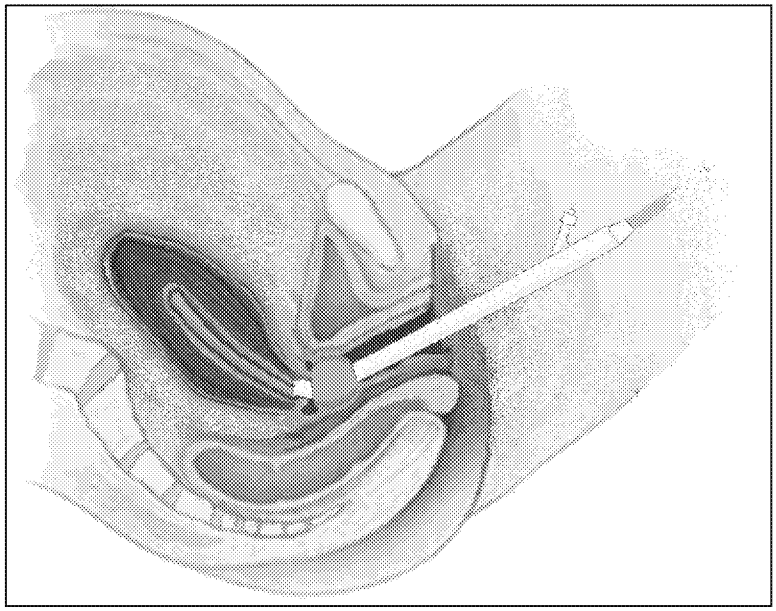


Figure 3: Negative pressure within the uterine cavity causing the uterus to collapse upon itself.

3.3.1 Mechanism of Action

The uterus is composed of a unique interlacing network of muscle fibers. Blood vessels that supply the placental bed pass through this latticework of uterine muscle, Figure 4. After delivery of the infant, when the placenta separates from the uterine wall, these fibers contract causing uterine retraction and constriction of these blood vessels. It is a physiologically efficient method for hemostasis. If the uterine muscle fibers do not contract as normal, PPH may occur.

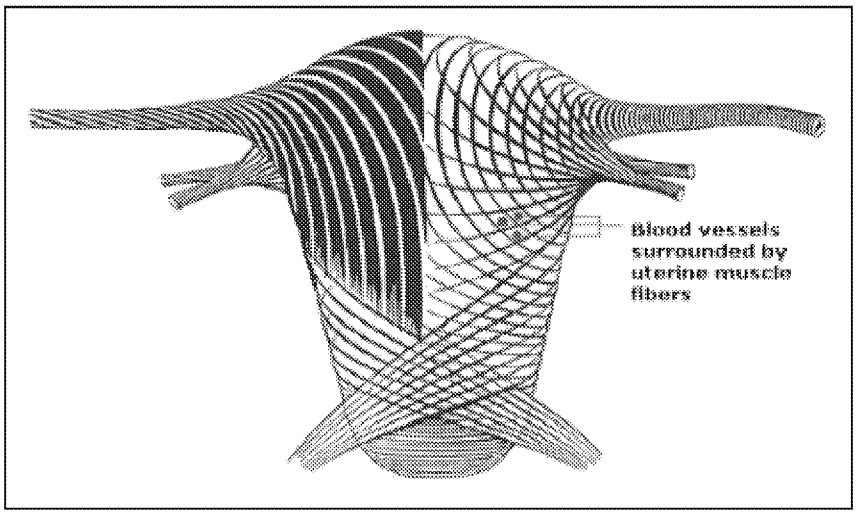


Figure 4: Muscular latticework basket weave diagram of the uterus

The Jada System facilitates an assisted physiologic restoration of normal postpartum uterine mechanisms. Jada establishes negative pressure within the atonic postpartum uterus, causing the uterus to collapse into and onto itself. The inner uterine walls press against one another, producing an immediate tamponade of the uterine cavity that causes rapid hemostasis. In this hemostatic state, the uterus is also stimulated to contract, and can retract down to its normal postpartum size and status without obstruction to optimal postpartum architecture. Additionally, by generating tamponade and stimulating contractions without distension of the uterus, there is no risk of rupturing the scarred or sutured uterus when prior surgery or current Cesarean section is a risk factor.

3.4 Prior Bench and Animal Testing

Benchtop, safety, and animal studies have been performed to verify the functionality and performance of the Jada System.

3.4.1 Benchtop Studies

Functionality Verification was conducted to verify Jada is built to the specifications in the Manufacturing and Functional Specifications documents. The shape integrity of the Jada was tested to verify that it would not collapse or break when being subjected to a vacuum of twice the recommended use. The Flow Rate test verified that the Jada System facilitated a flow rate of at least 400 ml/min when an internal vacuum of 70 mm Hg was applied. The connecting tube was tested to verify that it would facilitate a connection to a hospital-supplied collection vessel and vacuum line. The vacuum seal was tested to verify that it can withstand over-inflation to one and a half times its recommended size. The device was also tested in the presence of heavily clotted pig blood to verify that it can function within the presence of blood clots.

3.4.2 Safety Studies

Table 1: Safety Studies

Test Category	Tests Performed	Testing Performed per Standard		Pass/Fail
Sterilization Validation	Tests performed by SteriPro (through Sterigenics) to substantiate a 25 kGy dose and validate the effectiveness of Gamma batch release for sterilization of the Jada System.	ANSI/AAMI/ISO 11137-2		Pass
Packaging and Shelf Life Validation	Tests performed by Westpak to validate the packaging can withstand shipping & handling, various climates, and support a shelf life of 4 years.	Accelerated Aging	ASTM F1980-07	Pass
		Climatic Conditioning	ASTM D4332-14	
		Initial Manual Handling	ASTM D5276-98	
		Vehicle Stacking	ASTM D642-00	
		Loose Load Vibration	ASTM D999-08	
		Vehicle Vibration	ASTM D4728-06	
		Final Manual Handling	ASTM D5276-98	
		Gross Leak Detection (Bubble)	ASTM F2096-11	
		Seal Strength (Peel)	ASTM F88/F88M-09	
Biocompatibility Validation	Tests performed by NAMSA to validate the materials of the Jada System are biocompatible and nonirritating.	Cytotoxicity Study Using the ISO Elution Method (1X MEM Extract)	ISO 10993-5	Pass
		ISO Maximization Sensitization Study—Extract	ISO 10993-10	

		ISO Vaginal Irritation Study	ISO 10993-10	
		Acute Systemic Toxicity – Extract	ISO 10993-11	

3.4.3 Animal Studies

There is no adequate animal model that duplicates PPH that is observed in humans; however, animal studies were conducted to test technical aspects of the device. In the animal testing that was performed, Jada was evaluated in porcine and ovine bladders. Testing supported the theory that vacuum could contract a sealed organ, thus, could theoretically reduce bleeding.

3.5 First in Human Study Feasibility Study

A First-in-Human (FIH) feasibility investigational study with Ethics Committee oversight was conducted at two clinical sites in Indonesia. The purpose of the study was to demonstrate the placement, function, and operation of the Jada System to meet its intended use to reduce or control PPH.

Ten women were enrolled between July 2014 and February 2015. None of the subjects presented with a retained placenta, uterine lacerations, uterine scarring, or for any conditions other than atonic post-partum hemorrhage. The Jada was successfully placed and activated in all ten subjects. A vacuum force of 70 mmHg - 90 mmHg was used for treatment. The average time from placement of the Jada to removal was 152.0 ± 111.7 minutes (range 60-390 minutes).

Bleeding was controlled within two minutes for all ten subjects. Evaluation of the primary clinical data safety endpoints determined that: 1) no safety issues were observed relative to the placement, insertion, or removal of the Jada, 2) there were no complications related to delayed arrest of blood loss, 3) there was no damage to the uterus, cervix, or vagina, and 4) no uterine inversion or folding events were observed during the Jada procedure.

3.6 Risk Analysis

A risk analysis has been performed in accordance with ISO 14971 for the Jada System. The safety and risk profile of Jada have been further explored and substantiated in the FIH Feasibility study. Based on the risk analysis and FIH study results, there is no expectation or current evidence to suggest that the risks will be increased with Jada as compared to commercially available tamponade devices. Jada has the potential to work more quickly to treat PPH with less side effects. Thus, the potential benefits of the device are expected to outweigh the risks.

3.6.1 Potential Risks to Study Subjects

Risks due to use of the Jada System and recommended actions are described below.

Bleeding: Bleeding may be observed due to mechanical injury to blood vessels or tissue in the area where the Jada System is inserted and deployed. If bleeding due to the device is suspected, the Investigator should remove the device and repair the injured area, as indicated.

Pain / Cramping: Subjects may experience pain or discomfort during the intervention and possibly post-intervention for a short duration of time. Non-steroidal anti-inflammatory or other analgesic medication may be provided for relief.

Perforation of or injury to uterus, fallopian tubes, and adjacent structures: Perforation or injury to the vagina, uterus, fallopian tubes, or adjacent tissue is a possible risk during insertion of any foreign object into the uterus. If perforation due to Jada is suspected, the Investigator should remove the device and evaluate the subject for further treatment.

Infection: Infection is a possible complication following the placement of any foreign object into the uterus. If infection due to Jada is suspected, the Investigator should evaluate the subject and provide treatment (e.g. antibiotics) as indicated.

Failure to stop PPH: Patient monitoring is an integral part of managing PPH. Signs of deteriorating or non-improving condition should lead to a more aggressive treatment of uterine bleeding. There is a risk that the use of Jada will not achieve its intended goal of stopping the PPH; therefore, other treatments may be required. It is noted that while Jada is designed to stop PPH, it does not treat the effects of blood loss, so is not a replacement for fluid resuscitation and should be used along with proper treatment for blood loss (i.e., transfusions).

Unknown Risks: As with any investigational device, there may be risks that are currently unknown or unanticipated.

Inconvenience: There may be added inconvenience to the study subject for participating in the study. The potential for inconvenience is thought to be very minimal for this study as there are no additional requirements for visits outside of standard of care for study subjects.

Loss of confidentiality: There may be loss of confidentiality of a subject's study-related Protected Health Information (PHI) due to participation in the study. The investigational site and study sponsor will do everything possible to limit this risk by storing research records in secure areas and limited access to these records.

3.6.2 Risk Detection and Mitigation

Several precautionary measures have been built into the investigational protocol to protect the study subjects and to detect any potential adverse effects.

- Inclusion/exclusion criteria were identified to help assure that any study subject who may be at increased risk for an adverse event is not enrolled in the study. Also, study subjects will be observed during and following the intervention to assure that any acute adverse events are detected in a timely manner so that proper medical treatment can be initiated. Subjects will be followed at 6 weeks following the intervention in order to capture other possible intervention-related adverse events that do not manifest immediately.

3.7 Potential Benefits of the Intervention

The potential clinical benefits include:

- Treatment that mirrors the normal postpartum physiology of the body, which may result in a more rapid control of hemorrhage.
- Less invasive device than commonly used surgical interventions.
- Avoidance of the use of some uterotonics or shortening duration of use that have more systemic adverse effects.
- No outward physical pressure on a scarred or sutured uterus unlike other commonly used tamponade devices.
- Ability to measure blood loss after initiation of treatment due to the use of the in-line graduated canister.

If Jada proves effective and safe in treating PPH, there are also larger benefits expected for global health care systems:

- Control PPH rapidly, resulting in reduced costs
- Decrease physician time for the intervention and monitoring
- Reduce use of operating rooms or ICUs and decrease length of hospital stays
- Lower cost product than currently available balloon tamponade devices, allowing Jada to significantly benefit emerging countries.

4.0 Study Objectives

4.1 Purpose of the Study

The purpose of this Pivotal Study is to evaluate the safety and effectiveness of the Jada System in the control and reduction of primary PPH.

4.2 Study Endpoints

4.2.1 Primary Effectiveness Endpoint

Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada use is standard of care as long as such use does not exceed the maximum dose of the drug and does not constitute failure of the primary effectiveness endpoint.

4.2.2 Primary Safety Endpoint

Safety: Incidence, severity and seriousness of device-related Adverse Events.

4.2.3 Secondary Endpoints

1. Time to control hemorrhage, defined as the time from turning on the vacuum source until the time the *first* of any of the following occurs:
    - there is no blood being collected in the tubing or canister, or
    - the blood loss is observed as leveled off in the canister, or
    - blood loss is at a rate of < 500 ml in 24 hours.
2. Rate of surgical intervention required to control PPH after Jada use.
3. Rate of non-surgical intervention required to control PPH after Jada use.
4. Assessment of device usability as reported by the clinician using a dedicated data collection form.
5. Rate of blood product transfusion required after Jada use, and number of transfusion units when administered.

4.3 Overall Study Success

A thorough review of all known publications reporting on the use of the Bakri Balloon to treat PPH was performed. A meta-analysis methodology was used to aggregate the studies and provide a numerical estimate of the overall Treatment Success Rate. Based on a random effects model, the estimated pooled proportion of subjects who reached hemostasis (i.e., control of uterine hemorrhaging)

following Bakri Balloon (or equivalent) treatments was 82.0% (95% CI: 73.4% to 89.2%). See the Clinical Evaluation Report (G150265, Attachment H, pages 337-382).

The primary effectiveness objective of this Pivotal Study is to show that the observed Treatment Success Rate is not worse that the rate reported in the literature. The study is considered a success when the lower bound of the two-sided Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success is greater than or equal to 73.4%.

5.0 Study Design

5.1 Overview

This study design is prospective, single-arm, literature-controlled, and multi-center. Since this is a literature-controlled study, meta-analysis methodology was used to establish target endpoints which will demonstrate the safety and effectiveness of the Jada System. See the Clinical Evaluation Report (G150265, Attachment H, pages 337-382).

5.2 Site Selection

The study will be conducted at no less than five and no more than twenty sites, which may include both U.S. and O.U.S sites. Site selection will be conducted in accordance with sponsor Standard Operating Procedures. If O.U.S. sites are enrolled, they will comply with FDA's February 2018 guidance titled "Acceptance of Clinical Data to Support Medical Device Applications and Submissions, Frequently Asked Questions, Guidance for Industry and Food and Drug Administration Staff."

5.3 Study Training

The training program for sites participating in the study will include the following:

1. Didactic training;
2. Hands-on training;
3. Investigator Training Certification Quiz;
4. Procedure Guide Poster.

All investigators will be required to undergo both hands-on training and didactic training and successfully pass the Investigator Training Certification Quiz, which will be administered after the training is complete. The trainee will be considered to have passed the Investigator Training Certification Quiz once all questions have been answered correctly, which may involve a retake of the quiz.

Didactic Training

The didactic training will be performed by Alydia Health staff that are qualified to perform the training. The didactic training will be performed either in person or via videoconference.

Hands-On Training

Hands-on training will be provided by qualified persons who are familiar with the Jada System and PPH. Trainees will use demonstration samples of the Jada System in bench models built by Alydia Health to simulate anatomy in both transvaginal placement and transabdominal placement. This clinical experience simulation is intended to ensure operators master the Jada procedural steps prior to live study subject procedures. Trainees will be required to independently and individually demonstrate successful deployment of a minimum of one Jada System in each model before they are approved to use the device. Successful deployment is defined as following all of the procedural steps in

accordance with the Instructions for Use without prompting or correction by the trainer in the transvaginal model, and successfully completing the device positioning steps in the transabdominal model also without prompting or correction by the trainer. This may require more than one deployment attempt.

Procedure Guide Poster
Finally, as a post-training reminder and reference, each site is provided with a Procedure Guide Poster, which serves as a quick reference guide for the procedure.

5.4 Study Population

5.4.1 Number of Subjects and Sample Size Calculation

Up to 107 subjects will be enrolled in the study to ensure that 96 subjects are available for the analysis of the primary effectiveness endpoint. Sites are expected to enroll a minimum of 5 subjects. Site enrollment will be capped at 30% of the total expected enrollment, such that no site will enroll more than 32 subjects.

The study is powered to show that the Treatment Success Rate among the Jada subjects is not inferior to the Treatment Success Rate derived from a meta-analysis performed using all known publications reporting on the use of the Bakri Balloon (and equivalents) to treat PPH.

Based on a random effects model used in the meta-analysis, the estimated pooled proportion of subjects who reached hemostasis (i.e., control of uterine hemorrhaging) following Bakri Balloon treatments was 82.0% (95% CI: 73.4% to 89.2%). See the Clinical Evaluation Report (G150265, Attachment H, pages 337-382).

Non-inferiority will be achieved when the lower bound of the Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success Rate is greater than or equal to the lower bound of the 95% Confidence Interval of the Treatment Success Rate derived in the meta-analysis, or 73.4%. That is:

Statistical Hypothesis:	H_0: $\pi_{Jada} \leq \pi_{Literature\ CI\ LB}$ vs H_1: $\pi_{Jada} > \pi_{Literature\ CI\ LB}$ where π_{Jada} is the Treatment Success Rate for Jada treated subjects and $\pi_{Literature\ CI\ LB}$ is the lower bound of the 95% Confidence Interval for the Treatment Success Rate derived from the meta-analysis of the Bakri Balloon Literature.
Statistical Methodology:	Confidence Interval for π_{Jada}
Expected π_{Jada}:	0.82
Half-width of 95% CI:	0.086
Confidence Level:	Two-sided 95%
Minimum Sample Size:	n = 96 evaluable subjects
Statistical Power:	0.806 that the lower bound will be greater than or equal to 0.734

With 96 evaluable subjects, there is an 80.6% probability that the lower bound of the observed Exact Clopper-Pearson mid-p two-sided 95% confidence interval will be expected to be greater than 0.734 when the Jada Treatment Success is expected to be 82%. (Calculated using SAS v9.4 PROC POWER.)

For safety, with 96 subjects treated with Jada, there is a 95% chance of observing at least one adverse event when the underlying incidence of the event is at least 3.1%.

To account for up to 10% of the subjects withdrawing early or not having data available for the analysis of the primary effectiveness endpoint, a total of 107 subjects will be enrolled.

5.4.2 Source of Subjects

Subjects will be identified and recruited from inpatient and outpatient facilities affiliated with or at study sites. Any recruitment materials used that are intended for use with patients must be approved by the Sponsor and the reviewing IRB prior to use.

5.4.3 Inclusion/Exclusion Criteria

All patients must be carefully screened against all inclusion and exclusion criteria prior to enrollment in the study. Each Jada System will be shipped with a source worksheet listing all eligibility criteria, which should be used to ensure compliance with study eligibility criteria during subject enrollment.

Inclusion Criteria:

1. Adult Female, 18 years of age or older at time of consent.
2. Able to understand and provide informed consent to participate in the study.
3. Diagnosis of PPH with suspected atony within 24 hours after vaginal or c-section delivery.
4. EBL, determined when investigator is ready to have the Jada peel pack opened:
   Vaginal delivery: 500 – 1500 ml EBL or
   C-section delivery 1000 – 1500 ml EBL
5. Failed first-line intervention of uterotonics and uterine massage/bimanual uterine massage to stop bleeding.
   Note: Uterotonic administration may continue concomitant with and post Jada use, as long as such use does not exceed the maximum dose of the drug.

Exclusion Criteria:

1. EBL >1500ml, to be determined when investigator is ready to have the Jada peel pack opened.
2. Delivery at a gestational age < 34 weeks.
3. For C-sections: Cervix < 3 cm dilated before use of Jada.
4. PPH that the investigator determines to require more aggressive treatment, including any of the following:
   a) hysterectomy;
   b) b-lynch suture;
   c) uterine artery embolization or ligation;
   d) hypogastric ligation.
5. Known uterine anomaly.
6. Ongoing intrauterine pregnancy.
7. Placenta abnormality including any of the following:
   a) known placenta accreta;
   b) retained placenta with known risk factors for placenta accreta (e.g. history of prior uterine surgery, including prior c-section and placenta previa);
   c) retained placenta without easy manual removal.
8. Known uterine rupture.
9. Unresolved uterine inversion.

10. Subject has undergone intrauterine balloon therapy or uterine packing for tamponade treatment of this PPH prior to use of Jada.
11. Current cervical cancer.
12. Current purulent infection of vagina, cervix, uterus.
13. Diagnosis of coagulopathy.

5.4.4 Subject Withdrawal and Termination

Subjects will be advised that they may voluntarily withdraw from the study at any time and will be instructed to notify the Investigator immediately if they choose to withdraw. A subject may choose to withdraw for any reason and is not obligated to reveal reason(s) for withdrawal. Any data contributed up to the point of withdrawal will be included in the analyses. In addition, any adverse events that are ongoing at the time of the subject's withdrawal will be marked as such on the Adverse Event case report form. Subjects will be followed until the adverse event is resolved or is not expected to change.

Subjects may also be involuntarily terminated from the study by the Investigator if the Investigator believes it is in the best interest of the subject. This may occur if the investigator believes more aggressive treatment is necessary prior to the use of Jada. This may also occur if the Investigator decides to abort the treatment with Jada after it is inserted. If a Jada is inserted in the subject but treatment is aborted thereafter, the subject will be followed for six weeks.

5.5 Duration of Study and Subject Participation

All eligible study subjects who are enrolled in the study will be expected to continue participation in this clinical study for six weeks following the Jada intervention, except as provided in the section on subject withdrawal and termination. For this study, "enrolled" is defined as: 1) signing the Informed Consent Form and 2) meeting the inclusion/exclusion criteria.

The literature cites PPH prevalence rates ranging from 2% (severe PPH) to 5% (primary PPH) in the United States. This would mean 2000 to 5000 deliveries would be needed to reach the target enrollment of 107 subjects. Consequently, it is anticipated that it will take approximately 12-18 months to screen, enroll, intervene, and follow-up all 107 subjects.

5.6 Justification for Study

A feasibility clinical study of the Jada System has been completed with encouraging results. See the Clinical Evaluation Report (G150265, Attachment H, pages 337-382). In this feasibility study, Jada was used in a limited population of women who had failed first line conservative therapy. This study excluded subjects delivering by Cesarean section and subjects with other major identifiable causes of PPH other than atony. This conservative subject selection process was deliberately chosen to reduce the variance in the treated population in order to clearly demonstrate the device's mechanism of action and allow safety to be elucidated. In all ten subjects, PPH ceased within two minutes. The Jada System was left in place for up to 6.5 hours. None of the subjects experienced a device-related adverse event.

Subsequent to this Feasibility Study, clinical use of vacuum via uterine cannula (different device than the Jada) to create uterine tamponade was reported by Ram et al in 2014.[25] Sixteen women who had vaginal deliveries and four women who underwent Cesarean sections were included in the study. All women received 10 units of oxytocin at the appearance of the baby's anterior shoulder, 5 units of intravenous oxytocin after the delivery of the placenta, and then uterine massage. Carboprost 125 mcg was also given when the bleeding did not stop. All 20 women were then administered the uterine vacuum retraction system via rigid cannula and vacuum forces of 650 mmHg for 10 minutes at a time. Complete cessation of bleeding which was associated with contraction and firm retraction of the uterus

was observed in all women within 4 minutes of initiation of the procedure. The clinical outcomes for the vaginal deliveries and Cesarean sections were comparable. No adverse events were reported.

These early studies demonstrated the safety and initial effectiveness of the use of a vacuum to create uterine tamponade and treat postpartum hemorrhage. This Pivotal Study is designed to gather more data demonstrating the safety and effectiveness of the Jada System in a larger patient population. Meta-analysis methodology was used to establish target endpoints which will demonstrate the safety and effectiveness of the Jada System; as such, the resulting design is a literature-controlled study design.

6.0 Study Procedures

6.1 Subject Recruitment

Participants will not be recruited until the Institutional Review Board governing their treatment facility has approved the study.

The Investigator may begin recruiting participants at any time prior to the diagnosis of PPH in accordance with the requirements of the following section, Subject Consent. The supplied short Patient Study Brochure, the PEARLE Study Poster, or the Patient Study Information Video can be used at this point to introduce the study to all potential participants (provided these recruitment materials have been approved by the IRB at the site), prior to issuing the lengthier informed consent form. Use of the brochure, study poster and video information tools are optional.

6.2 Subject Consent

Principles of Informed Consent

As stated by US FDA,[1] *"To many, the term informed consent is mistakenly viewed as synonymous with obtaining a subject's signature on the consent form. FDA believes that obtaining a subject's oral or written informed consent is only part of the consent process. Informed consent involves providing a potential subject with adequate information to allow for an informed decision about participation in the clinical investigation, facilitating the potential subject's comprehension of the information, providing adequate opportunity for the potential subject to ask questions and to consider whether to participate, obtaining the potential subject's voluntary agreement to participate, and continuing to provide information as the clinical investigation progresses or as the subject or situation requires. To be effective, the process must provide sufficient opportunity for the subject to consider whether to participate. (21 CFR 50.20.) FDA considers this to include allowing sufficient time for subjects to consider the information and providing time and opportunity for the subjects to ask questions and have those questions answered. The Investigator (or other study staff who are conducting the informed consent interview) and the subject should exchange information and discuss the contents of the informed consent document. This process must occur under circumstances that minimize the possibility of coercion or undue influence."*

Study Requirements

Upon determination of subject eligibility (preliminary completion of study entry criteria), the patient will have the opportunity to discuss any risks, benefits, alternative therapies, and the study requirements with the Investigator prior to signing the informed consent document. Signed informed consent shall be obtained from each study subject prior to use of the investigational device.

[1] Informed Consent Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Draft issued July 2014

Consent Timing

Given the potential for duress, the timing for obtaining informed consent from women undergoing labor and delivery raises unique considerations. As such, considerations and requirements for timing of obtaining informed consent are discussed below.

Informed consent for this study can be obtained during several different phases of interaction with the patient:

Phase 1: At any antenatal obstetrical office visit prior to the onset of labor

Phase 2: After hospital admission, but before the onset of labor, including the following:

- Women making an antenatal visit at the hospital
- Women admitted for labor induction
- Women with ruptured membranes, but who are not in labor

Phase 3: After the onset of labor, **but before the diagnosis of PPH**

In all 3 phases, the patient must be provided adequate time to review the informed consent form and consider whether or not to participate. For women considered high risk for PPH, it is ideal to obtain informed consent during Phase 1. In order to avoid undue anxiety for those women who are not considered at high risk, consent can be obtained later, upon hospital admission, when many possible although unlikely interventions are routinely discussed.

During Phase 3, there is an increased likelihood that the woman will be under periods of duress. As such, the following safeguards will be applied to informed consent that is obtained during Phase 3.

Informed consent will not be obtained when any of the following apply:

1. The patient has been diagnosed with PPH.
2. The patient has arterial bleeding requiring surgical exploration or angiographic embolization.
3. The patient requires immediate life-saving hysterectomy.
4. The patient is in the second stage of labor.
5. The patient is experiencing a contraction.
6. The patient is experiencing pain or discomfort that prevents a lucid discussion of the elements of the informed consent form.
7. The patient is undergoing a gynecological examination.
8. The patient is distracted by the placement or adjustment of fetal or labor monitoring devices.
9. The patient is undergoing administration of an epidural regional anesthetic or spinal anesthetic.
10. The study Investigator believes that the patient's level of mental and/or physical stress prevents a lucid discussion of the elements of the informed consent form.

The patients will be informed by the Investigator or Investigator's designee that they are free to refuse participation in this research study. If they elect to participate, it will be made clear that they may withdraw from the study at any time without prejudicing further care.

The Investigator or the Investigator's designee will inform patients that their medical records will be subject to review by the sponsor and appropriate regulatory bodies. This information will be used during the analysis of the results of the clinical study, but the patients' identities will be treated as confidential. Patients will be assigned a unique study subject code that will not reveal the patient's identity, and this code will be used on all data and data collection forms during the study period.

The Investigator or their designee will explain the conditions of the study, giving the patient sufficient time to ask questions and to consider whether or not they want to participate. If the patient agrees, they shall be given an approved consent form for signature and date. A copy of the consent form will

be given to the patient. The original consent forms will be kept by the Investigator and will be subject to review by the sponsor or a representative of the sponsor, and by the appropriate regulatory bodies.

If the patient signs the informed consent form, the site must place a PEARLE Consent ID bracelet on their wrist to indicate that they have been consented.

Figure 5: PEARLE Consent ID Bracelet

6.3 Subject Pre-Enrollment Screening

All patients must be screened for all inclusion and exclusion criteria prior to being enrolled in the study.

At any time during the consent process or after, if the subject is known to screen fail the study for any inclusion or exclusion criterion, the process of working toward enrollment of that subject should cease. This includes any information that becomes known from subject interview, subject history, or examination at any point after admission. Once a person is known to not fulfill any criterion, the identification of their consent should be removed. For example, if they have a PEARLE Consent ID bracelet on, it should be removed from their wrist.

6.4 Subject Enrollment

The Investigator should consider all possible causes of bleeding, including evaluating for lacerations, retained placenta, broad ligament and vaginal hematomas, uterine rupture, and other causes requiring different treatment pathways. First line therapies should be attempted in accordance with the institution's PPH protocol. After first line therapies have been attempted and failed, the Investigator will make the decision to use Jada to attempt control or reduction of PPH. The subject will be considered "enrolled" after she: 1) signs the Informed Consent Form and 2) meets the inclusion/exclusion criteria.

6.5 Intervention

The Investigator will use Jada in conjunction with the device's Instructions for Use that is included with every device. Following the steps of the IFU and according to their training, the Investigator will place the Jada intrauterine loop into the uterus. For vaginal deliveries, the device will be placed transvaginally; for Cesarean deliveries, the device will be placed trans-abdominally or transvaginally (if the hysterotomy was closed first). The vacuum seal will be filled with 60 ml sterile IV fluid. Vacuum forces will be applied to suction residual blood and debris. Once the residual blood is removed, the pressure gradient from the vacuum creates a uniform mechanical stimulus on the uterus, causing it to collapse into and onto itself. At that time, tamponade occurs and hemorrhage is expected to be controlled. Vacuum forces will be maintained for at least one hour (from the time hemorrhage is controlled) until the subject is stable or until the Investigator determines that hemorrhage was not

controlled and further intervention is needed. If any further intervention is required to treat the PPH, it will be reported on the Procedure case report form, capturing details on the intervention.

Once the Investigator detaches the tubing from the device or "zero's" the vacuum source and the seal is emptied of the fluid, the device should remain in place and taped to the patient's inner thigh for at least 30 minutes, provided the subject is stable and there is no medically valid reason to remove the device. The 30-minute minimum observation period allows for the Investigator to re-initiate treatment should the uterus return to an atonic state with abnormal bleeding.

If the subject remains stable and the PPH does not return for 30 minutes, then the device can be removed and decommissioned (cut up) prior to final disposal. Device pieces should be discarded in accordance with hospital biohazardous waste policies. If there was a device malfunction, the Investigator or designee should wrap the device in a biohazardous disposal bag and contact Alydia Health for further instructions to return the device for evaluation.

Other standard of care medical evaluation and care must be ongoing during the use of the Jada System. If it is determined that blood products must be administered, then the Investigator should follow the local protocol to do so.

6.6 Post-procedure Follow-up

After removal of Jada and before subject discharge from the hospital, additional data collection is required. Information about the following will be collected on case reports forms:

- Physical Examination, including limited Pelvic Examination
- If done, CBC and coagulation panel results
- Clinician Assessment of Device Usability
- Assessment of any adverse events that occur from the beginning of device use to discharge

6.7 Six-week Follow-up

A study follow-up assessment will occur at the subject's normal 6-week postpartum follow-up visit. The following assessments will be performed:

- Physical Examination, including limited Pelvic Examination
- Assessment for any adverse events

Note: If a patient is unable to return for their normal 6-week postpartum visit after three documented attempts to complete the visit, follow-up should occur via phone to gather data related to adverse events from the discharge through this single follow-up time point.

6.8 Summary Table of Clinical Assessments

The schedule of clinical assessment is outlined in Table 2.

Table 2: Clinical Assessment Schedule

Procedure/Assessment	**Baseline**	**Jada Procedure through discharge**	**6-Week Follow-up** *42 days ± 14 days*
Screening for inclusion / exclusion	√		
Informed Consent and HIPAA authorization	√		
Enrollment		√	

Demographics, history and delivery data collection	√		
General exam	√ (after delivery but prior to PPH dx)	√ (after Jada use and prior to discharge)	√
Vital Signs (at admission)	√		
CBC / Coag Panel	√* (at admission)	√* (after Jada use and prior to discharge)	
Jada procedure and endpoint assessment		√	
Investigator assessment of device usability		√	
Adverse Event assessment		√	√
Assessment of medications that may affect bleeding	√	√	
Study exit			√

√* If an Investigator deems it medically important to conduct the CBC or coagulation panel, the results of these should be recorded in the Baseline and Post-Procedure Through Discharge case report forms.

7.0 Safety and Adverse Events

7.1 Definitions

7.1.1 Adverse event

An adverse event is any untoward medical occurrence (i.e., any unfavorable and unintended sign, including abnormal laboratory findings, symptom, or disease) in a clinical investigation subject after the subject enrolls in this study. Adverse events will be categorized as serious and non-serious, device-related and non-device-related, and anticipated and unanticipated.

7.1.2 Adverse device effect

An adverse device effect (ADE) is an AE related to the use of the device, including AEs resulting from insufficient or inadequate instructions for use, installation or operation, or any malfunction of the investigational medical device, use error or from intentional misuse of the medical device.

7.1.3 Device deficiency

A device deficiency is an inadequacy of device related to its identity, quality, durability, reliability, safety, or performance, such as malfunction, misuse, or use error and inadequate labeling.

7.1.4 Device failure

A device failure is a failure of the device to perform or function as intended, including any deviations from the performance specifications or intended use.

7.1.5 Device malfunction

A device malfunction is a failure of the device to meet its performance specifications or otherwise perform as intended when used in accordance with the Instructions For Use.

7.1.6 Device misuse

A device misuse occurs when the Investigator uses the device in a manner that is contradictory to the Instructions For Use. A device misuse will not be considered a malfunction.

7.1.7 Device-related adverse event

A device-related adverse event is any AE for which a causal relationship between the device and the AE is at least a reasonable possibility (i.e., the relationship cannot be excluded).

7.1.8 Near incident

A near incident is any malfunction or deterioration in the characteristics and/or performance of the device (an ADE) which might have led to death or serious deterioration in health. The incident occurred and is such that if it occurred again, it might lead to death or serious deterioration in health.

7.1.9 Serious adverse device effect

An ADE that results in any of the consequences of a serious adverse event "SAE". The term serious adverse device effect (SADE) is synonymous with "incident".

7.1.10 Serious adverse event (SAE)

Any adverse event that meets at least one of the following criteria (a—f):

a. Results in death.
b. Is life-threatening.
   The term 'life-threatening' in the definition refers to an event in which the subject was at risk of death at the time of the event, it does not refer to an event which hypothetically might have caused death if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization.
   A hospitalization or prolongation of hospitalization will not be regarded as an SAE if at least one of the following exceptions is met: the admission is pre-planned (i.e., elective or scheduled surgery arranged prior to the start of the study) OR the admission is not associated with an AE (e.g., social hospitalization for purposes of respite care). However, it should be noted that invasive treatment during any hospitalization may fulfill the criterion of 'medically important' and as such may be reportable as an SAE dependent on clinical judgment. In addition, where local regulatory authorities specifically require a more stringent definition, the local regulation takes precedence.
d. Results in persistent or significant disability / incapacity.
   Disability means a substantial disruption of a person's ability to conduct normal life's functions.
e. Results in fetal distress, fetal death or a congenital abnormality or birth defect.
f. Is considered an important medical event that jeopardizes the health of the subject or requires surgical intervention to prevent one of the outcomes listed above as judged by the Investigator.

7.1.11 Unanticipated adverse device effect

An unanticipated adverse device effect (UADE) is any SADE on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, intensity, or degree of incidence in the investigational plan or application or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

7.2 Classifications for Adverse Event Assessment

All AEs from beginning of device use to subject termination will be assessed and documented by the Investigator according to the categories detailed below:

7.2.1 Seriousness

For each AE, the seriousness must be determined according to the criteria given in section 7.1 (Definitions).

7.2.2 Severity

The severity of an AE is classified according to the following categories:

- Mild
- Moderate
- Severe

7.2.3 Causal relationship

The assessment of the causal relationship between an AE and the device or procedure is a clinical decision based on all available information at the time of the completion of the AE case report form. The assessment is based on the question whether there was a "reasonable causal relationship" to the procedure and/or device.

Possible responses to causal relationship are "related", "possibly related", or "not related".

- An assessment of "not related" would include (1) the existence of a clear alternative explanation (e.g., the subject develops a local infection from an unrelated laceration) or (2) non-plausibility (e.g., the subject is struck by an automobile when there is no indication that the device caused disorientation that may have caused the event).
- An assessment of "possibly related" indicates that there is a reasonable suspicion that the AE is associated with the procedure and/or device, but not definitively so.
- An assessment of "related" indicates that the AE is very likely associated with the procedure and/or device.

Important factors to be considered in assessing the relationship of the AE to the device or procedure include (1) the temporal sequence from the procedure—the event should occur after the procedure is initiated, (2) underlying, concomitant, intercurrent diseases—each event should be evaluated in the context of the natural history and course of the procedure and any other medical conditions the subject may have, and (3) concomitant medications or procedures—any drugs the subject is taking or the additional procedures the subject receives should be examined to determine whether any of them may be suspected to cause the event in question.

7.2.4 Anticipated

A list of anticipated adverse events is in Section 3.6.1. For this study, the applicable reference documents are this protocol and the Clinical Evaluation Report (G150265, Attachment H, pages 337-382). Classification of AEs as anticipated and unanticipated will be determined by the Investigator using the reference documents.

7.3 Assessments and documentation of adverse events

The Investigator must collect all AEs for each subject from the time of enrollment through the end of subject study participation, whether or not deemed related to the investigational device or procedure. A hospitalization or surgical procedure that was scheduled prior to subject enrollment should not be deemed an adverse event. All AE data will be recorded on the AE case report form. The Investigator must make an assessment and document it on the AE case report form. The Independent Medical Monitor will adjudicate all reported adverse events.

All AEs will be followed through resolution or until the AE is not expected to change. The subject will be referred to his or her primary care physician for any ongoing medical issues continuing beyond the completion of the study.

7.4 Reporting of serious adverse events and near incidents

The definition of SAE is provided in Section 7.1. These include device deficiencies that may have led to a SAE if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate.

Notification to sponsor: All serious adverse events (whether or not considered device-related) must be reported immediately (within 24 hours) to:

Kathryn D. Wine, MPH
Clinical Operations
415.990.4104
Kathryn@alydiahealth.com
If e-mail receipt is not confirmed, please call to provide notification.

Notification of the IRB: Notification of the IRB about all relevant events will be performed by the Investigator according to all applicable requirements.

7.5 Device Deficiencies

The Investigator must document all device failures, malfunctions, and use errors, including the assessment whether the event is considered a near incident (ADE) using the Device Deficiency case report form. The case report form must be faxed or emailed to the Sponsor within 24 hours of Investigator knowledge of the event. If a device malfunctions, the Investigator must contact the Sponsor to determine if the device should be returned.

7.6 Study Termination

If new information is discovered during the study that indicates that the device or intervention provides an unreasonable risk to subjects, study enrollment will be suspended or discontinued. Enrollment will only be resumed once the risk has been appropriately mitigated and authorization to resume is obtained from FDA and the reviewing IRB. Regardless of ability to resume the study, all treated subjects will be followed as required by the protocol (6 weeks post-intervention).

The study or any clinical study site may also be halted or terminated early by the Sponsor for business reasons.

8.0 Data Collection, Reporting and Quality Assurance

8.1 Case Report Forms

Case report forms will be used to record demographic, intervention, and follow-up data, as well as any protocol deviations, adverse events, or device malfunctions that may occur during the study period.

8.2 Protocol Deviations

A Protocol Deviation Form must be completed for each study protocol deviation (e.g., failure to obtain informed consent, enrolling a subject who does not meet inclusion/exclusion criteria[2], not performing

[2] There may be times when the pre-treatment EBL is re-estimated after Device use. If the re-estimation of the pre-treatment EBL is greater than the maximum EBL allowed for study entry by ≤ 20% (i.e. the re-estimate was ≤ 1800 ml), then the site is not required to report a protocol deviation to the EBL

required testing, missed follow-up window, etc.). The Investigator must notify the Sponsor and the reviewing IRB of any deviation from the investigational plan that was done to protect the life or physical well-being of a subject (medical emergencies). Such notice should be given within 24 hours after the emergency occurred.

8.3 Efforts to Minimize Data Loss

If a subject fails to comply with the follow up evaluations, the study site must attempt to contact the subject at least three times, including once as a registered letter. In order to minimize loss to follow-up, during the hospitalization, the study coordinator will request that the subject provide names and contact information of two individuals that have a close relationship with the subject. The contacts will be utilized in the event that the subject relocates or cannot be reached by mail or telephone. This information will be treated as confidential and for use by the investigative site only.

8.4 Data Confidentiality

All information and data sent to the Sponsor, Contract Research Organizations, or their designated agents concerning subjects or their participation in this study will be considered confidential and identifying information should be redacted. All data used in the analysis and reporting of this evaluation will be used in a manner without identifiable reference to the subject. The Principal Investigator consents to visits by the staff of the Sponsor and its authorized representatives and the U.S. Food and Drug Administration or any other local governmental body to review the study subjects' medical records including any test or laboratory data.

All information concerning the device, such as patent applications, formulas, manufacturing processes, scientific data, specific study designs, protocols, and formulation information supplied by the Sponsor and not previously published is considered confidential and will remain the sole property of the Sponsor. The Principal Investigator agrees to use this information only in accomplishing the purposes of this study and will not use it for other purposes without the Sponsor's written consent.

8.5 Quality Assurance of the Data

Subject case report forms will be reviewed against source documentation for completeness and accuracy. If any discrepancies are noted, they will be resolved with the Investigator and/or designee. If the data are incomplete, attempts will be made to obtain the missing data.

8.6 Monitoring Procedures

The Alydia Health Vice President of Clinical Operations will have responsibility over the clinical study. Monitors, the Independent Medical Monitor, and associated personnel will be recorded in the Trial Master File.

The Sponsor is responsible for monitoring the study data to verify that the subject rights and well-being are protected in accordance with applicable regulations, GCP, and Sponsor/CRO procedures. The Sponsor, or Sponsor designee, will perform clinical monitoring, including review of case report forms with verification to the source documentation. Both remote and on-site monitoring may be conducted in this study. The Investigator will allow direct access to all relevant subject files for the purpose of verifying entries made in the case report form and assist with the monitor's activities as required. Adequate time, office accommodations, and resources (e.g., copy machine, phone, and/or internet access) for monitoring visits should be made available to the monitor at clinical sites.

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eligibility criteria. If the re-estimated pre-treatment EBL is >1800 ml, then it must be reported as a protocol deviation.

Monitors will contact the site prior to the start of the study to review with the site staff the protocol, study requirements, and their responsibilities to satisfy regulatory, ethical, and Sponsor's requirements.

The Sponsor/designee will periodically monitor the site activity to verify:

- Data are authentic, accurate and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol (including study treatment being used in accordance with the protocol).
- Any other study agreements, GCP, and all applicable regulatory requirements are met.

The Investigator and the head of the medical institution (where applicable) agree to allow the monitor direct access to all relevant documents.

8.7 Publication Policy

The Principal Investigator may not publish information obtained during this study prior to obtaining the review and approval of the Sponsor, which shall be in writing. The Sponsor reserves the right to assert its proprietary interests regarding any confidential, technical or proprietary information that the Sponsor may have furnished the Principal Investigator in order to facilitate clinical studies under this agreement.

9.0 Statistical Analysis Plan

9.1 Introduction

This is a prospective, single-arm, literature-controlled, multi-center trial designed to assess the safety and effectiveness of the Jada System when treating primary PPH. The study is designed to demonstrate that Jada provides safe and effective control or reduction of primary PPH. Safety will be evaluated by analyzing all adverse events for device relatedness, seriousness, severity, and whether or not they were anticipated.

Up to 20 study sites will enroll a total of up to 107 subjects in the study to ensure that 96 subjects are available for the analysis of the primary effectiveness endpoint. Qualified sites will be located in the U.S. and potentially O.U.S. as well. Sites are expected to enroll a minimum of 5 subjects. Site enrollment will be capped at 30% of the total expected enrollment, such that no site will enroll more than 32 subjects. Also, no more than 50% of the study data will come from O.U.S. sites.

9.2 Study Endpoint Analysis

Reported Adverse Events

Adverse events will be categorized as:

- serious or non-serious,
- severe, moderate or mild,
- device-related, possibly device-related or non-device-related,
- anticipated or unanticipated.

The frequency of each event will be summarized according to the above categories. Since some subjects may report the same event several times (e.g., headache), the first occurrence of the worst reported case of the event will be used for the purpose of analysis.

9.3 Primary Effectiveness Endpoint – Treatment Success

Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada use is standard of care as long as such use does not exceed the maximum dose of the drug and does not constitute failure of the primary effectiveness endpoint.

9.4 Study Success

A thorough review of all known publications reporting on the use of the Bakri Balloon and other balloon tamponade methodologies to treat PPH was conducted. A meta-analysis methodology was used to aggregate the studies and provide a numerical estimate of the overall Literature Treatment Success Rate. Based on a random effects model, the estimated pooled proportion of subjects who reached hemostasis (i.e., control of uterine hemorrhaging) following Bakri Balloon treatments was 82.0% (95% CI: 73.4% to 89.2%). See the Clinical Evaluation Report (G150265, Attachment H, pages 337-382).

The primary effectiveness objective of this Pivotal Study is to show that the observed Study Treatment Success Rate is not worse that the rate reported in the literature. The study is considered a success when the lower bound of the two-sided Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success is greater than or equal to 73.4%.

9.5 Secondary Endpoints

1. Time to control hemorrhage, defined as the time from turning on the vacuum source until the time the *first* of any of the following occurs:
    - there is no blood being collected in the tubing or canister, or
    - the blood loss is observed as leveled off in the canister, or
    - blood loss at a rate of < 500 ml in 24 hours.
2. Rate of surgical intervention required to control PPH after Jada use.
3. Rate of non-surgical intervention required to control PPH after Jada use.
4. Assessment of device usability as reported by the clinician using a dedicated data collection form.
5. Rate of blood product transfusion required after Jada use, and number of transfusion units when administered.

The secondary endpoints will be summarized, and confidence intervals will be provided to support interpretation of the results. No specific hypothesis tests will be performed for the secondary endpoints.

9.6 Analysis Cohorts

Different groups of subjects, or Analysis Cohorts, will be identified depending on the type and extent of analysis being performed.

Only subjects from study centers located within the United States and study centers located O.U.S. that have been enrolled under this version of the protocol (2.6) will be included in the analyses and data presentations defined in this protocol.

Screening Cohort
All subjects who are consented and screened for the study will be included in the Screening Cohort. Subjects excluded during the procedure from receiving Jada treatment for non-device related reasons are included in this Cohort. Only an accounting of the numbers of subjects screened in the study, plus the reasons given for subjects not enrolled in the study will be performed on this Cohort.

Safety/ITT (Intent to Treat) Cohort
All subjects in whom treatment was attempted with Jada (device inserted and vacuum turned on) are included in the Safety/ITT Cohort.

Per-Protocol Cohort
The Per-Protocol Cohort is defined as the group of subjects who are treated and complete treatment with the Jada System per the device's Instructions for Use, and who complete their 6-week visit without any major protocol deviations.

Cohort for Primary and Secondary Effectiveness Endpoints
Analyses of all primary and secondary effectiveness endpoints will be repeated both for the Safety/ITT Cohort and for the Per-Protocol Cohort. Study Success will be based on the Safety/ITT Cohort.

Cohort for Safety Endpoints
Analyses for all safety related endpoints will be performed using the Safety/ITT Cohort.

9.7 Derived Data – Change-from-Baseline Parameters

Within-subject change-from-baseline (pre-treatment baseline) values for a parameter are calculated as:

Change-from-Baseline = Pre-Treatment value – Follow-Up value

such that a positive value indicates a reduction from the pre-treatment value to the follow-up value, whereas a negative result indicates the opposite.

9.8 Statistical Methods

Categorical data will be summarized using frequency tables, presenting the subject counts and relative percentages. McNemar's chi-square may be used to assess within-subject changes in a bivariate response variable.

Continuous variables will be summarized by the mean, standard deviation, median, minimum and maximum. Within-subject changes (Change-from-Baseline) will be analyzed parametrically using the Paired t-test if the differences are normally distributed, or non-parametrically using the Sign-Rank Test if the differences are not normally distributed.

The SAS system or equivalent statistical package will be used to perform all analyses. Exact confidence intervals will be generated for estimates of proportions. Asymptotic confidence intervals will be generated for estimates of means. The p-values of all tests will be reported without any correction for the multiplicity of tests performed.

9.9 Subgroup Analysis

Analysis of the primary safety and effectiveness endpoints will be repeated for two subgroups of subjects: subjects with vaginal delivery and subjects with surgical delivery by Cesarean section.

9.10 Poolability

Data will be pooled from multiple study sites for this analysis. The justification for pooling is made on a clinical basis[3]. The basis for pooling comes from three critical factors: the study sites must implement one common protocol; the sponsor must provide monitoring of study site compliance; the study sites must use common data collection procedures.

Poolability across study sites will be assessed by presenting Treatment Success Rates by site and analyzing site-to-site differences using the Chi-square Test. Other methods for assessing site-to-site differences in Treatment Success Rates will be considered if the assumptions underlying the Chi-square Test are not met. Site-to-site differences will be assessed at a 0.15 level of significance. A non-significant site-to-site effect will support poolability of study sites. Note that prior to assessing site-to-site differences, sites with less than 5 subjects will be combined. To avoid the scenario that the data from the combined super-site dominate the trial conclusion, sites with less than 5 enrolled subjects be combined according to their geographical closeness, and once a super-site has five or more enrolled subjects, then the forming of this super-site will stop and the forming of a new super-site will start. Site-to-site differences of a quantitative nature, (e.g., all sites show the treatment to be beneficial, but perhaps to a different degree by study site) will not be considered to be an impediment to pooling. Site-to-site differences qualitative in nature (e.g., the vast majority of sites show the treatment to be beneficial, but one or more sites show the treatment to be detrimental) will require extensive evaluation of the sites with contrary results to attempt to determine what factors at those sites led to the result.

9.11 Lost to Follow-up

Data on subjects who are lost to follow-up or who withdraw from the study will be maintained and analyzed up to the point at which they discontinued. The reason for withdrawal will be recorded if known. Subjects who discontinue participation, for whatever reason, will remain in the study and be subject to follow-up in the same manner as those who complete the study except as noted above. The only confirmed lost to follow-up subject will be a subject who dies or refuses to continue to participate in the study and thereby withdraws.

9.12 Dropout Mechanism and Analysis

Subjects who are missing data necessary to assess Treatment Success will be considered a failure (Treatment Success = No) in the analysis of the primary effectiveness endpoint. If the subject withdraws from the study prior to completing the assessment of Treatment Success, it will be considered missing data. All other endpoints will be analyzed "as-is" without any special data imputation methods used to replace missing data.

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SECTION 7: TRUTHFUL AND ACCURATE STATEMENT

Provided below is the Truthful and Accurate Statement as required by 21 CFR 807.87(l).

I certify that, in my capacity as Interim CEO of Alydia Health, I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

(b)(6)

(Signature)

Colby Holtshouse

Typed Name

May 1, 2020

(Date)

*(Premarket Notification [510(k)] Number)

*For a new submission, leave the 510(k) number blank.

Must be signed by a responsible person of the firm required to submit the premarket notification [e.g., not a consultant for the 510(k) submitter].

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? **If possible, please provide a response by noon on Tuesday, August 25, 2020.**

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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From: Qu, Yanping
To: Colden, Kelly
Cc: Avery, Reginald
Subject: RE: (b)(5) c K201199/S001
Date: Tuesday, August 25, 2020 6:41:50 PM
Attachments: image014.png
image001.png

Hi Kelly,

(b)(5)

Yanping

Yanping Qu, PhD | Mathematical Statistician
Biostatistics Team 1 | Division of Biostatistics
Office of Clinical Evidence and Analysis | Office of Product Evaluation and Quality
Center for Devices and Radiological Health
U.S. Food and Drug Administration
Telephone: (301)796-2867
Email: yanping.qu@fda.hhs.gov

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Sent: Tuesday, August 25, 2020 4:58 PM
To: Qu, Yanping <Yanping.Qu@fda.hhs.gov>
Cc: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Subject (b)(5) K201199/S001

Yanping,

(b)(5)

(b)(5)

Best,

Kelly

Kelly Colden MD, MPH
Medical Officer
Obstetrical and Reproductive Health Devices Team
Division of Reproductive, Gynecology, and Urology Devices (DHT3B)
FDA/CDRH/OPEQ/OHT3

WO 66, 2660B
Silver Spring, MD 20993
Phone: 240-402-5341
kelly.colden@fda.hhs.gov

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Hello,

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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[cid:image002.jpg@01D1C57E.DFA022A0]<https://www.facebook.com/FDA>
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From: Cindy Domecus <domecusconsulting@comcast.net>

Sent: Thursday, August 27, 2020 6:36 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello Cindy,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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From: Cindy Domecus
<DomecusConsulting@comcast.net<mailto:DomecusConsulting@comcast.net>>

Sent: Thursday, August 27, 2020 10:41 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 27, 2020, at 4:47 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

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Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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From: Cindy Domecus
<DomecusConsulting@comcast.net<mailto:DomecusConsulting@comcast.net>>

Sent: Thursday, August 27, 2020 12:50 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

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White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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Exhibit C: Clean copy of revised Jada System Instructions for Use

Jada SYSTEM

Vacuum-induced Hemorrhage Control System
INSTRUCTIONS FOR USE

Important Information – Please Read Before Use

CAUTION

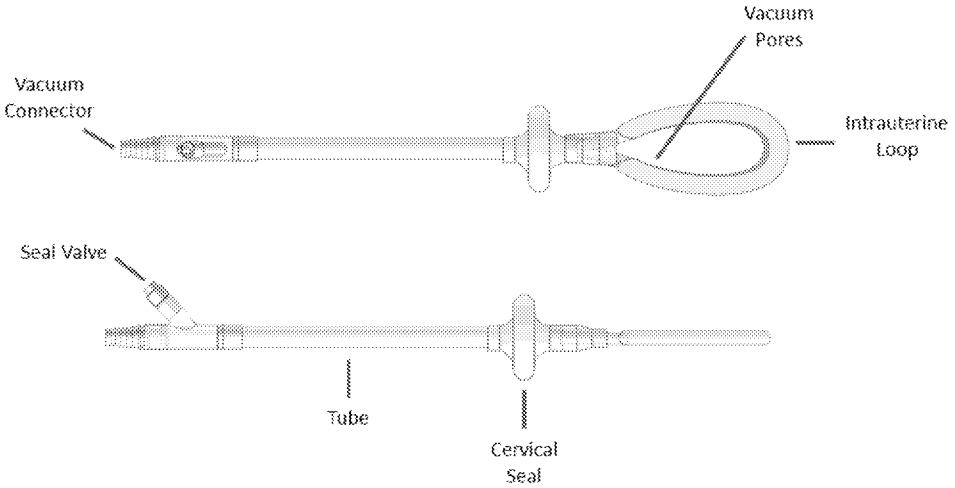
Federal law (USA) restricts this device to sale by or on the order of a physician. This medical device is intended for use by healthcare providers trained and experienced in obstetrics and gynecological techniques.

INDICATIONS FOR USE

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

DESCRIPTION

The Jada System is a 41 cm long intrauterine device made of silicone. Jada consists of an Intrauterine Loop on the distal end of a Tube. The proximal end of the Tube has a Vacuum Connector for connection to sterile vacuum tubing. The Cervical Seal proximal to the Intrauterine Loop is filled and emptied with a sterile luer tapered syringe filled with sterile fluid via the Seal Valve. The Intrauterine Loop consists of a loop tube with 20 Vacuum Pores oriented toward the inside diameter of the Intrauterine Loop. The outer surface of the Intrauterine Loop is covered by a Shield which overhangs the Vacuum Pores to protect tissue from vacuum and the Vacuum Pores from plugging with tissue and blood clots.



CONTRAINDICATIONS

The following are contraindications to Jada use:

- Ongoing intrauterine pregnancy
- Untreated uterine rupture
- Unresolved uterine inversion
- Current cervical cancer
- Known uterine anomaly
- Current purulent infection of vagina, cervix, or uterus
- For C-sections: Cervix < 3 cm dilated before use of Jada

WARNINGS

- The safety and effectiveness of the Jada System in delivery at a gestational age < 34 weeks or, if multiples, uterus judged < 34 weeks size, have not been established. With smaller uterine size, there is potential for increased risk of perforation and expulsion.
- Signs of patient deterioration or failure to improve indicate the need for reassessment and possibly more aggressive treatment and management of postpartum hemorrhage (PPH)/abnormal postpartum uterine bleeding.
- Jada is not a substitute for surgical management and fluid resuscitation of life-threatening PPH/abnormal postpartum uterine bleeding.
- Remove air from Cervical Seal prior to device use to minimize risk of air embolism if Cervical Seal bursts.
- Always fill the Cervical Seal with sterile fluid. Never inflate with air, carbon dioxide, or any other gas to minimize risk of air embolism if Cervical Seal bursts.

PRECAUTIONS

- The safety and effectiveness of the use of Jada in patients with placenta accreta have not been evaluated.
- Use care when suturing any lacerations to avoid puncturing or damaging the material of the Cervical Seal.
- Avoid excessive force when inserting the Jada into the uterus or trauma to uterine wall may occur.
- The maximum vacuum pressure is 90 mm Hg. Do not increase the vacuum pressure higher than 90 mm Hg. (90 mm Hg = 1.7 psi = 12.0 kPa = 3.5 in Hg = 120.0 mbar) or tissue trauma may occur.

- After initiation of vacuum, blood flow into Jada or the vacuum tubing and/or improvement in uterine tone should be noted. If this does not occur, the Cervical Seal and/or the vacuum may not be effective. If so, refer to Troubleshooting section.
- During treatment, the presence of intermittent or continuous air flow through Jada and vacuum tubing may indicate an issue with the Cervical Seal location or Cervical Seal coverage. If so, refer to the Troubleshooting section.
- Jada should not be left within the uterus for longer than 24 hours due to the possibility of an adverse tissue reaction or infection.
- The safety and effectiveness of the use of Jada in patients with Disseminated Intravascular Coagulation (DIC) have not been evaluated.

SUMMARY OF CLINICAL DATA

The safety and effectiveness of the Jada System was evaluated in the PEARLE study (**P**rospectiv**e**, Single Arm, Pivotal Clinic**a**l T**r**i**a**l D**e**signed to Assess the Safety and Effectiveness of the Jada System In Treating Primary Postpartum Hemorrhage "PPH") under an approved IDE from the U.S. Food and Drug Administration (FDA).

Study Design

PEARLE was a prospective, single-arm, literature-controlled, multi-center treatment study where each enrolled subject was treated with the Jada System. The primary endpoints of the study were:

- Primary Effectiveness Endpoint: control of postpartum hemorrhage, defined as the avoidance of non-surgical, second line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use.
- Primary Safety Endpoint: incidence, severity and seriousness of adverse events related to Jada.

The following Secondary Endpoints were evaluated in the PEARLE study:

- Time to hemorrhage control.
- Rate of non-surgical intervention required to control PPH after Jada use.
- Rate of surgical intervention required to control PPH after Jada use.
- Assessment of device usability.
- Rate of blood product transfusion required after Jada use, and number of transfusion units when administered.

Use of the Jada System occurred after failure of first line uterotonics and uterine massage.

The comparator to the Jada System was a literature meta-analysis of the Bakri® Postpartum Balloon. Based on a random effects model used in the meta-analysis, the estimated pooled proportion of subjects who reached control of uterine hemorrhage

following Bakri Postpartum Balloon treatments was 82.0% (95% CI: 73.4% to 89.2%). By this definition, the study was considered a success if the lower bound of the two-sided Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success was greater than or equal to 73.4%.

A total of 107 subjects were enrolled in PEARLE at 12 investigational centers in the United States.

Cohort	Subjects (N)
Total Subjects Enrolled*	107
Safety/Intent to Treat (ITT)**	106
Modified Intent to Treat (mITT)***	104
Per Protocol (PP)****	97

*All subjects in whom Jada insertion was attempted.
** All subjects in whom treatment was attempted with Jada (device inserted and vacuum turned on).
***All subjects in whom treatment was attempted with Jada (device inserted and vacuum turned on) and whose treatment was not aborted early for non-Jada reasons.
**** All subjects who completed Jada treatment per Jada's Instructions for Use, and who completed their 6-week visit without any major protocol deviations.

Primary Endpoints

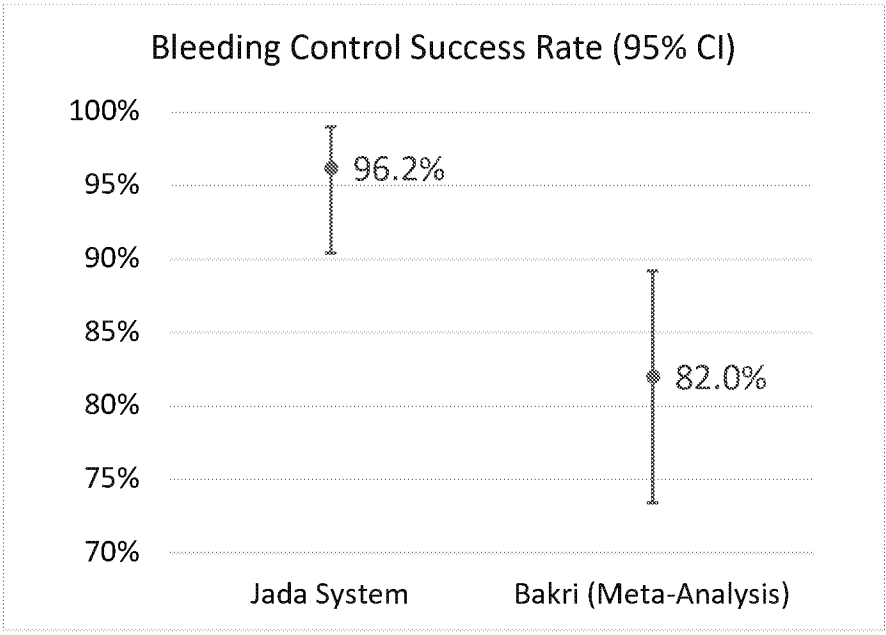
Effectiveness

The analysis of effectiveness was based on the 106 subjects in the ITT Cohort. Results from the 104 subjects in the mITT and 97 subjects in the PP Cohort are also presented. The treatment success rate in the ITT Cohort was 94.3% (100/106, p<0.001), with a lower bound 95% confidence limit of 88.1%. One subject counted as a success in the study was treated with uterine balloon tamponade (UBT) prior to meeting the minimum EBL threshold. The UBT treatment was unsuccessful and continued blood loss occurred. After meeting the EBL threshold, the subject was treated with Jada which controlled hemorrhage without requiring further treatment. The treatment success rate of the comparator, the Bakri Postpartum Balloon, was 82.0% (95% CI: 73.4% to 89.2%). The treatment success rate in the mITT Cohort was 96.2 (95% CI: 90.4%, 98.9%). The confidence intervals for the mITT cohort and the meta-analysis of the comparator do not overlap.

Primary Effectiveness			
Cohort (N)	**Treatment Success**	**95% Confidence Limit (2-sided)**	***P* value**

Primary Effectiveness			
ITT (N=106)	94.3% (100/106)	88.1%, 97.9%	<0.001
mITT (N=104)	96.2% (100/104)	90.4%, 98.9%	<0.001
PP (N=97)	99.0% (96/97)	94.4%, 100%	<0.001

Jada Success Rate Compared to Bakri Postpartum Balloon (mITT Cohort).



Safety

The analysis of safety was based on the 106 subjects in the Safety / ITT Cohort. There were no adverse events judged definitely related to the device or the procedure and there was a low rate of possibly related adverse events, all of which were anticipated in this patient population and with introduction of an intrauterine device. Five possibly device-related adverse events were rated as "mild" and three were rated as "moderate" without any event in this group rated "severe". The three moderate events were cases of endometritis, which is a known risk of long labor, vaginal exam, and PPH.

Secondary Endpoints

Control of hemorrhage was defined in the protocol as the time from connecting the vacuum source to Jada to the time the first of any of the following occurs: there is no blood being collected in the tubing or canister, or the blood loss is observed as leveled off in the canister, or blood loss is at a rate of < 500 mL in 24 hours. The median time to control of PPH in the ITT, mITT and PP population was 3 minutes.

Timing of the procedure and duration of treatment was tracked from diagnosis through treatment and patient discharge for subjects enrolled in PEARLE. Jada was used most often within one hour after delivery. Bleeding was controlled quickly from the time of connection of vacuum, with a median control in three minutes. The duration of treatment with active vacuum connected was a median of 2 hours and 24 minutes with total in-dwelling time median of 3 hours and 11 minutes.

Duration of Treatment (ITT Cohort (N=106*))				
Procedural Steps	**Time (minutes)**			
	Mean	**SD**	**Median**	**Min, Max**
Time to control of hemorrhage	4.2	5.3	3.0	0, 35.0
Duration of Vacuum Treatment (Protocol: ≥ 60 minutes)	248.8	261.1	144.0	57, 1276
Total in-dwelling time (Treatment + Verification)	306.0	274.9	191.0	70, 1400

*Timing of steps was available in 100 subjects in whom bleeding was successfully controlled with Jada alone.

The median hospital length of stay from delivery time was 2.2 days.

The need for non-surgical intervention after use of Jada was rare, with only 2 subjects receiving non-surgical intervention in the ITT Cohort.

Surgical intervention after Jada treatment was reported in three subjects: one subject received a B-Lynch compression suture in conjunction with Jada, one subject received B-Lynch compression suture followed by hysterectomy, and one subject underwent hysterectomy.

Rate of Non-surgical and Surgical Intervention After Jada Use			
Cohort	**Non-Surgical Intervention**	**Surgical Intervention**	**No Intervention Needed**
ITT	2/106 (1.9%) (95% CI: 0.2%, 6.7%)	3/106 (2.8%) (95% CI: 0.6%, 8.1%)	101*/106 (95.3%)
mITT	1/104 (0.9%) (95% CI: 0%, 5.2%)	3/104 (2.9%) (95% CI: 0.6%, 8.2%)	100/104 (96.2%)
PP	0/97 (0%)	1/97 (1.0%)	96/97 (99%)

*One subject who did not meet the success criteria in the ITT Cohort did not have any further intervention for uterine bleeding post Jada use.

The device usability was notably positive by investigators on all measurements.

Investigators Experience with Jada Use (N=107)	
Category Evaluated	**Response (Agreed or Strongly Agreed)**
IFU and device training clearly explained use	100%
Jada was easy to insert and position	96.3%
Jada was easy to remove	98.1%
Jada use did not inhibit other care	98.1%
Jada was easy to use	98.1%
Would recommend Jada to treat PPH	97.2%

In the study, 40 subjects (37.7%) in the ITT Cohort, 38 subjects (36.5%) in the mITT Cohort, and 33 subjects (34.0%) in the PP Cohort received any blood product replacement. Transfusion of four or more units of packed red blood cells (PRBC) occurred in five subjects (4.7%) in the ITT Cohort, five subjects (4.8%) in the mITT Cohort, and four subjects (4.1%) in the PP Cohort. No subject developed disseminated intravascular coagulation (DIC) on the study.

Additional Treatment

A subset of subjects received tranexamic acid (TXA) along with uterotonics and uterine massage for treatment of PPH. TXA was used in 41/106 (39%) subjects in the ITT cohort.

Summary of TXA Usage in Study Subjects (ITT Cohort (N=106))	
Timing of TXA Usage	**Number of Subjects (%)**
Any use of TXA in Study Subject	41/106 (39%)
Before Jada Use	22/106 (21%)
During Jada Use	10/106 (9%)
After Jada Use	3/106 (3%)
Before and During Jada Use	4/106 (4%)
Before and After Jada Use	2/106 (2%)

The safety data evaluation showed there were no device deficiencies or adverse events reported related to use of TXA in study subjects.

Summary of Effectiveness Results for Subjects With and Without TXA (ITT Cohort (N=106))	
TXA Usage Timing	**Success Rate per Primary Effectiveness Endpoint % (n/N)**
No TXA Use	100% (65/65)
Any TXA Use	85% (35/41)
Before Jada Use	96% (21/22)
During Jada Use	80% (8/10)
After Jada Use	33% (1/3)
Before and During Jada Use	100% (4/4)
Before and After Jada Use	50% (1/2)

Additional Analyses by Delivery Mode

Sub-group analysis of effectiveness rate was evaluated by mode of delivery, vaginal or c-section. For the ITT population of 106 subjects, there were 91 vaginal deliveries with three failures, and 15 c-sections with three failures. One subject counted as a success in the study was treated after vaginal delivery with uterine balloon tamponade (UBT) prior to meeting the minimum EBL threshold. The UBT treatment was unsuccessful and continued blood loss occurred. After meeting the EBL threshold, the subject was treated with Jada which controlled hemorrhage without requiring further treatment. The success rates in the ITT Cohort were 96.7% and 80.0% after vaginal and c-section birth, respectively. In the mITT Cohort, success rates were 98.9% and 80.0%, respectively. In the PP Cohort, the success rates were 100.0% and 91.7%, respectively.

Effectiveness of Jada by Delivery Type/Cohort						
	Vaginal Delivery			C-Section		
Primary Effectiveness	**ITT (N=91)**	**mITT (N=89)**	**PP (N=85)**	**ITT (N=15)**	**mITT (N=15)**	**PP (N=12)**
	88/91 (96.7%)	88/89 (98.9%)	85/85 (100.0%)	12/15 (80.0%)	12/15 (80.0%)	11/12 (91.7%)
Time to Hemorrhage Control with Jada Success (minutes)	**ITT (N=88)**	**mITT (N=88)**	**PP (N=85)**	**ITT (N=12)**	**mITT (N=12)**	**PP (N=11)**
Mean	3.8	3.8	3.8	7.1	7.1	7.2
SD	4.6	4.6	4.6	8.7	8.7	9.1
Median	3.0	3.0	3.0	4.0	4.0	3.0
Min, Max	0, 35	0, 35	0, 35	0, 29	0, 29	0, 29

Summary

The results of the PEARLE study demonstrated that the Jada System is safe with an effectiveness rate of 94.3% for its intended use. The effectiveness rates in the mITT and PP Cohorts were 96.2% and 99.0%, respectively. There were no adverse events judged definitely related to the device or the procedure, and there was a low rate of possibly related adverse events, all of which were anticipated in this patient population and with introduction of an intrauterine device.

The secondary endpoints were also overwhelmingly positive. Bleeding was controlled in 3 minutes in the ITT, mITT and PP populations. The rate of further surgical or non-surgical intervention after Jada was very low. The rate of blood transfusion was expected in this patient population, treated at U.S. hospitals with ready access to these resources. The median reported total time for Jada treatment with vacuum in this study was 2 hours and 24 minutes, and total in-dwelling time was 3 hours and 11 minutes.

Additional clinical data collected outside the United States

First-in-Woman Study Results

A First-in-Woman (FIW) feasibility study with Ethics Committee oversight was conducted at two clinical sites in Indonesia. The purpose of the study was to demonstrate the placement, function, and operation of the Jada System to meet its intended use.

Ten subjects were enrolled in the feasibility study. None of the subjects presented with a retained placenta, uterine lacerations, uterine scarring, or for any conditions other than

atonic postpartum hemorrhage. Bleeding was controlled within two minutes for all ten subjects. Evaluation of the primary clinical data safety endpoints determined that: 1) no safety issues were observed relative to the placement, insertion, or removal of the Jada, 2) there were no complications related to delayed arrest of blood loss, 3) there was no damage to the uterus, cervix, or vagina, and 4) no uterine inversion or folding events were observed during the Jada procedure.

Case Series Outside the United States

Thirteen subjects were enrolled at the clinical trial site at St. Francis Hospital Nsambya, in Kampala, Uganda under an earlier iteration of the PEARLE study protocol with similar inclusion/exclusion criteria.

Jada was effective at treating PPH in all 13 subjects, including three subjects who were enrolled despite estimated blood loss (EBL) at study entry significantly higher than allowed per study inclusion criterion. Hemorrhage was controlled in each subject but two subjects subsequently died due to lack of blood product supply for transfusion to treat their severe blood loss. There were no adverse events designated definitely related to the device or the procedure.

INSTRUCTIONS FOR USE

Pre-Jada Patient Evaluation

Precaution: The safety and effectiveness of the use of Jada in patients with placenta accreta have not been evaluated.

1. Evaluate for lacerations, retained products of conception, or other causes of bleeding prior to using Jada.

Note: Prioritization of laceration repair and placement of Jada for atony-related bleeding is up to the judgment of the provider. Repair of vaginal and external genital lacerations can be performed with the Jada in place.

Precaution: Use care when suturing any lacerations to avoid puncturing or damaging the material of the Cervical Seal.

Jada Preparation

2. Inspect the packaging and Jada before use.
3. Ensure that the bladder is empty (straight cath or place Foley) in order to facilitate palpation and contraction of the uterus.
4. Connect a vacuum canister and sterile standard vacuum tubing to a regulated vacuum source.

5. Use a sterile luer tapered syringe to remove any air that is in the Cervical Seal.
6. Fill sterile luer tapered syringe with 60 mL of sterile fluid.

Jada Placement: Post Vaginal Delivery or Post Cesarean Section After Closure of Hysterotomy

7. Secure visualization of the cervix to confirm it is dilated ≥ 3 cm to allow for placement of Jada.
8. Grasp and compress the Intrauterine Loop near the distal tip for support and insert Jada transvaginally, leading with the Intrauterine Loop (**See Figure 1**). Use gentle traction on the anterior cervical lip to stabilize the cervical opening, if needed.
9. Place Jada such that the Intrauterine Loop is located in the uterus and is oriented in the frontal plane of the body by assuring the Seal Valve is oriented at either 6 or 12 o'clock. Ultrasound may be used to confirm proper placement of the Intrauterine Loop within the uterus.
10. After insertion, the Intrauterine Loop should be within the uterus while the Cervical Seal should be located within the vagina at the external cervical os (**See Figure 2**).

Note: If clinically relevant, a B-Lynch compression suture may be used in conjunction with Jada.

Filling of Cervical Seal and Connection of Vacuum

11. While securely holding the Seal Valve and avoiding unintentional proximal or distal movement of the Cervical Seal away from the external cervical os, use a sterile luer tapered syringe to fill the Cervical Seal with 60 mL of sterile fluid. If needed, add up to another 60 mL of sterile fluid to achieve coverage of the external cervical os and create a seal for vacuum (**See Figure 3**).
12. Set the vacuum source to 80 mm Hg +/- 10 mm Hg while occluding the end of the tubing (80 mm Hg = 1.5 psi = 10.7 kPa = 3.2 in Hg = 106.7 mbar) (**See Figure 4**).

Precaution: The maximum vacuum pressure is 90 mm Hg. Do not increase the vacuum pressure higher than 90 mm Hg. (90 mm Hg = 1.7 psi = 12.0 kPa = 3.5 in Hg = 120.0 mbar) or tissue trauma may occur.

13. After the vacuum pressure has been set and confirmed, connect Jada to the sterile vacuum tubing (**See Figure 5**). Blood flow into the vacuum tubing and/or improvement in uterine tone should be noted after initiation of vacuum.

Note: Confirm that the Cervical Seal is positioned at the external cervical os after the system is in place (Cervical Seal is filled and the vacuum is connected). Reposition Jada if required to facilitate a seal.

14. After initial evacuation of any pooled blood, presentation may vary during treatment: there may be no further blood evacuation, or additional blood moving into the tubing, or accumulation of blood in the canister. If blood flow does not stop or slow sufficiently, consider increasing the vacuum pressure in accordance with your clinical judgment, not to exceed a maximum pressure of 90 mm Hg.
15. Tape Jada to the patient's inner thigh without tension.

Precaution: Ensure Jada is secured with tape to avoid unintentional dislodgement.

16. Leave Jada in place with the vacuum applied until:

    - PPH/abnormal postpartum uterine bleeding is controlled for at least 1 hour,
    - The uterus is firm,
    - Patient is stable.

17. Consider prophylactic antibiotics for prolonged use.

Verify and End Treatment

18. Before disconnecting vacuum, assess the patient to confirm that treatment is no longer needed.
19. Disconnect vacuum tubing from Jada while vacuum is on to collect any blood from the tubing into the canister. Secure tubing in case re-application of vacuum is needed.
20. Using a luer tapered syringe, remove the fluid from the Cervical Seal and keep the Jada System in place for at least 30 minutes while monitoring for any recurrent uterine bleeding.

Jada Removal

Precaution: to avoid uterine inversion, do not remove the Jada while vacuum is applied. Always disconnect Jada from vacuum tubing before removal.

Precaution: remove all fluid from the Cervical Seal prior to removing Jada to avoid disruption of the vaginal mucosa or any sutured lacerations.

21. If PPH/abnormal postpartum uterine bleeding remains controlled and the uterus remains firm for a minimum of 30 minutes after vacuum is disconnected, remove Jada.
22. Place one hand on the abdomen to secure the uterine fundus while the other hand slowly withdraws the device

TROUBLESHOOTING

SITUATION	RECOMMENDED ACTION
Vacuum is not detected at the end of the vacuum tubing.	a) Check connection on all system components: • Confirm vacuum source is functional, including regulator. • Confirm lid of vacuum canister is fully seated and that canister is not cracked. • Confirm vacuum tubing is securely connected at both ends and any connection in between. b) Confirm desired vacuum level is regulated in the appropriate units (i.e. mm Hg vs. cm Hg).
Vacuum system is connected and working but uterus does not collapse and/or bleeding does not stop.	a) Increase vacuum pressure to maximum (90 mm Hg). b) Disconnect the vacuum tubing from Jada and occlude the end of the tubing to check vacuum. c) Confirm appropriate Jada placement, with ultrasound if needed: • Confirm proper placement of Intrauterine Loop in uterus (vs. misplacement in posterior vaginal fornix). • Confirm proper placement of Cervical Seal outside of the cervical os (vs. misplacement into uterus). • Ensure Cervical Seal is sufficiently filled with sterile fluid to create adequate seal at the cervix. d) Re-evaluate patient for other sources of bleeding.

HOW SUPPLIED

Jada is supplied sterilized by gamma radiation in a peel-open package. Jada is sterile if package is unopened or undamaged. Do not use Jada if there is doubt as to whether the device is sterile.

MATERIALS REQUIRED BUT NOT SUPPLIED

- Sterile vacuum tubing: 10'- 12'
- Sterile luer tapered syringe: 60 mL recommended
- Sterile fluids

- Vacuum canister
- Regulated vacuum source
- Tape

STORAGE

Handle with care. Store in original packaging in a clean, cool, and dry location. Avoid exposure to temperature and humidity extremes.

RE-STERILIZATION/RE-USE

Jada is for single-patient use only. Do not reuse, reprocess, or re-sterilize. Reuse of Jada may lead to cross contamination, infection, or patient death.

SYMBOL GLOSSARY

Sources: **21 CFR 801** Labeling and **ISO 15223-1:2016** *Medical devices — Symbols to be used with medical device labels, labelling and information to be supplied — Part 1: General requirements.*

Symbol	Title	Meaning/Definition	Standard/ Ref. Number
	Catalog Number	Indicates the manufacturer's catalogue number so that the medical device can be identified.	ISO 15223-1 5.1.6
	Batch Code	Indicates the manufacturer's batch code so that the batch or lot can be identified.	ISO 15223-1 5.1.5
	Date of manufacture	Indicates the date when the medical device was manufactured.	ISO 15223-1 5.1.3
	Use-by date	Indicates the date after which the medical device is not to be used.	ISO 15223-1 5.1.4
	Prescription Only	"CAUTION: FEDERAL (USA) LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN."	21 CFR 801.109
	Consult instructions for use or consult electronic instructions for use	Indicates the need for the user to consult the instructions for use.	ISO 15223-1 5.4.3

Symbol	Title	Meaning/Definition	Standard/ Ref. Number
	Caution	To indicate that caution is necessary when operating the device or control close to where the symbol is placed, or to indicate that the current situation needs operator awareness or operator action in order to avoid undesirable consequences.	ISO 15223-1 5.4.4
	Keep away from sunlight	Indicates a medical device that needs protection from light sources.	ISO 15223-1 5.3.2
	Sterilized Using Irradiation	Indicates a medical device that has been sterilized using irradiation.	ISO 15223-1 5.2.4
	Does not contain natural rubber latex	Indicates the absence of dry natural rubber or natural rubber latex as a material of construction within the medical device or the packaging of a medical device.	ISO 15223-1 5.4.5
	Keep Dry	Indicates a medical device that needs to be protected from moisture.	ISO 15223-1 5.3.4
	Do not re-use	Indicates a medical device that is intended for one single use only.	ISO 15223-1 5.4.2
	Do not use if package is damaged and consult instructions for use	Indicates a medical device that should not be used if the package has been damaged or opened and that the user should consult the instructions for use for additional information.	ISO 15223-1 5.2.8
	Do not resterilize	Indicates a medical device that is not to be resterilized.	ISO 15223-1 5.2.6
	Manufacturer	Indicates the medical device manufacturer	ISO 15223-1 5.1.1

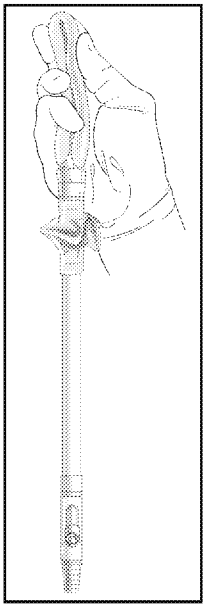


Figure 1

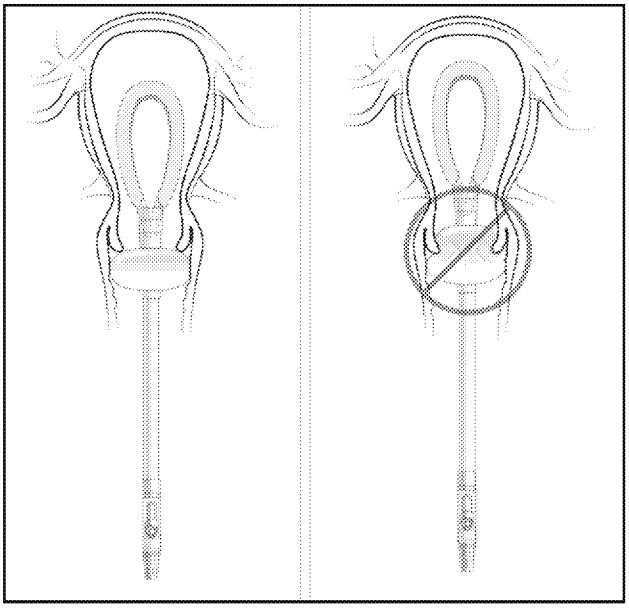


Figure 2

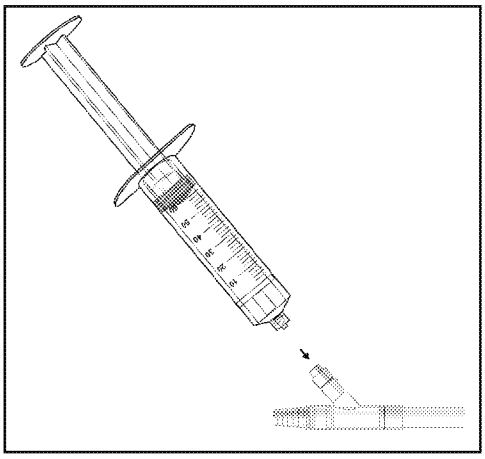


Figure 3

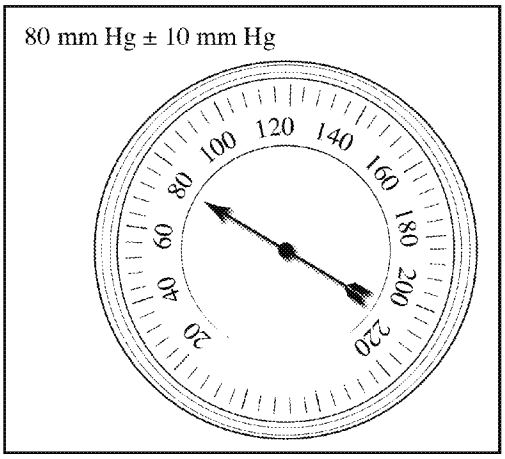


Figure 4

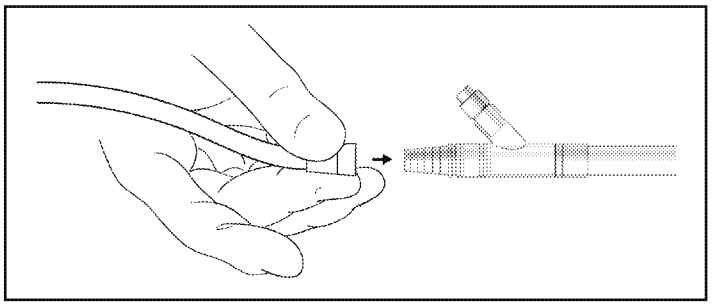


Figure 5

Alydia Health
3495 Edison Way
Menlo Park, CA 94025 USA
Tel: 844-JADAMOM
844-523-2666
www.alydiahealth.com

LBL-15 v3.0
Bakri® Postpartum Balloon is a registered trademark of Cook Incorporated.

U.S. FOOD & DRUG ADMINISTRATION

Food and Drug Administration
CDRH/OPEQ/OHT3/DHT3B
WO66 RM2647
10903 New Hampshire Ave
Silver Spring, MD 20993-0002
240-402-6152

Premarket Notification 510(k) Review

Date: August 28, 2020

Reviewer: Reginald Avery

Subject: Traditional 510(k)# K201199/S001

Applicant: Alydia Health	**Device Trade Name:** Jada System
Contact Name: Cindy Domecus	**Contact Title:** Principal
Correspondent Firm: Domecus Consulting Services LLC	**Phone:** (650) 343-4813 **Email:** domecusconsulting@comcast.net
Received Date: May 4, 2020	**Due Date:** August 2, 2020
Pro Code(s): OQY **Class:** II **Reg #:** 884.4530	**Reg Name:** Obstetric-Gynecologic Specialized Manual Instrument

Predicate Devices:

Submission #	Pro Code	Device Trade Name	Applicant
K170622	OQY	Bakri Postpartum Balloon, Bakri Postpartum Balloon with Rapid Instillation Component	Cook Incorporated

(b)(5) FDA drafts

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Hello Cindy,

I am replacing Dr. Nandy as the lead reviewer for this file and will complete the review for the Jada System. I have discussed the file with Dr. Nandy to ensure our review is consistent. Please let me know if you have any questions.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>

Sent: Friday, August 21, 2020 4:20 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov

Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thank you for your reivew of our file. I am writing to confirm receipt of your below request and that we will respond by the requested date. We stand ready to respond to any further questions FDA may have as the review team completes its review of our file.

Can you please clarify if you are replacing Poulomi as the lead reviewer for this file or is she just on vacation at this time? Thanks.

Have a nice weekend.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? If possible, please provide a response by noon on Tuesday, August 25, 2020.

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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Hello Cindy,

She has not left FDA. Due to an increased workload during the COVID-19 public health emergency, some files were reassigned.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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From: Cindy Domecus <DomecusConsulting@comcast.net>

Sent: Friday, August 21, 2020 5:08 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov

Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thanks for the update! Did Dr. Nandy leave FDA (just curious)?

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 21, 2020, at 2:04 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello Cindy,

I am replacing Dr. Nandy as the lead reviewer for this file and will complete the review for the Jada System. I have discussed the file with Dr. Nandy to ensure our review is consistent. Please let me know if you have any questions.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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From: Cindy Domecus <DomecusConsulting@comcast.net<mailto:DomecusConsulting@comcast.net>>

Sent: Friday, August 21, 2020 4:20 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

Thank you for your reivew of our file. I am writing to confirm receipt of your below request and that we will respond by the requested date. We stand ready to respond to any further questions FDA may have as the review team completes its review of our file.

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Have a nice weekend.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? If possible, please provide a response by noon on Tuesday, August 25, 2020.

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Response to August 25, 2020 Interactive Review Request

Provided below are Alydia Health's responses to FDA's requests identified in its Interactive Review Request dated August 25, 2020. FDA's requests are repeated below in bold font followed by Alydia Health's response in plain font.

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

Clinical comments to Team:

(b)(5) FDA drafts

(b)(5) FDA drafts

(b)(5) FDA drafts

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

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From: Cindy Domecus <DomecusConsulting@comcast.net>

Sent: Thursday, August 27, 2020 12:50 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Thanks Reginald. FYI, I have a Pre-Sub call for another client from 3:00 to 4:00 ET today, so will be â€œout of pocketâ€ for that hour.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 27, 2020, at 4:37 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

>

> Thank you. We will let you know if we have any additional requests as soon as possible.

>

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

> OPEQ: Office of Product Evaluation and Quality

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> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 12:50 AM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

> Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

>

>

>

>

> On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov
<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

> Thanks,

> Reginald

>

> Reginald Avery, Ph.D.

> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

>

> DHT3B: Division of Reproductive, Gynecology and Urology Devices

> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

> OPEQ: Office of Product Evaluation and Quality

> CDRH | Food and Drug Administration

>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

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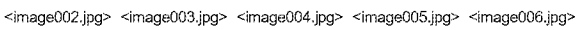

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K201199

Device Name
Jada® System

Indications for Use *(Describe)*
The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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(b)(4) Deficiencies

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Appendix 14.B: Jada System Product Labels

(b)(4) Draft Labeling

(b)(4) Draft Labeling

May 13, 2020</br></br>

Acceptance Review Notification - Accepted

An administrative acceptance review was conducted on your premarket notification (510(k)) K201199, and it was found to contain all of the necessary elements and information needed to proceed with the substantive review. We will contact you should we require any additional information during the course of the substantive review. The lead reviewer assigned to your submission is Poulomi Nandy.

 *** This is a system-generated email notification ***

(b)(4)

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Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

SECTION 6: 510(k) SUMMARY (21 CFR § 807.92(a))

The 510(k) Summary is provided in this section. The 510(k) Summary complies with 807.92(a) and has been prepared in accordance with the formatting in Appendix C of FDA's July 28, 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

510(k) Summary

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TEST FACILITY

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InPress Technologies
955 Morro Street
San Luis Obispo, CA 93401

STUDY TITLE

ISO Vaginal Irritation Study in Rabbits

TEST ARTICLE NAME

Postpartum Hemorrhage Intrauterine Suction Device

TEST ARTICLE IDENTIFICATION

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Exhibit 14.C: Jada System Quick Reference

(b)(4) Draft Package Insert

(b)(4) Draft Package Insert

CE 0088

Bakri Postpartum Balloon
Instructions for Use

Tampónovací balónek Bakri
Návod k použití

Bakri postpartum-ballon
Brugsanvisning

Bakri Postpartum-Ballon
Gebrauchsanweisung

Επιλόχειο μπαλόνι Bakri
Οδηγίες χρήσης

Balón de postparto de Bakri
Instrucciones de uso

Ballonnet post-partum de Bakri
Mode d'emploi

Bakri post partum ballon
Használati utasítás

Palloncino post-parto Bakri
Istruzioni per l'uso

Bakri-postpartumballon
Gebruiksaanwijzing

Bakri-postpartumballong
Bruksanvisning

Balon poporodowy Bakriego
Instrukcja użycia

Balão pós-parto Bakri
Instruções de utilização

Bakri postpartumballong
Bruksanvisning

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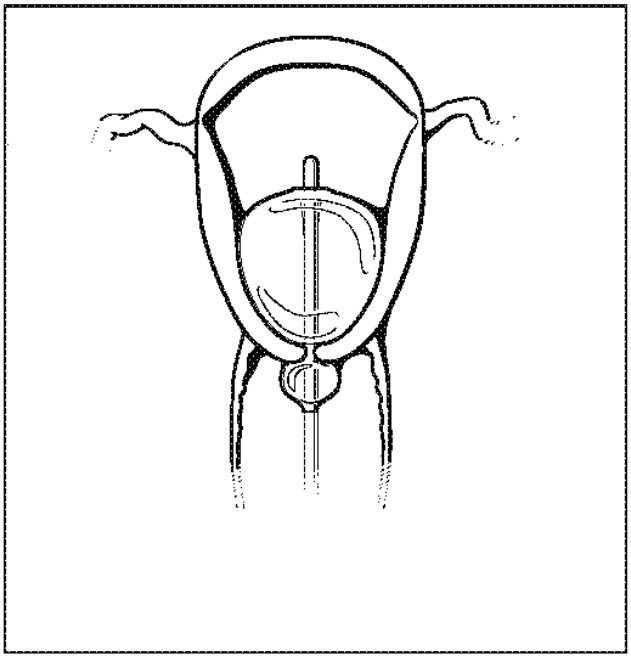

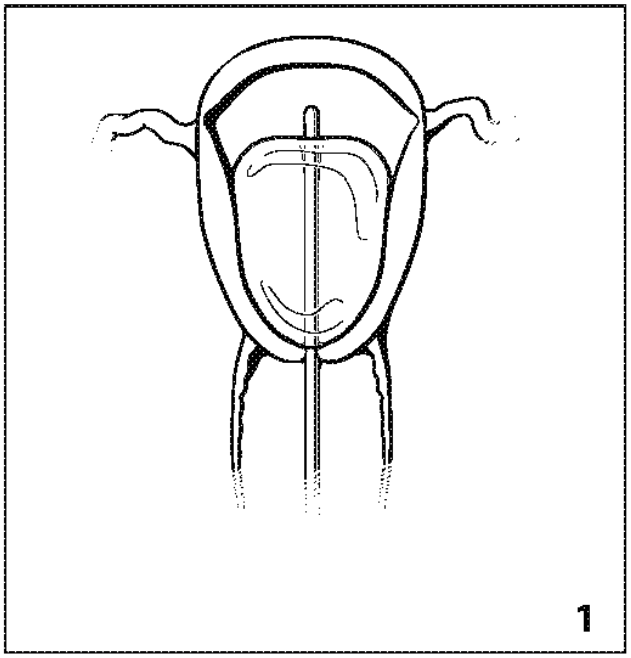

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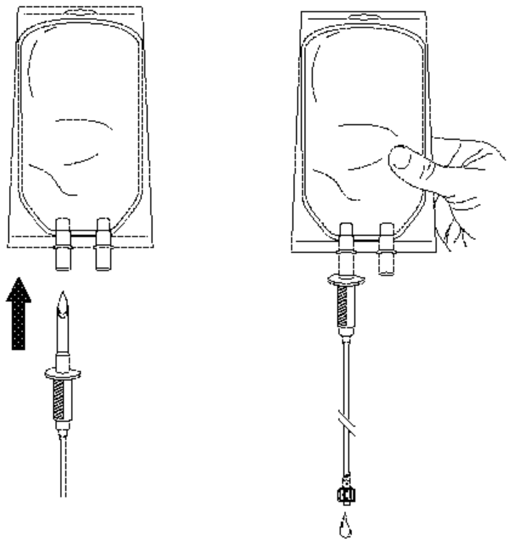
Improper Placement

Nesprávné umístění
Ukorrekt anlæggelse
Falsche Platzierung
Εσφαλμένη τοποθέτηση
Colocación incorrecta
Mise en place incorrecte
Nem megfelelő behelyezés
Posizionamento errato
Verkeerd geplaatst
Feil plassering
Umieszczenie nieprawidłowe
Colocação incorreta
Felaktig placering

Proper Placement

Správné umístění
Korrekt anlæggelse
Richtige Platzierung
Σωστή τοποθέτηση
Colocación correcta
Mise en place correcte
Megfelelő behelyezés
Posizionamento corretto
Correct geplaatst
Riktig plassering
Umieszczenie prawidłowe
Colocação correta
Korrekt placering



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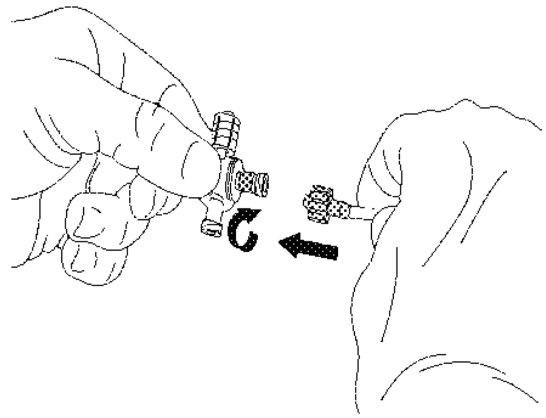

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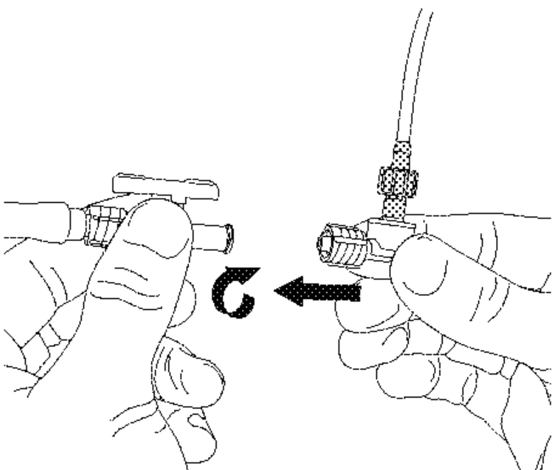

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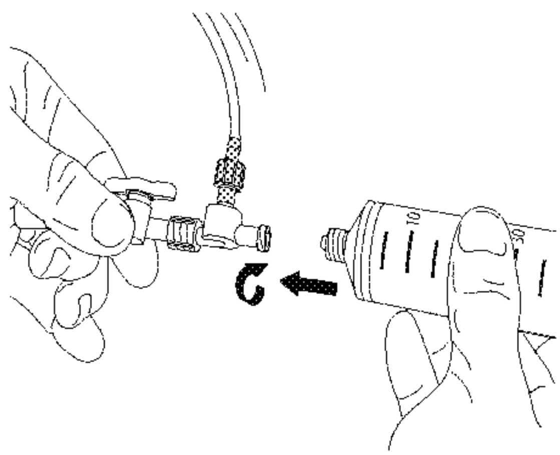

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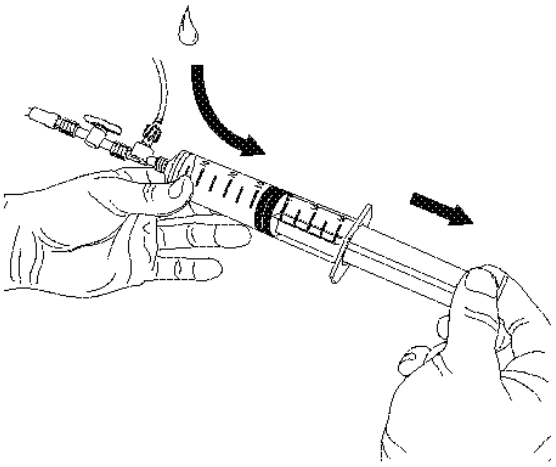

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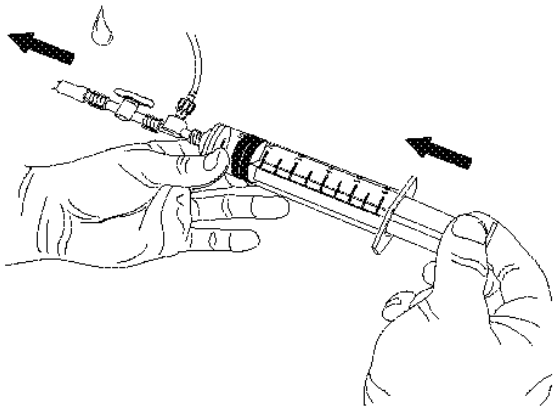

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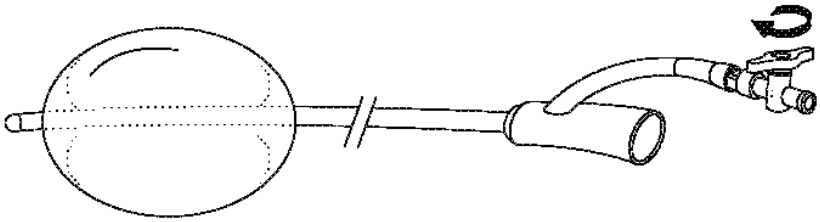

8

BAKRI POSTPARTUM BALLOON

CAUTION: U.S. federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

DEVICE DESCRIPTION

The Bakri Postpartum Balloon is a silicone balloon catheter with a maximum inflation volume of 500 mL. The Rapid Instillation Components include polymer tubing with an IV bag spike and three-way valve.

INTENDED USE

This device is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.

CONTRAINDICATIONS

- Arterial bleeding requiring surgical exploration or angiographic embolization
- Cases indicating hysterectomy
- Pregnancy
- Cervical cancer
- Purulent infections in the vagina, cervix, or uterus
- Untreated uterine anomaly
- Disseminated intravascular coagulation
- A surgical site that would prohibit the device from effectively controlling bleeding

WARNINGS

- This device is intended as a temporary means of establishing hemostasis in cases indicating conservative management of postpartum uterine bleeding.
- The Bakri Postpartum Balloon is indicated for use in the event of primary postpartum hemorrhage within 24 hours of delivery.
- The device should not be left indwelling for more than 24 hours.
- The balloon should be inflated with a sterile liquid such as sterile water, sterile saline, or lactated ringers solution. The balloon should never be inflated with air, carbon dioxide or any other gas.
- The maximum inflation is 500 mL. Do not overinflate the balloon. Overinflation of the balloon may result in the balloon being displaced into the vagina.
- Patients in whom this device is being used should be closely monitored for signs of worsening bleeding and/or disseminated intravascular coagulation (DIC). In such cases, emergency intervention per hospital protocol should be followed.
- There are no clinical data to support use of this device in the setting of DIC.
- Patient monitoring is an integral part of managing postpartum hemorrhage. Signs of deteriorating or non-improving condition should lead to a more aggressive treatment and management of patient uterine bleeding.
- Patient urine output should be monitored while the Bakri Postpartum Balloon is in use.

PRECAUTIONS

- This product is intended for use by physicians trained and experienced in obstetrics and gynecological techniques.
- Avoid excessive force when inserting the balloon into the uterus.

INSTRUCTIONS FOR USE

IMPORTANT: Prior to transvaginal or transabdominal placement of the Bakri Postpartum Balloon, the uterus should be free of all placental fragments, and the patient should be evaluated to ensure that there are no lacerations or trauma to the genital tract and that the source of the bleeding is not arterial.

Transvaginal Placement

1. Determine uterine volume by direct examination or ultrasound examination.
2. Insert the balloon portion of the catheter into the uterus, making certain that the entire balloon is inserted past the cervical canal and internal ostium.
3. Place an indwelling urinary bladder Foley catheter at this time, if not already in place, to collect and monitor urine output.

Transabdominal Placement, Post-Cesarean Section

1. Determine uterine volume by direct examination.
2. From above, via access of the cesarean incision, pass the tamponade balloon, inflation port first, through the uterus and cervix.

NOTE: Remove the stopcock to aid in placement and reattach prior to filling balloon.

3. Have an assistant pull the shaft of the balloon through the vaginal canal until the deflated balloon base comes into contact with the internal cervical ostium.
4. Close the incision per normal procedure, taking care to avoid puncturing the balloon while suturing.

NOTE: Ensure that all product components are intact and the hysterotomy is securely sutured prior to inflating the balloon. If clinically relevant, the abdomen may remain open upon inflation of the balloon to closely monitor uterine distention and confirm the hysterotomy closure.

NOTE: If clinically relevant, a B-Lynch compression suture may be used in conjunction with the Bakri Postpartum Balloon.

Balloon Inflation

With Syringe

WARNING: Always inflate the balloon with sterile liquid. Never inflate with air, carbon dioxide or any other gas.

WARNING: The maximum inflation is 500 mL. Do not overinflate the balloon. Overinflation of the balloon may result in the balloon being displaced into the vagina.

NOTE: To ensure that the balloon is filled to the desired volume, it is recommended that the predetermined volume of fluid be placed in a separate container, rather than relying on a syringe count to verify the amount of fluid that has been instilled into the balloon.

1. Place an indwelling urinary bladder Foley catheter at this time, if not already in place, to collect and monitor urine output.
2. Using the enclosed syringe, begin filling the balloon to the predetermined volume through the stopcock.
3. Once the balloon has been inflated to the predetermined volume, confirm placement via ultrasound. **NOTE: See Fig. 1 for proper placement.**
4. If desired, traction can be applied to the balloon shaft. In order to maintain tension, secure the balloon shaft to the patient's leg or attach to a weight, not to exceed 500 grams.

NOTE: To prevent displacement of the balloon into the vagina, counterpressure can be applied by packing the vaginal canal with iodine- or antibiotic-soaked vaginal gauze.

5. Connect the drainage port to a fluid collection bag to monitor hemostasis.

NOTE: To adequately monitor hemostasis, the balloon drainage port and tubing may be flushed clear of clots with sterile isotonic saline.

6. Monitor the patient continuously for signs of increased bleeding and uterine cramping.

Balloon Inflation

With Rapid Instillation Components

See **Figs. 2-8**, at the front of this booklet.

NOTE: Ultrasound should be used to confirm proper placement of the balloon once the balloon is inflated to the predetermined volume.

Balloon Removal

NOTE: The timing of balloon removal should be determined by the attending clinician upon evaluation of the patient once bleeding has been controlled and the patient has been stabilized. The balloon may be removed sooner upon the clinician's determination of hemostasis. The maximum indwell time is 24 hours.

1. Remove tension from the balloon shaft.
2. Remove any vaginal packing.
3. Using an appropriate syringe, aspirate the contents of the balloon until fully deflated. The fluid may be removed incrementally to allow periodic observation of the patient.

NOTE: In an emergent situation, the catheter shaft may be cut to facilitate more rapid deflation.

4. Gently retract the balloon from the uterus and vaginal canal and discard.
5. Monitor patient for signs of bleeding.

HOW SUPPLIED

Supplied sterilized by ethylene oxide gas in peel-open packages. Intended for one-time use. Sterile if package is unopened and undamaged. Do not use the product if there is doubt as to whether the product is sterile. Store in a dark, dry, cool place. Avoid extended exposure to light. Upon removal from the package, inspect the product to ensure no damage has occurred.

REFERENCE

These instructions for use are based on experience from physicians and (or) their published literature. Refer to your local Cook sales representative for information on available literature.

ČESKY

TAMPÓNOVACÍ BALÓNEK BAKRI

POZOR: Federální zákony USA dovolují prodej tohoto prostředku pouze lékařům nebo na předpis lékaře (nebo kvalifikovaného zdravotníka s licencí).

POPIS PROSTŘEDKU

Tampónovací balónek Bakri je silikonový balónkový katetr s maximálním plnicím objemem 500 mL. Komponenty pro rychlé vstřikování zahrnují polymerovou hadičku s bodcem na IV vak a trojcestný ventil.

URČENÉ POUŽITÍ

Tento prostředek je určen k dočasnému zvládnutí nebo ke snížení postpartálního krvácení z dělohy, pokud jsou důvody ke konzervativní léčbě.

KONTRAINDIKACE

- Tepenné krvácení vyžadující chirurgickou revizi nebo angiografickou embolizaci
- Případy, kdy je indikována hysterektomie
- Těhotenství
- Rakovina děložního hrdla
- Hnisavé infekce pochvy, děložního hrdla nebo dělohy
- Neléčený abnormální stav dělohy

- Diseminovaná intravaskulární koagulopatie
- Místo chirurgického zákroku, kde prostředek nemůže účinně fungovat při zástavě krvácení

VAROVÁNÍ

- Tento prostředek je určen k dočasnému navození hemostáze v případech, kde je indikována konzervativní léčba postpartálního děložního krvácení.
- Tampónovací balónek Bakri je indikován k použití v případě primárního postpartálního krvácení v období 24 hodin po porodu.
- Prostředek se nesmí ponechat zavedený v těle déle než 24 hodin.
- Balónek se plní sterilní kapalinou, např. sterilní vodou, sterilním fyziologickým roztokem nebo složeným roztokem mléčnanu sodného (Ringer-laktátový roztok). Balónek nikdy nenaplňujte vzduchem, oxidem uhličitým ani jiným plynem.
- Maximální objem náplně je 500 mL. Balónek nepřeplňte. Přeplnění balónků může vést k jeho dislokaci do vagíny.
- Pacientky, u kterých se tento prostředek použije, musí být pečlivě sledovány, zda nejeví známky zhoršeného krvácení nebo diseminované intravaskulární koagulopatie. V takových případech se musí provést nouzová intervence podle nemocničního protokolu.
- Neexistují žádné klinické údaje na podporu použití tohoto prostředku v případech diseminované intravaskulární koagulopatie.
- Monitorování pacientky je nedílnou součástí léčby postpartálního krvácení. Známky nezlepšujícího se nebo zhoršeného stavu musí vést k agresivnějším způsobům léčby pacientky s děložním krvácením.
- Při použití tampónovacího balónku Bakri se musí u pacientky monitorovat výdej moči.

UPOZORNĚNÍ

- Tento výrobek je určen k použití lékaři, kteří jsou vyškoleni v porodnických a gynekologických výkonech a mají s nimi zkušenosti.
- Při zavádění balónku do dělohy nepoužívejte nadměrnou sílu.

NÁVOD K POUŽITÍ

DŮLEŽITÉ: Před transvaginálním (pochvou) nebo transabdominálním (břichem) umístěním tampónovacího balónku Bakri nesmí být v děloze zbytky placenty a pacientka musí být vyhodnocena, zda nemá tržné rány nebo jiná poranění genitálií, a zda se nejedná o tepenné krvácení.

Zavedení pochvou

1. Zjistěte objem dělohy přímým nebo ultrazvukovým vyšetřením.
2. Zaveďte balónkovou část katetru do dělohy a zkontrolujte, že je celý balkónek zaveden za kanál děložního hrdla a vnitřního ústí.
3. V této fázi zaveďte trvalou cévku Foley do močového měchýře, pokud již není zavedena, pro sledování odtoku moči a její sběr.

Zavedení břichem, po císařském řezu

1. Zjistěte objem dělohy přímým vyšetřením.
2. Přístupem skrz incizi císařského řezu shora zaveďte tampónovací balónek skrz dělohu a děložní hrdlo, plnicím portem napřed.

POZNÁMKA: Na pomoc při zavedení sejměte uzavírací kohout a před plněním balónku jej znovu připevněte.

3. Požádejte asistenta, aby zatáhl za tubus balónku skrz poševní kanál, až se základna vyprázdněného balónku dotkne vnitřního ústí děložního hrdla.
4. Normální technikou uzavřete incizi a dávejte pozor, aby při šití nedošlo k propíchnutí balónku.

POZNÁMKA: Před naplněním balónku se přesvědčte, že všechny součásti výrobku jsou intaktní a že

hysterotomie je bezpečně uzavřená suturou. Pokud je to klinicky relevantní, břicho může po naplnění balónku zůstat otevřené pro sledování distenze dělohy a potvrzení uzavření hysterotomie.

POZNÁMKA: Pokud je to klinicky relevantní, může se společně s tampónovacím balónkem Bakri použít kompresní steh B-Lynch.

Plnění balónku

Se stříkačkou

VAROVÁNÍ: Balónek naplňujte vždy sterilní tekutinou. Nikdy je nenaplňujte vzduchem, oxidem uhličitým ani jiným plynem.

VAROVÁNÍ: Maximální objem náplně je 500 mL. Balónek nepřeplňte. Přeplnění balónků může vést k jeho dislokaci do vagíny.

POZNÁMKA: Je nutno zajistit, aby balónek byl naplněn na požadovaný objem. Doporučujeme připravit předem určený objem kapaliny do samostatné nádobky. Pro ověření objemu, který byl vstříknut do balónku, nespoléhejte na dávkování stříkačkou.

1. V této fázi zaveďte trvalou cévku Foley do močového měchýře, pokud již není zavedena, pro sledování odtoku moči a její sběr.
2. Přiloženou stříkačkou začněte plnit balónek skrz uzavírací kohout na předem určený objem.
3. Jakmile je balónek naplněn na předem určený objem, potvrďte umístění ultrazvukem.
   POZNÁMKA: Správné umístění ilustruje obr. 1.
4. Pokud je to žádoucí, je možné aplikovat tah na tubus balónku. Pro udržení tahu připevněte tubus balónku k noze pacientky nebo na něj připevněte závaží o maximální hmotnosti 500 g.

POZNÁMKA: Abyste předešli nesprávnému umístění balónku v pochvě, lze aplikovat protitlak vyložením poševního kanálu gázovými tampony namočenými v jódovém nebo antibiotikovém přípravku.

5. Připojte drenážní port k vaku určenému pro sběr tekutin a monitorujte hemostázu.

POZNÁMKA: Pro adekvátní monitorování hemostázy se drenážní port balónku a hadičky mohou propláchnout sterilním izotonickým fyziologickým roztokem, aby v nich nebyly krevní sraženiny.

6. Nepřetržitě sledujte, zda se u pacientky neobjevují známky zvýšeného krvácení a děložních křečí.

Plnění balónku

S komponentami pro rychlé vstřikování

Viz **obr. 2-8** na začátku této brožurky.

POZNÁMKA: Jakmile je balónek naplněn na předem určený objem, musí se ultrazvukem potvrdit správná poloha balónku.

Vyjmutí balónku

POZNÁMKA: Dobu odstranění balónku určí ošetřující lékař po vyhodnocení pacientky, jakmile se krvácení dostane pod kontrolu a pacientka je stabilizována. Balónek lze vyjmout dříve, podle lékařova hodnocení hemostázy. Maximální doba zavedení je 24 hodin.

1. Odstraňte tah aplikovaný na tubus balónku.
2. Vyjměte všechny tampónovací materiály z pochvy.
3. Vhodnou stříkačkou odsajte obsah balónku a zcela jej vyprázdněte. Kapalina se může odstraňovat po částech, aby bylo možné pravidelné sledování pacientky.

POZNÁMKA: V naléhavé situaci se může tubus katetru odstřihnout, aby se urychlilo vyprazdňování.

4. Jemně vytáhněte balónek z dělohy a poševního kanálu a zlikvidujte jej.
5. Sledujte, zda u pacientky nedochází ke krvácení.

STAV PŘI DODÁNÍ

Výrobek je dodáván v odtrhovacím obalu a je sterilizován plynným ethylenoxidem. Určeno pro jednorázové použití. Sterilní, pokud obal není otevřen nebo poškozen. Nepoužívejte výrobek, pokud existují pochybnosti o jeho sterilitě. Skladujte na tmavém, suchém a chladném místě. Zamezte dlouhodobému vystavení světlu. Po odstranění obalu výrobek prohlédněte a zkontrolujte, zda není poškozený.

LITERATURA

Tento návod k použití je založen na zkušenostech lékařů a (nebo) na jejich publikované odborné literatuře. S otázkami na dostupnou literaturu se obraťte na svého nejbližšího obchodního zástupce společnosti Cook.

DANSK

BAKRI POSTPARTUM-BALLON

FORSIGTIG: I henhold til amerikansk lovgivning må dette produkt kun sælges af en læge eller efter en læges ordination (eller en autoriseret behandler).

BESKRIVELSE AF PRODUKTET

Bakri postpartum-ballonen er et silikoneballonkateter med et maksimalt inflationsvolumen på 500 mL. De hurtige instillationskomponenter omfatter polymerslange med en kanyle og trevejs ventil til I.V.-pose.

TILSIGTET ANVENDELSE

Denne anordning er beregnet til at give midlertidig kontrol eller reduktion af postpartum blødning i uterus, hvor konservativ behandling er berettiget.

KONTRAINDIKATIONER

- Arterieblødning, der kræver en kirurgisk undersøgelse eller angiografisk embolisering
- Tilfælde, hvor hysterektomi er indiceret
- Graviditet
- Livmoderhalskræft
- Pusdannende infektioner i vagina, cervix eller uterus
- Ubehandlet anomali i uterus
- Dissemineret intravaskulær koagulation
- Et operationssted, der ville forhindre anordningen i at kontrollere blødning effektivt

ADVARSLER

- Anordningen er beregnet som et midlertidigt middel til etablering af hæmostase i tilfælde, hvor konservativ behandling af postpartum blødning i uterus er indiceret.
- Bakri postpartum-ballonen er indiceret til brug i tilfælde af primær postpartum blødning inden 24 timer efter fødslen.
- Anordningen må ikke forblive indlagt længere end 24 timer.
- Ballonen skal inflateres med en steril væske såsom sterilt vand, sterilt saltvand eller Ringers laktat. Ballonen må aldrig inflateres med luft, kuldioxid eller nogen anden luftart.
- Maksimal fyldning er 500 mL. Ballonen må ikke overudspiles. Overudspiling af ballonen kan resultere i, at ballonen forskubbes i vagina.
- Patienter, hos hvem anordningen anlægges, skal overvåges nøje for tegn på forværret blødning og/eller dissemineret intravaskulær koagulation (DIC). I disse tilfælde skal akut intervention finde sted, i henhold til hospitalsprotokollen.
- Der findes ingen kliniske data til understøttelse af brugen af anordningen ved DIC.
- Patientovervågning er en integreret del af behandlingen af postpartum blødning. Tegn på en tilstand i forværring og som ikke viser tegn på bedring, bør følges af mere aggressiv behandling og styring af patientens blødning i uterus.
- Patientens urinproduktion skal overvåges, så længe Bakri postpartum-ballonen er i brug.

FORHOLDSREGLER

- Dette produkt er beregnet til brug for læger med uddannelse og erfaring i obstetrik og gynækologiske teknikker.

- Undgå for stor kraft ved indsætning af ballonen i uterus.

BRUGSANVISNING

VIGTIGT: Inden transvaginal eller transabdominal anlæggelse af Bakri postpartum-ballonen skal uterus være fri for alle placentarester, og patienten skal evalueres for at sikre, at der ikke er rifter eller traume i genitaltrakten, og at årsagen til blødningen ikke er arteriel.

Transvaginal anlæggelse

1. Bestem volumen af uterus ved direkte undersøgelse eller med ultralyd.
2. Indsæt ballondelen af kateteret i uterus, og sørg for, at hele ballonen føres forbi cervikalkanalen og interne ostium.
3. Anlæg et indlagt Foley-kateter i urinblæren på dette tidspunkt, hvis dette ikke allerede er gjort, for at opsamle og overvåge urinproduktionen.

Transabdominal anlæggelse, efter kejsersnit

1. Bestem volumen af uterus ved direkte undersøgelse.
2. Fra oven føres tamponadeballonen via kejsersnitåbningen, og med inflationsporten først, igennem uterus og cervix.

BEMÆRK: Fjern stophanen for at lette anlæggelse og sæt den på igen, inden ballonen fyldes.

3. Få en assistent til at trække ballonens skaft igennem vaginalkanalen, indtil det nederste af den tømte ballon kommer i kontakt med interne cervicale ostium.
4. Luk incisionen på normal vis. Udvis forsigtighed for at undgå at stikke hul i ballonen ved sutureringen.

BEMÆRK: Sørg for at alle produktkomponenter er intakte, og at hysterotomien er sutureret korrekt, inden ballonen inflateres. Hvis det er klinisk relevant, kan abdomen forblive åbent efter fyldning af ballonen, så udspilingen af uterus kan overvåges, og lukning af hysterotomien bekræftes.

BEMÆRK: Hvis det er klinisk relevant, kan der anvendes en B-Lynch-sutur sammen med Bakri postpartum-ballonen.

Balloninflation

Med sprøjte

ADVARSEL: Ballonen skal altid inflateres med steril væske. Ballonen må aldrig inflateres med luft, kuldioxid eller nogen anden luftart.

ADVARSEL: Maksimal fyldning er 500 mL. Ballonen må ikke overudspiles. Overudspiling af ballonen kan resultere i, at ballonen forskubbes i vagina.

BEMÆRK: For at sikre, at ballonen fyldes til det ønskede volumen, anbefales det, at det forudfastlagte væskevolumen hældes i en særskilt beholder frem for at stole på en måling med sprøjten til at bekræfte den mængde væske, der er instilleret i ballonen.

1. Anlæg et indlagt Foley-kateter i urinblæren på dette tidspunkt, hvis dette ikke allerede er gjort, for at opsamle og overvåge urinproduktionen.
2. Brug den vedlagte sprøjte, og start påfyldningen af ballonen til det forudfastlagte volumen via stophanen.
3. Når ballonen er fyldt til det forudfastlagte volumen, skal anlæggelsen bekræftes med ultralyd.
   BEMÆRK: Se fig. 1 vedrørende korrekt anlæggelse.
4. Hvis ønsket, kan der påføres træk på ballonskaftet. For at opretholde spændingen fastgøres ballonskaftet til patientens ben eller til en vægt, der ikke må overstige 500 gram.

BEMÆRK: For at forhindre at ballonen forskubbes i vagina, kan der påføres modtryk ved at udfylde vaginalkanalen med vaginalgazetamponer gennemvædet med jod eller antibiotika.

5. Tilslut drænageporten til en væskeopsamlingspose for at overvåge hæmostase.

BEMÆRK: For at overvåge hæmostase på korrekt vis, kan ballonens drænageport og slange skylles fri for koagler med sterilt isotonisk saltvand.

6. Overvåg patienten konstant for tegn på øget blødning og uteruskramper.

Balloninflation

Med komponenter til hurtig instillation

Se **fig. 2-8** forrest i denne brochure.

BEMÆRK: Der skal bruges ultralyd til at bekræfte den korrekte placering af ballonen, efter at ballonen er fyldt til det forudfastlagte volumen.

Fjernelse af ballonen

BEMÆRK: Tidspunktet for fjernelse af ballonen skal bestemmes af den tilsynsførende læge efter evaluering af patienten, når blødningen er under kontrol og patienten er stabiliseret. Ballonen kan fjernes tidligere afhængigt af lægens bedømmelse af hæmostase. Den maksimale indlæggelsestid er 24 timer.

1. Udløs spændingen på ballonens skaft.
2. Fjern eventuelle gazetamponer fra vagina.
3. Brug en passende sprøjte, og aspirér indholdet af ballonen, indtil den er helt tom. Væsken kan fjernes gradvist, så patienten kan observeres regelmæssigt.

BEMÆRK: I en nødsituation kan kateterskaftet skæres, så tømningen sker hurtigere.

4. Træk ballonen forsigtigt ud af uterus og vaginalkanalen, og kassér den.
5. Overvåg patienten for tegn på blødning.

LEVERING

Leveres steriliseret med ethylenoxid i peel-open pakninger. Beregnet til engangsbrug. Steril, hvis pakningen er uåbnet eller ubeskadiget. Produktet må ikke bruges, hvis der er tvivl om produktets sterilitet. Opbevares mørkt, tørt og køligt. Undgå længere eksponering for lys. Inspicér produktet efter udtagning fra pakningen for at sikre, at det ikke er beskadiget.

LITTERATUR

Denne brugsanvisning er baseret på lægers erfaring og (eller) lægers publicerede litteratur. Kontakt den lokale salgsrepræsentant for Cook for at få information om tilgængelig litteratur.

DEUTSCH

BAKRI POSTPARTUM-BALLON

VORSICHT: Laut US-Gesetzgebung darf dieses Instrument nur von einem Arzt oder im Auftrag eines Arztes gekauft werden.

BESCHREIBUNG DES INSTRUMENTS

Der Bakri Postpartum-Ballon ist ein Ballonkatheter aus Silikon mit einem maximalen Inflationsvolumen von 500 mL. Die Schnell-Instillationskomponenten umfassen einen Polymerschlauch mit IV-Beuteldorn und Drei-Wege-Ventil.

VERWENDUNGSZWECK

Dieses Produkt dient zur vorübergehenden Kontrolle bzw. Reduzierung postpartaler Uterusblutungen, wenn eine konservative Behandlung gerechtfertigt ist.

KONTRAINDIKATIONEN

- Arterielle Blutungen, die eine chirurgische Sondierung oder angiographische Embolisation erfordern
- Bestehende Indikation für eine Hysterektomie
- Schwangerschaft
- Zervixkarzinom
- Eitrige Infektionen in Vagina, Zervix oder Uterus
- Unbehandelte Uterusanomalien

- Disseminierte intravasale Koagulopathie
- Operationsstelle, die eine wirksame Blutungskontrolle durch das Produkt verhindern würde

WARNHINWEISE

- Dieses Produkt ist zur vorübergehenden Anwendung bei der Stillung von postpartalen Uterusblutungen bestimmt, wenn eine konservative Behandlung gerechtfertigt ist.
- Der Bakri Postpartum-Ballon ist zur Anwendung im Falle von primären postpartalen Blutungen innerhalb von 24 Stunden nach der Geburt bestimmt.
- Das Produkt darf nicht länger als 24 Stunden im Körper verweilen.
- Der Ballon ist mit einer sterilen Flüssigkeit wie sterilem Wasser, steriler Kochsalzlösung oder Ringer-Laktat-Lösung zu inflatieren. Der Ballon darf niemals mit Luft, Kohlendioxid oder sonstigem Gas inflatiert werden.
- Das maximale Inflationsvolumen beträgt 500 mL. Den Ballon nicht überinflatieren. Wird der Ballon überinflatiert, kann es dazu kommen, dass der Ballon in die Vagina verschoben wird.
- Patientinnen mit diesem Produkt müssen sorgfältig auf Anzeichen einer verschlimmerten Blutung und/oder disseminierten intravasalen Koagulopathie (DIC) überwacht werden. In solchen Fällen ist eine Notintervention nach dem Protokoll des jeweiligen Krankenhauses einzuleiten.
- Zum Einsatz dieses Produkts bei DIC liegen keine klinischen Daten vor.
- Die Überwachung der Patientin ist ein integraler Bestandteil der Beherrschung postpartaler Blutungen. Bei Anzeichen einer Verschlimmerung oder ausbleibenden Besserung der Symptome ist eine aggressivere Behandlung der Uterusblutung einzuleiten.
- Während der Anwendung des Bakri Postpartum-Ballons ist die ausgeschiedene Urinmenge der Patientin zu überwachen.

VORSICHTSMASSNAHMEN

- Dieses Produkt ist zur Verwendung durch Ärzte bestimmt, die in obstetrischen und gynäkologischen Techniken geschult und erfahren sind.
- Beim Einführen des Ballons in den Uterus keine übermäßige Kraft aufwenden.

GEBRAUCHSANWEISUNG

WICHTIG: Vor der transvaginalen bzw. transabdominalen Einführung des Bakri Postpartum-Ballons sollte der Uterus frei von Plazentaresten sein und es sollte eine Beurteilung der Patientin stattfinden, um sicherzustellen, dass im Genitaltrakt weder Lazerationen noch Traumata vorliegen und dass der Ursprung der Blutung nicht arteriell ist.

Transvaginale Einführung

1. Uterusvolumen durch direkte Untersuchung oder Ultraschall ermitteln.
2. Den Ballonanteil des Katheters in den Uterus einführen und darauf achten, dass der gesamte Ballon den Zervixkanal und den inneren Muttermund passiert.
3. Zum Auffangen von Urin und zur Kontrolle des Urinvolumens einen Foley-Verweilkatheter in die Harnblase legen, falls nicht bereits geschehen.

Transabdominale Einführung nach einer Kaiserschnittentbindung

1. Uterusvolumen durch direkte Untersuchung ermitteln.
2. Den Tamponadeballon von oben her und mit dem Inflationszugang voran über die Kaiserschnittinzision durch Uterus und Zervix führen.

HINWEIS: Zur leichteren Einführung Absperrhahn entfernen und vor der Füllung des Ballons wieder anbringen.

3. Die Assistenz bitten, den Ballonschaft durch den Vaginalkanal zu ziehen, bis die Basis des deflatierten Ballons den inneren Muttermund berührt.
4. Die Inzision wie üblich verschließen und dabei darauf achten, dass der Ballon beim Anlegen der Naht nicht punktiert wird.

HINWEIS: Vor der Inflation des Ballons sicherstellen, dass alle Produktkomponenten intakt sind und die Hysterotomie gut vernäht ist. Falls klinisch relevant, kann das Abdomen bei der Inflation des Ballons geöffnet bleiben, um die Uterusdistension engmaschig zu überwachen und den Verschluss der Hysterotomie zu bestätigen.

HINWEIS: Falls klinisch relevant, kann in Verbindung mit dem Bakri Postpartum-Ballon eine B-Lynch-Kompressionsnaht angebracht werden.

Balloninflation

mittels Spritze

WARNHINWEIS: Den Ballon grundsätzlich mit einer sterilen Flüssigkeit inflatieren. Zur Inflation niemals Luft, Kohlendioxid oder ein anderes Gas verwenden.

WARNHINWEIS: Das maximale Inflationsvolumen beträgt 500 mL. Den Ballon nicht überinflatieren. Wird der Ballon überinflatiert, kann es dazu kommen, dass der Ballon in die Vagina verschoben wird.

HINWEIS: Um sicherzustellen, dass der Ballon auf das vorgesehene Volumen gefüllt wird, wird empfohlen, das zuvor ermittelte Flüssigkeitsvolumen in einen separaten Behälter zu füllen. Dies erleichtert die Kontrolle über die in den Ballon instillierte Flüssigkeitsmenge im Vergleich zum Zählen der Spritzen.

1. Zum Auffangen von Urin und zur Kontrolle des Urinvolumens einen Foley-Verweilkatheter in die Harnblase legen, falls nicht bereits geschehen.
2. Mithilfe der beiliegenden Spritze den Ballon durch den Absperrhahn bis zum zuvor bestimmten Volumen füllen.
3. Sobald der Ballon bis zum zuvor bestimmten Volumen gefüllt wurde, die Platzierung mittels Ultraschall bestätigen.

   HINWEIS: Die richtige Platzierung ist aus Abb. 1 ersichtlich.
4. Bei Bedarf kann Zug auf den Ballonschaft ausgeübt werden. Um den Zug aufrecht zu erhalten, den Ballonschaft am Bein der Patientin befestigen oder ein Gewicht (maximal 500 g) anbringen.

HINWEIS: Um ein Abrutschen des Ballons in die Vagina zu vermeiden, kann ein Gegendruck aufgebaut werden, indem der Vaginalkanal mit in Iodtinktur oder Antibiotika getränktem Vaginalmull ausgefüllt wird.

5. Den Drainageanschluss zur Kontrolle der Hämostase an einen Auffangbeutel für Flüssigkeiten anschließen.

HINWEIS: Um die Hämostase adäquat zu überwachen, können Gerinnsel mit steriler isotonischer Kochsalzlösung aus dem Drainageanschluss des Ballons und dem Schlauch gespült werden.

6. Die Patientin muss kontinuierlich auf Anzeichen für eine verstärkte Blutung oder Uteruskrämpfe überwacht werden.

Balloninflation

mit Schnell-Instillationskomponenten

Siehe **Abb. 2-8** vorne in diesem Handbuch.

HINWEIS: Sobald der Ballon bis zum zuvor bestimmten Volumen gefüllt wurde, sollte seine richtige Platzierung mittels Ultraschall bestätigt werden.

Entfernung des Ballons

HINWEIS: Der Zeitpunkt zur Entfernung des Ballons sollte vom behandelnden Arzt nach erfolgter Auswertung der Patientin, sobald die Blutung kontrolliert und die Patientin stabilisiert wurde, festgelegt werden. Der Ballon kann nach Einschätzung der Hämostase durch den Arzt früher entfernt werden. Die maximale Verweildauer beträgt 24 Stunden.

1. Den Zug am Ballonschaft lösen.
2. Mullfüllung (falls verwendet) aus der Vagina entfernen.
3. Den Inhalt des Ballons mit einer geeigneten Spritze aspirieren, bis dieser vollständig deflatiert ist. Die Flüssigkeit kann schrittweise entfernt werden, um eine periodische Überwachung der Patientin zu ermöglichen.

HINWEIS: In einer Notfallsituation kann der Katheterschaft zur rascheren Deflation eingeschnitten werden.

4. Den Ballon vorsichtig aus dem Uterus und dem Vaginalkanal ziehen und entsorgen.
5. Die Patientin auf Anzeichen für eine Blutung überwachen.

LIEFERFORM

Produkt mit Ethylenoxid gassterilisiert; in Aufreißverpackungen. Nur für den einmaligen Gebrauch. Bei ungeöffneter und unbeschädigter Verpackung steril. Produkt nicht verwenden, falls Zweifel an der Sterilität bestehen. An einem dunklen, trockenen, kühlen Ort lagern. Längere Lichteinwirkung vermeiden. Nachdem das Produkt der Verpackung entnommen wurde, auf Beschädigungen überprüfen.

LITERATUR

Diese Gebrauchsanweisung basiert auf der Erfahrung von Ärzten und/oder auf Fachliteratur. Informationen über verfügbare Literatur erhalten Sie bei Ihrem Cook Außendienstmitarbeiter.

ΕΛΛΗΝΙΚΑ

ΕΠΙΛΟΧΕΙΟ ΜΠΑΛΟΝΙ BAKRI

ΠΡΟΣΟΧΗ: Η ομοσπονδιακή νομοθεσία των Η.Π.Α. επιτρέπει την πώληση της συσκευής αυτής μόνον από ιατρό ή κατόπιν εντολής ιατρού (ή επαγγελματία υγείας ο οποίος έχει λάβει την κατάλληλη άδεια).

ΠΕΡΙΓΡΑΦΗ ΤΗΣ ΣΥΣΚΕΥΗΣ

Το επιλόχειο μπαλόνι Bakri είναι ένας καθετήρας με μπαλόνι σιλικόνης με μέγιστο όγκο πλήρωσης 500 mL. Τα εξαρτήματα ταχείας ενστάλλαξης περιλαμβάνουν σωλήνωση από πολυμερές με ακίδα ασκού ενδοφλέβιας έγχυσης και τρίοδη βαλβίδα.

ΧΡΗΣΗ ΓΙΑ ΤΗΝ ΟΠΟΙΑ ΠΡΟΟΡΙΖΕΤΑΙ

Αυτή η συσκευή προορίζεται για την παροχή προσωρινού ελέγχου ή μείωσης της επιλόχειας αιμορραγίας της μήτρας, όταν είναι επιβεβλημένη η συντηρητική αντιμετώπιση.

ΑΝΤΕΝΔΕΙΞΕΙΣ

- Αρτηριακή αιμορραγία που απαιτεί χειρουργική διερεύνηση ή αγγειογραφικό εμβολισμό
- Περιπτώσεις στις οποίες ενδείκνυται υστερεκτομή
- Κύηση
- Καρκίνος του τραχήλου της μήτρας
- Πυώδεις λοιμώξεις στον κόλπο, στον τράχηλο ή στη μήτρα
- Μη αντιμετωπισθείσα ανωμαλία της μήτρας
- Διάχυτη ενδαγγειακή πήξη
- Θέση χειρουργικής επέμβασης, η οποία δεν θα επέτρεπε τον αποτελεσματικό έλεγχο της αιμορραγίας από τη συσκευή

ΠΡΟΕΙΔΟΠΟΙΗΣΕΙΣ

- Αυτή η συσκευή προορίζεται για χρήση ως προσωρινό μέτρο εξασφάλισης αιμόστασης σε περιπτώσεις στις οποίες ενδείκνυται η συντηρητική αντιμετώπιση της επιλόχειας αιμορραγίας της μήτρας.
- Το επιλόχειο μπαλόνι Bakri ενδείκνυται για χρήση σε περίπτωση πρωτοπαθούς επιλόχειας αιμορραγίας, εντός 24 ωρών από τον τοκετό.
- Η συσκευή δεν θα πρέπει να παραμένει εντός του σώματος για περισσότερες από 24 ώρες.
- Το μπαλόνι θα πρέπει να πληρώνεται με στείρο υγρό, όπως στείρο νερό, στείρος φυσιολογικός ορός ή διάλυμα Ringer's lactate. Η πλήρωση του μπαλονιού δεν θα πρέπει να γίνεται ποτέ με αέρα, διοξείδιο του άνθρακα ή οποιοδήποτε άλλο αέριο.

- Ο μέγιστος όγκος πλήρωσης είναι 500 mL. Μην πληρώσετε υπερβολικά το μπαλόνι. Η υπερβολική πλήρωση του μπαλονιού ενδέχεται να προκαλέσει παρεκτόπιση του μπαλονιού μέσα στον κόλπο.
- Οι ασθενείς στις οποίες χρησιμοποιείται αυτή η συσκευή θα πρέπει να παρακολουθούνται στενά για σημεία επιδείνωσης της αιμορραγίας ή/και διάχυτης ενδαγγειακής πήξης (ΔΕΠ). Σε τέτοιες περιπτώσεις, θα πρέπει να ακολουθείται επείγουσα παρέμβαση σύμφωνα με το πρωτόκολλο του νοσοκομείου.
- Δεν υπάρχουν κλινικά δεδομένα που να υποστηρίζουν τη χρήση αυτής της συσκευής σε περίπτωση ΔΕΠ.
- Η παρακολούθηση της ασθενούς αποτελεί αναπόσπαστο μέρος της αντιμετώπισης της επιλόχειας αιμορραγίας. Σημεία επιδείνωσης ή μη βελτίωσης της κατάστασης θα πρέπει να οδηγήσουν σε πιο επιθετική θεραπεία και αντιμετώπιση της αιμορραγίας της μήτρας της ασθενούς.
- Θα πρέπει να παρακολουθείται η παραγωγή ούρων της ασθενούς για όσο διάστημα χρησιμοποιείται το επιλόχειο μπαλόνι Bakri.

ΠΡΟΦΥΛΑΞΕΙΣ

- Αυτό το προϊόν προορίζεται για χρήση από ιατρούς εκπαιδευμένους και πεπειραμένους σε μαιευτικές και γυναικολογικές τεχνικές.
- Αποφύγετε την άσκηση υπερβολικής δύναμης κατά την εισαγωγή του μπαλονιού στη μήτρα.

ΟΔΗΓΙΕΣ ΧΡΗΣΗΣ

ΣΗΜΑΝΤΙΚΟ: Πριν από τη διακοπλική ή τη διακοιλιακή τοποθέτηση του επιλόχειου μπαλονιού Bakri, θα πρέπει να έχουν αφαιρεθεί από τη μήτρα όλα τα τμήματα του πλακούντα και η ασθενής θα πρέπει να αξιολογείται για να διασφαλιστεί ότι δεν φέρει ρήξεις ή τραύματα στο ουρογεννητικό σύστημα και ότι η πηγή της αιμορραγίας δεν είναι αρτηριακή.

Διακολπική τοποθέτηση

1. Προσδιορίστε τον όγκο της μήτρας με άμεση εξέταση ή με υπερηχογραφική εξέταση.
2. Εισαγάγετε το τμήμα του μπαλονιού του καθετήρα στη μήτρα, επιβεβαιώνοντας ότι ολόκληρο το μπαλόνι έχει εισαχθεί πέρα από τον αυλό του τραχήλου και το έσω στόμιο.
3. Τοποθετήστε έναν μόνιμο καθετήρα Foley ουροδόχου κύστης, εάν δεν έχει ήδη τοποθετηθεί, για συλλογή και παρακολούθηση της παραγωγής ούρων.

Διακοιλιακή τοποθέτηση, μετά από καισαρική τομή

1. Προσδιορίστε τον όγκο της μήτρας με άμεση εξέταση.
2. Από επάνω, διαμέσου της καισαρικής τομής, περάστε το μπαλόνι επιπωματισμού, εισάγοντας πρώτη τη θύρα πλήρωσης, διαμέσου της μήτρας και του τραχήλου της μήτρας.

ΣΗΜΕΙΩΣΗ: Αφαιρέστε τη στρόφιγγα ώστε να διευκολυνθεί η τοποθέτηση και η εκ νέου προσάρτηση πριν από την πλήρωση του μπαλονιού.

3. Ζητήστε από έναν βοηθό να τραβήξει το στέλεχος του μπαλονιού διαμέσου του αυλού του κόλπου μέχρι η βάση του συμπτυγμένου μπαλονιού να έρθει σε επαφή με το έσω τραχηλικό στόμιο.
4. Συγκλείστε την τομή σύμφωνα με την τυπική διαδικασία, προσέχοντας να αποφύγετε την τρώση του μπαλονιού κατά τη συρραφή.

ΣΗΜΕΙΩΣΗ: Βεβαιωθείτε ότι όλα τα εξαρτήματα του προϊόντος είναι άθικτα και ότι η υστεροτομή έχει συρραφεί καλά πριν από την πλήρωση του μπαλονιού. Εάν ενδείκνυται κλινικά, η κοιλιά μπορεί να παραμείνει ανοικτή μετά την πλήρωση του μπαλονιού για τη στενή παρακολούθηση της διάτασης της μήτρας και για την επιβεβαίωση της σύγκλεισης της υστεροτομής.

ΣΗΜΕΙΩΣΗ: Εάν ενδείκνυται κλινικά, μπορεί να χρησιμοποιηθεί ράμμα συμπίεσης B-Lynch σε συνδυασμό με το επιλόχειο μπαλόνι Bakri.

Πλήρωση του μπαλονιού

Με σύριγγα

ΠΡΟΕΙΔΟΠΟΙΗΣΗ: Η πλήρωση του μπαλονιού πρέπει να γίνεται πάντα με στείρο υγρό. Η πλήρωση δεν πρέπει να γίνεται ποτέ με αέρα, διοξείδιο του άνθρακα ή οποιοδήποτε άλλο αέριο.

ΠΡΟΕΙΔΟΠΟΙΗΣΗ: Ο μέγιστος όγκος πλήρωσης είναι 500 mL. Μην πληρώσετε υπερβολικά το μπαλόνι. Η υπερβολική πλήρωση του μπαλονιού ενδέχεται να προκαλέσει παρεκτόπιση του μπαλονιού μέσα στον κόλπο.

ΣΗΜΕΙΩΣΗ: Για να διασφαλίσετε ότι το μπαλόνι θα πληρωθεί έως τον επιθυμητό όγκο, συνιστάται η τοποθέτηση του προκαθορισμένου όγκου του υγρού σε ξεχωριστό περιέκτη, αντί να βασίζεστε στην ποσότητα που μετράται με τη σύριγγα για την επιβεβαίωση της ποσότητας του υγρού που ενσταλάζεται στο μπαλόνι.

1. Τοποθετήστε έναν μόνιμο καθετήρα Foley ουροδόχου κύστης, εάν δεν έχει ήδη τοποθετηθεί, για συλλογή και παρακολούθηση της παραγωγής ούρων.
2. Χρησιμοποιώντας την εσωκλειόμενη σύριγγα, ξεκινήστε την πλήρωση του μπαλονιού έως τον προκαθορισμένο όγκο διαμέσου της στρόφιγγας.
3. Μετά από την πλήρωση του μπαλονιού έως τον προκαθορισμένο όγκο, επιβεβαιώστε την τοποθέτηση με υπέρηχο. **ΣΗΜΕΙΩΣΗ: Για τη σωστή τοποθέτηση, δείτε την Εικ. 1.**
4. Εάν επιθυμείτε, μπορείτε να εφαρμόσετε ήπια έλξη στο στέλεχος του μπαλονιού. Για να διατηρήσετε την τάση, σταθεροποιήστε το στέλεχος του μπαλονιού στην κνήμη της ασθενούς ή προσαρτήστε το σε βάρος που δεν υπερβαίνει τα 500 g.

ΣΗΜΕΙΩΣΗ: Για να αποτραπεί η παρεκτόπιση του μπαλονιού εντός του κόλπου, μπορείτε να εφαρμόσετε αντίθετη πίεση επιπωματίζοντας το κολπικό κανάλι με κολπική γάζα εμποτισμένη με ιώδιο ή αντιβιοτικό.

5. Συνδέστε τη θύρα παροχέτευσης σε ασκό συλλογής υγρών για να παρακολουθείτε την αιμόσταση.

ΣΗΜΕΙΩΣΗ: Για επαρκή παρακολούθηση της αιμόστασης, η θύρα παροχέτευσης του μπαλονιού και η σωλήνωση είναι δυνατόν να εκπλυθούν με στείρο ισότονο φυσιολογικό ορό για να απομακρυνθούν οι θρόμβοι.

6. Παρακολουθείτε συνεχώς την ασθενή για σημεία αυξημένης αιμορραγίας και σπασμών της μήτρας.

Πλήρωση του μπαλονιού

Με εξαρτήματα ταχείας ενστάλαξης

Δείτε τις **Εικ. 2-8**, στο πρόσθιο τμήμα αυτού του φυλλαδίου.

ΣΗΜΕΙΩΣΗ: Θα πρέπει να χρησιμοποιείται υπέρηχος για την επιβεβαίωση της σωστής τοποθέτησης του μπαλονιού μετά από την πλήρωση του μπαλονιού έως τον προκαθορισμένο όγκο.

Αφαίρεση μπαλονιού

ΣΗΜΕΙΩΣΗ: Ο χρόνος αφαίρεσης του μπαλονιού θα πρέπει να προσδιορίζεται από τον θεράποντα κλινικό ιατρό, μετά από αξιολόγηση της ασθενούς, αφού τεθεί υπό έλεγχο η αιμορραγία και σταθεροποιηθεί η κατάσταση της ασθενούς. Είναι δυνατή η αφαίρεση του μπαλονιού νωρίτερα, αφού προσδιοριστεί η επίτευξη αιμόστασης από τον κλινικό ιατρό. Ο μέγιστος χρόνος παραμονής εντός του σώματος είναι 24 ώρες.

1. Άρετε την τάση από το στέλεχος του μπαλονιού.
2. Αφαιρέστε τυχόν επιπωματισμό του κόλπου.
3. Χρησιμοποιώντας κατάλληλη σύριγγα, αναρροφήστε το περιεχόμενο του μπαλονιού μέχρι να συμπτυχθεί πλήρως. Η αφαίρεση του υγρού μπορεί να γίνει σταδιακά για να είναι δυνατή η περιοδική παρακολούθηση της ασθενούς.

ΣΗΜΕΙΩΣΗ: Σε κατάσταση έκτακτης ανάγκης, μπορεί να αποκοπεί το στέλεχος του καθετήρα για να διευκολυνθεί η ταχύτερη σύμπτυξη.

4. Αποσύρετε με ήπιες κινήσεις το μπαλόνι από τη μήτρα και τον αυλό του κόλπου και απορρίψτε το.
5. Παρακολουθείτε την ασθενή για σημεία αιμορραγίας.

ΤΡΟΠΟΣ ΔΙΑΘΕΣΗΣ

Παρέχεται αποστειρωμένο με αέριο οξείδιο του αιθυλενίου σε αποκολλούμενες συσκευασίες. Προορίζεται για μία χρήση μόνο. Στείρο, εφόσον η συσκευασία δεν έχει ανοιχτεί ή δεν έχει υποστεί ζημιά. Μη χρησιμοποιείτε το προϊόν εάν υπάρχει αμφιβολία για τη στειρότητά του. Φυλάσσετε σε σκοτεινό, στεγνό και δροσερό χώρο. Αποφεύγετε την παρατεταμένη έκθεση στο φως. Κατά την αφαίρεση από τη συσκευασία, επιθεωρήστε το προϊόν για να βεβαιωθείτε ότι δεν έχει υποστεί ζημιά.

ΒΙΒΛΙΟΓΡΑΦΙΚΕΣ ΑΝΑΦΟΡΕΣ

Αυτές οι οδηγίες χρήσης βασίζονται στην εμπειρία από ιατρούς ή/και τη δημοσιευμένη βιβλιογραφία τους. Απευθυνθείτε στον τοπικό σας σντιπρόσωπο πωλήσεων της Cook για πληροφορίες σχετικά με τη διαθέσιμη βιβλιογραφία.

ESPAÑOL

BALÓN DE POSTPARTO DE BAKRI

AVISO: Las leyes federales estadounidenses restringen la venta de este dispositivo a médicos o por prescripción facultativa (o a profesionales con la debida autorización).

DESCRIPCIÓN DEL DISPOSITIVO

El balón de postparto de Bakri es un catéter balón de silicona con un volumen máximo de hinchado de 500 mL. Los componentes para instilación rápida incluyen un tubo de polímero con una púa para bolsa intravenosa y una válvula de tres vías.

INDICACIONES DE USO

Este dispositivo está indicado para detener o reducir temporalmente hemorragias uterinas postparto cuando sea adecuado emplear un tratamiento conservador.

CONTRAINDICACIONES

- Hemorragia arterial que requiera exploración quirúrgica o embolización angiográfica
- Casos en los que esté indicada una histerectomía
- Embarazo
- Cáncer de cuello uterino
- Infecciones purulentas de la vagina, el cuello uterino o el útero
- Anomalía uterina sin tratar
- Coagulación intravascular diseminada
- Una zona quirúrgica que impida que el dispositivo controle de manera eficaz la hemorragia

ADVERTENCIAS

- Este dispositivo está indicado como medio temporal para el establecimiento de la hemostasia en casos en que esté indicado el tratamiento conservador de la hemorragia uterina postparto.
- El balón de postparto de Bakri está indicado para utilizarse en casos de hemorragia postparto primaria en las 24 horas posteriores al parto.
- El dispositivo no debe permanecer implantado más de 24 horas.
- El balón debe hincharse con un líquido estéril, como agua estéril, solución salina estéril o solución láctica de Ringer. El balón nunca debe hincharse con aire, dióxido de carbono ni ningún otro gas.
- El hinchado máximo es de 500 mL. No hinche demasiado el balón. Si se hincha demasiado, el balón puede desplazarse en el interior de la vagina.
- Se debe vigilar estrechamente a las pacientes en las que se esté utilizando este dispositivo para detectar cualquier signo de aumento de la hemorragia o de coagulación intravascular diseminada (CID). En esos casos, se debe realizar una intervención de urgencia siguiendo el protocolo del hospital.
- No hay datos clínicos que apoyen el uso de este dispositivo en caso de CID.
- La vigilancia de la paciente forma parte integral del tratamiento de la hemorragia postparto. Si hay signos de deterioro o el proceso no mejora, se debe aplicar un tratamiento y un control más intensivos de la hemorragia uterine de la paciente.
- Cuando se esté utilizando el balón de postparto de Bakri, deberá vigilarse la emisión de orina de la paciente.

PRECAUCIONES

- Este producto está concebido para que lo utilicen médicos con formación y experiencia en obstetricia y técnicas ginecologicas.
- Evite utilizar una fuerza excesiva al introducir el balón en el útero.

INSTRUCCIONES DE USO

IMPORTANTE: Antes de la colocación transvaginal o transabdominal del balón de postparto de Bakri, el útero debe estar libre de todos los fragmentos de la placenta, y la paciente debe evaluarse para comprobar que no haya laceraciones o traumatismos en el aparato genital, y que el origen de la hemorragia no sea arterial.

Colocación transvaginal

1. Determine el volumen uterino mediante examen directo o ecográfico.
2. Introduzca en el útero la parte del catéter en la que está el balón y asegúrese de introducir todo el balón hasta que haya sobrepasado el canal cervical y el ostium interno.
3. Introduzca un catéter Foley permanente en la vejiga urinaria, si no hay uno ya colocado, para recoger y vigilar la emisión de orina.

Colocación transabdominal tras cesárea

1. Determine el volumen uterino por visualización directa.
2. Desde arriba, y empleando como acceso la incisión de la cesárea, haga pasar el balón de taponamiento, con el orificio de hinchado primero, a través del útero y del cuello uterino.

NOTA: Retire la llave de paso para facilitar la colocación y vuelva a colocarla antes de llenar el balón.

3. Haga que un ayudante tire del cuerpo del balón para hacerlo pasar a través del canal vaginal hasta que la base del balón deshinchado entre en contacto con el ostium cervical interno.
4. Cierre la incisión mediante el procedimiento normal, con cuidado para no pinchar el balón al suturar.

NOTA: Asegúrese de que todos los componentes del producto estén intactos y de que la histerotomía esté bien suturada antes de hinchar el balón. Si es conveniente por motivos clínicos, el abdomen puede permanecer abierto tras el hinchado del balón, para vigilar estrechamente la distensión uterina y confirmar el cierre de la histerotomía.

NOTA: Si es conveniente por motivos clínicos, puede utilizarse una sutura compresiva de B-Lynch junto con el balón de postparto de Bakri.

Hinchado del balón

con jeringa

ADVERTENCIA: Hinche siempre el balón con un líquido estéril. No lo hinche nunca con aire, dióxido de carbono ni ningún otro gas.

ADVERTENCIA: El hinchado máximo es de 500 mL. No hinche demasiado el balón. Si se hincha demasiado, el balón puede desplazarse en el interior de la vagina.

NOTA: Para asegurarse de llenar el balón con el volumen deseado, se recomienda colocar el volumen de líquido predeterminado en un recipiente aparte, en vez de ir calculando con la jeringa la cantidad de líquido que se ha introducido en el balón.

1. Introduzca un catéter Foley permanente en la vejiga urinaria, si no hay uno ya colocado, para recoger y vigilar la emisión de orina.
2. Con la jeringa suministrada, empiece a llenar el balón hasta el volumen predeterminado a través de la llave de paso.
3. Una vez que el balón se haya hinchado al volumen predeterminado, confirme su colocación mediante ecografía. **NOTA: Vea la colocación correcta en la figura 1.**
4. Si lo desea, puede aplicar tracción al cuerpo del balón. Para mantener la tensión, fije el cuerpo del balón a la pierna de la paciente o póngale encima un peso de no más de 500 g.

NOTA: Para evitar el desplazamiento del balón hacia el interior de la vagina, puede aplicarse contrapresión rellenando el canal vaginal con gasa vaginal empapada en yodo o antibiótico.

5. Conecte el orificio de drenaje a una bolsa de recogida de líquido para vigilar la hemostasia.

NOTA: El orificio de drenaje del balón y el tubo pueden lavarse con solución salina isotónica estéril para eliminar los coágulos y poder así vigilar correctamente la hemostasia.

6. Vigile continuamente a la paciente para comprobar si presenta signos de aumento de la hemorragia o de calambres uterinos.

Hinchado del balón

con componentes para instilación rápida

Vea las **figuras 2-8**, incluidas al principio de este folleto.

NOTA: Una vez hinchado el balón al volumen predeterminado, debe utilizarse ecografía para confirmar la colocación correcta del balón.

Extracción del balón

NOTA: El momento de la extracción del balón debe ser determinado por el médico a cargo tras la evaluación de la paciente una vez que se haya detenido la hemorragia y estabilizado a la paciente. El balón puede extraerse antes si el médico determina que se ha conseguido la hemostasia. El tiempo de permanencia máximo es de 24 horas.

1. Libere la tensión del cuerpo del balón.
2. Retire el material que se haya empleado para el relleno vaginal.
3. Con una jeringa adecuada, aspire el contenido del balón hasta que se deshinche por completo. El líquido puede extraerse poco a poco para permitir la observación periódica de la paciente.

NOTA: En situaciones de urgencia, el cuerpo del catéter puede cortarse para facilitar un deshinchado más rápido.

4. Retire suavemente el balón del útero y del canal vaginal, y deséchelo.
5. Vigile a la paciente por si hubiera signos de hemorragia.

PRESENTACIÓN

El producto se suministra esterilizado con óxido de etileno en envases de apertura pelable. Producto indicado para un solo uso. El producto se mantendrá estéril si el envase no está abierto y no ha sufrido ningún daño. No utilice el producto si no está seguro de que esté estéril. Almacénelo en un lugar fresco, seco y oscuro. Evite la exposición prolongada a la luz. Tras extraerlo del envase, inspeccione el producto para asegurarse de que no haya sufrido ningún daño.

REFERENCIA

Estas instrucciones de uso se basan en la experiencia de médicos y (o) en la bibliografía publicada por ellos. Si desea más información sobre la bibliografía disponible, consulte a su representante comercial local de Cook.

FRANÇAIS

BALLONNET POST-PARTUM DE BAKRI

MISE EN GARDE : En vertu de la législation fédérale des États-Unis, ce dispositif ne peut être vendu que par un médecin (ou un praticien autorisé) ou sur ordonnance médicale.

DESCRIPTION DU DISPOSITIF

Le ballonnet post-partum de Bakri est un cathéter à ballonnet en silicone avec un volume d'inflation maximum de 500 mL. Les composants d'instillation rapide incluent une tubulure en polymère avec un perforateur de poche IV et une valve à trois voies.

UTILISATION

Ce dispositif est prévu pour assurer le contrôle temporaire ou la réduction de l'hémorragie utérine post-partum lorsqu'une prise en charge conservatrice est justifiée.

CONTRE-INDICATIONS

- Toute hémorragie artérielle nécessitant une exploration chirurgicale ou une embolisation angiographique
- Cas nécessitant une hystérectomie
- Grossesse
- Cancer du col de l'utérus
- Infections purulentes du vagin, du col de l'utérus ou de l'utérus
- Anomalie utérine non traitée
- Coagulation intravasculaire disséminée
- Site chirurgical empêchant le contrôle efficace de l'hémorragie par le dispositif

AVERTISSEMENTS

- Ce dispositif est destiné à être utilisé comme un moyen provisoire pour obtenir l'hémostase dans des cas où une prise en charge conservatrice d'un saignement utérin post-partum est préconisée.
- Le ballonnet post-partum de Bakri est indiqué pour une utilisation en cas d'hémorragie primaire du post-partum dans les 24 heures après l'accouchement.
- La durée à demeure du dispositif ne doit pas dépasser 24 heures.
- Le ballonnet doit être gonflé à l'aide d'un liquide stérile tel que de l'eau stérile, du sérum physiologique stérile ou un soluté lactate de Ringer. Le ballonnet ne doit jamais être gonflé avec de l'air, du dioxyde de carbone ou tout autre gaz.
- Le volume d'inflation maximal est de 500 mL. Ne pas inflater excessivement le ballonnet. L'inflation excessive du ballonnet peut entraîner le déplacement du ballonnet dans le vagin.
- Les patientes chez lesquelles ce dispositif est utilisé doivent faire l'objet d'une surveillance étroite pour déceler tout signe de saignement aggravé et/ou de coagulation intravasculaire disséminée (CIVD). Dans de tels cas, procéder à une intervention d'urgence conformément au protocole hospitalier.
- Il n'existe aucune donnée clinique soutenant l'utilisation de ce dispositif dans le cadre d'une CIVD.
- La surveillance de la patiente est un composant essentiel de la prise en charge des hémorragies du post-partum. Si l'état de la patiente montre des signes de détérioration ou ne s'améliore pas, envisager un traitement et une prise en charge plus agressifs du saignement utérin de la patiente.
- L'écoulement d'urine de la patiente doit être surveillé pendant l'utilisation du ballonnet post-partum de Bakri.

MISES EN GARDE

- Ce produit est destiné à être utilisé par des médecins ayant acquis la formation et l'expérience nécessaires aux techniques obstétriques et gynécologiques.
- Éviter d'utiliser une force excessive lors de l'introduction du ballonnet dans l'utérus.

MODE D'EMPLOI

IMPORTANT : Avant la mise en place transvaginale ou transabdominale du ballonnet post-partum de Bakri, l'utérus doit être exempt de tout fragment de placenta et la patiente doit être examinée pour s'assurer que les voies génitales ne présentent aucune lacération ni traumatisme et que la source de l'hémorragie n'est pas artérielle.

Mise en place transvaginale

1. Déterminer le volume utérin par examen direct ou examen échographique.
2. Introduire la section à ballonnet du cathéter dans l'utérus, en s'assurant que la totalité du ballonnet est introduite au-delà du canal cervical et de l'orifice interne.

3. À ce stade, mettre en place dans la vessie urinaire une sonde de Foley à demeure, si ce n'est pas déjà fait, pour recueillir et surveiller l'écoulement d'urine.

Mise en place transabdominale, après une césarienne

1. Déterminer le volume utérin par examen direct.
2. Par le haut, introduire le ballonnet de tamponnement avec l'orifice d'inflation en premier, à travers l'incision de la césarienne, puis l'utérus et le col de l'utérus.

REMARQUE : Retirer le robinet afin de faciliter la mise en place, puis réinstaller avant de remplir le ballonnet.

3. Demander à un assistant de tirer l'âme du ballonnet à travers le canal vaginal jusqu'à ce que le bas du ballonnet déflaté vienne au contact de l'orifice interne du col.
4. Fermer l'incision selon la procédure habituelle, en prenant garde de ne pas transpercer le ballonnet durant la suture.

REMARQUE : S'assurer que tous les composants du produit sont intacts et l'hystérotomie est suturée de manière correcte avant d'inflater le ballonnet. Si cela est cliniquement pertinent, l'abdomen peut rester ouvert lors de l'inflation du ballonnet pour permettre au chirurgien de surveiller étroitement la distension de l'utérus et confirmer la fermeture de l'hystérotomie.

REMARQUE : Si cela est cliniquement pertinent, une suture de compression de type B-Lynch peut être utilisée avec le ballonnet post-partum de Bakri.

Inflation du ballonnet

Avec une seringue

AVERTISSEMENT : Toujours inflater le ballonnet avec un liquide stérile. Ne jamais inflater avec de l'air, du dioxyde de carbone ou un autre gaz.

AVERTISSEMENT : Le volume d'inflation maximum est de 500 mL. Ne pas inflater excessivement le ballonnet. L'inflation excessive du ballonnet peut entraîner le déplacement du ballonnet dans le vagin.

REMARQUE : Pour s'assurer que le ballonnet est rempli au volume souhaité, il est recommandé de placer le volume prédéterminé de liquide dans un récipient à part plutôt que de se fier au volume mesuré avec la seringue pour confirmer la quantité de liquide injectée dans le ballonnet.

1. À ce stade, mettre en place dans la vessie urinaire une sonde de Foley à demeure, si ce n'est pas déjà fait, pour recueillir et surveiller l'écoulement d'urine.
2. À l'aide de la seringue fournie, commencer à remplir le ballonnet avec le volume prédéterminé de liquide à travers le robinet.
3. Une fois le ballonnet inflaté au volume prédéterminé, vérifier sa mise en place par échographie.
   REMARQUE : Voir la Fig. 1 pour la mise en place correcte.
4. Si cela est souhaité, une traction peut être exercée sur l'âme du ballonnet. Pour maintenir la tension, fixer l'âme du ballonnet sur la jambe de la patiente ou y fixer un poids ne dépassant pas 500 grammes.

REMARQUE : Pour empêcher le déplacement du ballonnet dans le vagin, une contre-pression peut être appliquée en remplissant le canal vaginal avec des compresses vaginales imprégnées d'iode ou d'antibiotique.

5. Raccorder l'orifice de drainage à une poche de recueil de liquide pour surveiller l'hémostase.

REMARQUE : Afin de surveiller correctement l'hémostase, l'orifice de drainage du ballonnet et la tubulure peuvent être rincés avec du sérum physiologique isotonique stérile pour éliminer d'éventuels caillots.

6. Surveiller la patiente continuellement pour détecter tout signe d'augmentation du saignement ou de crampes utérines.

Inflation du ballonnet

Avec les composants d'instillation rapide

Voir les **Fig. 2 à 8**, au début de cette brochure.

REMARQUE : La mise en place correcte du ballonnet doit être confirmée par échographie une fois que celui-ci a été inflaté au volume prédéterminé.

Retrait du ballonnet

REMARQUE : Le moment du retrait du ballonnet doit être déterminé par le clinicien traitant après examen de la patiente une fois que l'hémorragie a été maîtrisée et que l'état de la patiente a été stabilisé. Le ballonnet peut être retiré plus tôt si le médecin juge qu'une hémostase adéquate a été obtenue. La durée à demeure maximum du dispositif est de 24 heures.

1. Relâcher la tension exercée sur l'âme du ballonnet.
2. Retirer tout pansement vaginal.
3. À l'aide d'une seringue appropriée, aspirer le contenu du ballonnet jusqu'à ce que celui-ci soit entièrement déflaté. Le liquide peut être retiré progressivement pour permettre une observation périodique de la patiente.

REMARQUE : Dans une situation d'urgence, l'âme du cathéter peut être coupée pour faciliter une déflation plus rapide.

4. Retirer doucement le ballonnet de l'utérus et du canal vaginal et le jeter.
5. Surveiller la patiente pour détecter tout signe de saignement.

PRÉSENTATION

Produit(s) fourni(s) stérilisé(s) à l'oxyde d'éthylène, sous emballage déchirable. Produit(s) destiné(s) à un usage unique. Contenu stérile lorsque l'emballage est scellé d'origine et intact. En cas de doute quant à la stérilité du produit, ne pas l'utiliser. Conserver à l'obscurité, au sec et au frais. Éviter une exposition prolongée à la lumière. Examiner le produit après son déballage pour s'assurer de son bon état.

BIBLIOGRAPHIE

Le présent mode d'emploi a été rédigé en fonction de l'expérience de médecins et/ou de leurs publications médicales. Pour obtenir des renseignements sur la documentation existante, s'adresser au représentant Cook local.

MAGYAR

BAKRI POST PARTUM BALLON

FIGYELEM: Az USA szövetségi törvényeinek értelmében ez az eszköz kizárólag orvos (vagy megfelelő engedéllyel rendelkező egészségügyi szakember) által vagy rendeletére forgalmazható.

AZ ESZKÖZ LEÍRÁSA

A Bakri post partum ballon 500 mL maximális feltöltési térfogatú szilikon ballonkatéter. A gyors feltöltő komponensek között polimer csővezeték is található infúziós zsákhoz való kiszúró tüskével és háromutas szeleppel.

RENDELTETÉS

Ez az eszköz a post partum méhvérzés ideiglenes kontrollálására vagy csökkentésére szolgál olyan esetekben, amikor konzervatív kezelés indokolt.

ELLENJAVALLATOK

- Sebészeti feltárást vagy angiográfiás embolizációt igénylő artériás vérzés
- Olyan esetek, amikor hysterectomia alkalmazása javallott
- Terhesség
- Méhnyakrák
- Gennyes fertőzés a hüvelyben, a méhnyakban vagy a méhben
- Méh nem kezelt anomáliája

- Disszeminált intravaszkuláris koaguláció
- Olyan műtéti hely, amely akadályozná az eszközt a vérzés hatékony kontrollálásában

„VIGYÁZAT" SZINTŰ FIGYELMEZTETÉSEK

- Az eszköz a vérzéscsillapítás ideiglenes biztosítására szolgál olyan esetekben, amikor a post partum méhvérzés konzervatív kezelése javallott.
- A Bakri post partum ballon használata a szüléstől számított 24 órán belül jelentkező primer post partum vérzés esetén javallott.
- Az eszköz nem maradhat a testben 24 óránál hosszabb ideig.
- A ballont steril folyadékkal, például steril vízzel, steril fiziológiás sóoldattal vagy Ringer-laktát oldattal kell feltölteni. A ballont soha nem szabad levegővel, szén-dioxiddal vagy bármilyen más gázzal feltölteni.
- A maximális feltöltési térfogat 500 mL. Ne töltse túl a ballont. A ballon túltöltésének eredményeképp a ballon átkerülhet a hüvelybe.
- Szorosan nyomon kell követni azokat a betegeket, akikben ez az eszköz használatos, és figyelni kell a vérzés rosszabbodására és/vagy a disszeminált intravaszkuláris koagulációra (DIC) utaló jeleket. Ilyen esetekben a sürgősségi beavatkozást a kórház protokolljának megfelelően kell végrehajtani.
- Az eszköz használatát DIC-ben szenvedő betegek esetében nem támasztják alá klinikai adatok.
- A betegek monitorozása a post partum vérzés kezelésének részét képezi. Az állapot romlását vagy javulásának elmaradását mutató jelek esetén a beteg méhvérzésének terápiájához és kezeléséhez agresszívebb módszert kell választani.
- A betegből távozó vizeletet monitorozni kell a Bakri post partum ballon használata folyamán.

ÓVINTÉZKEDÉSEK

- Ez a termék a szülészeti és nőgyógyászati technikákra kiképzett és azokban járatos orvosok általi használatra készült.
- A ballon méhbe történő behelyezése során ne alkalmazzon túl nagy erőt.

HASZNÁLATI UTASÍTÁS

FONTOS: A Bakri post partum ballon hüvelyen vagy hason keresztüli behelyezése előtt a méhnek minden méhlepénydarabtól mentesnek kell lennie, és a beteg állapotát értékelni kell, hogy meggyőződjön arról: a nemi szerveket nem érte szakadás vagy sérülés, és a vérzés nem arteriális eredetű.

Hüvelyen keresztüli behelyezés

1. Közvetlen vizsgálattal vagy ultrahangos vizsgálattal állapítsa meg a méh térfogatát.
2. Helyezze a katéter ballonrészét a méhbe, ügyelve arra, hogy a ballon egésze túljusson a méhcsatornán és a belső méhszájon.
3. Ha még nem lett behelyezve, akkor helyezzen be egy testben maradó Foley-típusú húgyhólyagkatétert, hogy összegyűjtse és monitorozza a távozó vizeletet.

Hason keresztüli behelyezés, császármetszés után

1. Közvetlen vizsgálattal állapítsa meg a méh térfogatát.
2. Felülről, a császármetszésen keresztül hozzáférve vezesse át a tamponáló ballont a méhen és a méhnyakon, feltöltőnyílásával előre.

MEGJEGYZÉS: A behelyezés elősegítése érdekében távolítsa el az elzárócsapot, majd a ballon feltöltése előtt helyezze vissza.

3. Utasítsa asszisztensét, hogy húzza a ballon szárát a hüvelycsatornán keresztül, egészen addig, amíg a leeresztett ballon alapja hozzá nem ér a belső méhszájhoz.
4. A szokásos eljárással zárja le a bemetszést, ügyelve arra, hogy ne szúrja meg a ballont az öltések során.

MEGJEGYZÉS: A ballon feltöltése előtt győződjön meg arról, hogy a termék valamennyi komponense sértetlen, és hogy a méhen ejtett vágás biztonságosan össze van varrva. Ha ez klinikailag fontos, a ballon

feltöltése után a has nyitva hagyható a méh kitágításának szoros megfigyelése és a méhen ejtett vágás záródásának igazolása céljából.

MEGJEGYZÉS: Ha ez klinikailag fontos, a Bakri post partum ballonnal együtt B-Lynch öltés is alkalmazható.

A ballon feltöltése

Fecskendővel

FIGYELMEZTETÉS: Mindig steril folyadékkal töltse fel a ballont. A ballon feltöltésére tilos levegőt, szén-dioxidot, vagy bármilyen egyéb gázt használni!

FIGYELMEZTETÉS: A maximális feltöltési térfogat 500 mL. Ne töltse túl a ballont. A ballon túltöltésének eredményeképp a ballon átkerülhet a hüvelybe.

MEGJEGYZÉS: A ballon kellő térfogatra történő feltöltésének biztosításához ajánlott az előre meghatározott térfogatú folyadékot egy külön edénybe helyezni, nem pedig a fecskendő feltöltéseinek megszámolására hagyatkozni a ballonba töltött folyadék mennyiségének vonatkozásában.

1. Ha még nem lett behelyezve, akkor helyezzen be egy testben maradó Foley-típusú húgyhólyagkatétert, hogy összegyűjtse és monitorozza a távozó vizeletet.
2. A mellékelt fecskendővel kezdje meg a ballon feltöltését az előre meghatározott térfogatra az elzárócsapon keresztül.
3. Miután megtörtént a ballon feltöltése az előre meghatározott térfogatra, ultrahanggal ellenőrizze a behelyezését. **MEGJEGYZÉS: A megfelelő behelyezést az 1. ábra mutatja.**
4. Ha szükséges, alkalmazzon húzást a ballon szárára. A feszesség fenntartásához rögzítse a ballon szárát a beteg lábához, vagy kapcsoljon hozzá 500 g-nál nem nehezebb súlyt.

MEGJEGYZÉS: Annak megelőzésére, hogy a ballon áthelyeződjék a hüvelybe, ellennyomást lehet alkalmazni a hüvelycsatorna jódba vagy antibiotikumba áztatott hüvelygézzel való kitömésével.

5. Csatlakoztassa a lecsapolónyílást egy folyadékgyűjtő tasakhoz a vérzéscsillapítás monitorozása céljából.

MEGJEGYZÉS: A vérzéscsillapítás megfelelő monitorozásához a ballon lecsapolónyílását és csövezetét steril izotóniás sóoldattal tisztára lehet mosni a véralvadéktól.

6. Folyamatosan monitorozza a beteget, és figyelje, hogy vannak-e a vérzés fokozódására vagy a méh görcsére utaló jelek.

A ballon feltöltése

Gyorsfeltöltő komponensekkel

Lásd a **2-8. ábrákat**, e könyvecske elején.

MEGJEGYZÉS: A ballon előre meghatározott térfogatra történő feltöltése után ultrahanggal kell ellenőrizni a ballon megfelelő behelyezését.

A ballon eltávolítása

MEGJEGYZÉS: A ballon eltávolításának időzítését a beteget ellátó orvosnak kell meghatároznia a beteg állapotának értékelését követően, amint a vérzést elállították és a beteg állapota stabilizálódott. Miután az orvos megállapította a vérzéscsillapítást, a ballon hamarabb eltávolítható. A ballon legfeljebb 24 óráig maradhat a testben.

1. Szüntesse meg a ballon szárának feszességét.
2. Távolítsa el a hüvelyből az összes kitöltőanyagot.
3. Megfelelő fecskendővel aspirálja a ballon tartalmát, amíg a ballon teljesen le nem ereszt. A folyadék lépésenként is eltávolítható a beteg időszakos megfigyelése érdekében.

MEGJEGYZÉS: Vészhelyzetben a katéter szárát el lehet vágni a gyorsabb leeresztés megkönnyítése érdekében.

4. Finoman húzza vissza a ballont a méhből és a hüvelycsatornából, majd helyezze a hulladékba.
5. Monitorozza, hogy fellépnek-e vérzésre utaló jelek a betegben.

KISZERELÉS

Kiszerelés: etilén-oxiddal sterilizálva, széthúzható csomagolásban. Egyszeri használatra. Felbontatlan vagy sértetlen csomagolásban steril. Ha a termék sterilitása kétséges, ne használja. Száraz, sötét, hűvös helyen tárolandó. Tartós megvilágítása kerülendő. A csomagolásból való eltávolítás után vizsgálja meg a terméket annak ellenőrzésére, hogy az nem sérült-e meg.

REFERENCIA

Ez a használati utasítás orvosok tapasztalatán és/vagy az általuk közölt szakirodalmon alapul. A rendelkezésre álló szakirodalomról a Cook helyi értékesítési képviselője tud felvilágosítással szolgálni.

ITALIANO

PALLONCINO POST-PARTO BAKRI

ATTENZIONE - Le leggi federali degli Stati Uniti d'America limitano la vendita del presente dispositivo a medici, a personale autorizzato o a operatori sanitari abilitati.

DESCRIZIONE DEL DISPOSITIVO

Il palloncino post-parto Bakri è un catetere a palloncino in silicone con un volume massimo di gonfiaggio di 500 mL. I componenti per l'instillazione rapida includono un tubo in polimero con un puntale di foratura della sacca endovenosa e una valvola a tre vie.

USO PREVISTO

Questo dispositivo è previsto per il controllo o la riduzione temporanei del sanguinamento uterino post-parto nei casi in cui sia indicata una gestione terapeutica conservativa.

CONTROINDICAZIONI

- Sanguinamento arterioso che richieda esplorazione chirurgica o embolizzazione angiografica
- Casi in cui è indicata un'isterectomia
- Gravidanza
- Cancro della cervice
- Infezioni purulente della vagina, della cervice o dell'utero
- Anomalia uterina non trattata
- Coagulazione intravascolare disseminata
- Un sito chirurgico che impedirebbe al dispositivo di controllare efficacemente il sanguinamento

AVVERTENZE

- Questo dispositivo è previsto come mezzo temporaneo di emostasi nei casi in cui sia indicata la gestione conservativa del sanguinamento uterino post-parto.
- Il palloncino post-parto Bakri è indicato per l'uso nei casi di emorragia primaria post-parto entro 24 ore dal parto.
- Il periodo di permanenza del dispositivo non deve superare le 24 ore.
- Il palloncino deve essere gonfiato con un liquido sterile come acqua sterile, soluzione fisiologica sterile o soluzione di Ringer lattato. Non gonfiarlo mai con aria, anidride carbonica o altri gas.
- Il volume massimo di gonfiaggio è di 500 mL. Non gonfiare eccessivamente il palloncino. Il gonfiaggio eccessivo del palloncino può causarne lo sposizionamento nella vagina.
- Le pazienti sulle quali viene usato il presente dispositivo devono essere sottoposte ad attento monitoraggio per evidenziare la presenza di eventuali segni di aggravamento del sanguinamento e/o coagulazione intravascolare disseminata (CID). In tali casi, seguire le procedure interventistiche di emergenza secondo quanto previsto dal protocollo ospedaliero.

- Non vi sono dati clinici a supporto dell'uso di questo dispositivo nei casi di CID.
- Il monitoraggio della paziente costituisce parte integrante della gestione dell'emorragia post-parto. Segni di deterioramento oppure il mancato miglioramento della condizione richiedono un trattamento e una gestione del sanguinamento uterino più aggressivi.
- Durante l'uso del palloncino post-parto Bakri è necessario monitorare la produzione di urina della paziente.

PRECAUZIONI

- Questo prodotto è previsto per essere usato da medici debitamente addestrati ed esperti nelle tecniche ostetriche e ginecologiche.
- Evitare di forzare eccessivamente nell'introdurre il palloncino nell'utero.

ISTRUZIONI PER L'USO

IMPORTANTE - Prima del posizionamento transvaginale o transaddominale del palloncino post-parto Bakri, eliminare dall'utero tutti i frammenti di placenta ed esaminare la paziente per escludere la presenza di lacerazioni o traumi al tratto genitale e accertarsi che il sanguinamento non sia di origine arteriosa.

Posizionamento transvaginale

1. Determinare il volume uterino mediante esame diretto o esame ecografico.
2. Inserire nell'utero la sezione a palloncino del catetere, assicurandosi che il palloncino sia interamente posizionato oltre il canale cervicale e l'ostio interno.
3. A questo punto inserire un catetere a permanenza Foley per vescica urinaria (nel caso non fosse già inserito), per raccogliere e monitorare la produzione di urina.

Posizionamento transaddominale in seguito a taglio cesareo

1. Determinare il volume uterino mediante esame diretto.
2. Accedendo dal taglio cesareo e procedendo dall'alto, fare passare il palloncino per tamponamento attraverso l'utero e la cervice, inserendo per primo il raccordo per il gonfiaggio.

NOTA - Togliere il rubinetto per agevolare il posizionamento e riapplicarlo prima di riempire il palloncino.

3. Avvalersi di un assistente che eserciti trazione sullo stelo del palloncino attraverso il canale vaginale, fino a portare la base del palloncino sgonfio a contatto con l'ostio cervicale interno.
4. Chiudere l'incisione con la prassi consueta, facendo attenzione a evitare di pungere il palloncino durante le operazioni di sutura.

NOTA - Prima di gonfiare il palloncino, assicurarsi che tutti i componenti del prodotto siano integri e che l'isterotomia sia stata adeguatamente suturata. Se clinicamente rilevante, l'addome può rimanere aperto al momento del gonfiaggio del palloncino, al fine di monitorare attentamente la distensione uterina e confermare la chiusura dell'isterotomia.

NOTA - Se clinicamente rilevante, insieme al palloncino post-parto Bakri si può usare una sutura compressiva di B-Lynch.

Gonfiaggio del palloncino

Mediante siringa

AVVERTENZA - Gonfiare sempre il palloncino con un liquido sterile. Non gonfiarlo mai con aria, anidride carbonica o alcun altro gas.

AVVERTENZA - Il volume massimo di gonfiaggio è di 500 mL. Non gonfiare eccessivamente il palloncino. Il gonfiaggio eccessivo del palloncino può causarne lo sposizionamento nella vagina.

NOTA - Per essere certi che il palloncino sia riempito fino al volume desiderato, si consiglia di collocare in un contenitore separato il volume predeterminato di fluido, invece di affidarsi al conteggio delle siringhe per verificare la quantità di fluido instillato nel palloncino.

1. A questo punto inserire un catetere a permanenza Foley per vescica urinaria (nel caso non fosse già inserito), per raccogliere e monitorare la produzione di urina.

2. Utilizzando la siringa acclusa, iniziare a gonfiare il palloncino attraverso il rubinetto fino a raggiungere il volume predeterminato.
3. Dopo avere gonfiato il palloncino con il volume predeterminato, confermare il posizionamento per via ecografica. **NOTA - La Fig. 1 illustra il posizionamento corretto.**
4. Se lo si desidera, è possibile applicare trazione allo stelo del palloncino. Per mantenere la tensione, fissare lo stelo del palloncino alla gamba della paziente oppure collegarlo a un peso che non superi i 500 grammi.

NOTA - Per impedire lo sposizionamento del palloncino nella vagina, è possibile applicare una contropressione inserendo nel canale vaginale compresse di garza imbevute di iodio o antibiotico.

5. Collegare il raccordo di drenaggio a una sacca di raccolta dei fluidi per monitorare l'emostasi.

NOTA - Per un adeguato monitoraggio dell'emostasi, il raccordo di drenaggio del palloncino e il tubicino possono essere liberati dai coaguli mediante lavaggio con soluzione fisiologica isotonica sterile.

6. Mantenere la paziente sotto monitoraggio continuo per rilevare segni di aumentato sanguinamento e crampi uterini.

Gonfiaggio del palloncino

Mediante componenti a instillazione rapida

Vedere le **Figg. 2-8**, all'inizio di questo opuscolo.

NOTA - Confermare per via ecografica il corretto posizionamento del palloncino, dopo averlo gonfiato con il volume predeterminato.

Rimozione del palloncino

NOTA - Sta al medico curante decidere quando è giunto il momento di rimuovere il palloncino dopo aver valutato la paziente, una volta tenuto sotto controllo il sanguinamento e stabilizzata la paziente. Il palloncino può essere rimosso in anticipo dopo che il medico ha determinato l'ottenimento dell'emostasi. Il tempo massimo di permanenza è di 24 ore.

1. Eliminare la tensione dallo stelo del palloncino.
2. Rimuovere l'eventuale impaccatura vaginale.
3. Utilizzando una siringa adeguata, aspirare il contenuto del palloncino fino a sgonfiarlo completamente. Il liquido può essere rimosso a poco a poco per consentire l'osservazione periodica della paziente.

NOTA - In una situazione di emergenza si può tagliare il corpo del catetere per sgonfiare più rapidamente il palloncino.

4. Estrarre delicatamente il palloncino dall'utero e dal canale vaginale e gettarlo.
5. Monitorare la paziente per individuare eventuali segni di sanguinamento.

CONFEZIONAMENTO

Il prodotto è sterilizzato mediante ossido di etilene ed è fornito in confezione con apertura a strappo. Esclusivamente monouso. Il prodotto è sterile se la sua confezione è chiusa e non danneggiata. Non utilizzare il prodotto in caso di dubbi sulla sua sterilità. Conservarlo in luogo fresco e asciutto, al riparo dalla luce. Evitarne l'esposizione prolungata alla luce. Dopo l'estrazione dalla confezione, esaminare il prodotto per accertarsi che non abbia subito danni.

BIBLIOGRAFIA

Le presenti istruzioni per l'uso sono basate sull'esperienza dei medici e/o sulle loro pubblicazioni specialistiche. Per ottenere informazioni sulla letteratura specializzata disponibile, rivolgersi al rappresentante Cook di zona.

BAKRI-POSTPARTUMBALLON

LET OP: Krachtens de federale wetgeving van de Verenigde Staten mag dit hulpmiddel uitsluitend worden verkocht door, of op voorschrift van, een arts (of een naar behoren gediplomeerde zorgverlener).

BESCHRIJVING VAN HET HULPMIDDEL

De Bakri-post-partumballon is een van silicone vervaardigde ballonkatheter met een vulvolume maximaal van 500 mL. De snel indruppelbare componenten bevatten polymeren slangen met een infuuszakspike en een driewegklep.

BEOOGD GEBRUIK

Dit hulpmiddel is bedoeld om postpartumbloedingen uit de baarmoeder tijdelijk te beheersen of te verminderen wanneer conservatieve behandeling verantwoord is.

CONTRA-INDICATIES

- Arteriële bloeding waarvoor chirurgische exploratie of angiografische embolisatie is vereist
- Gevallen die hysterectomie indiceren
- Zwangerschap
- Baarmoederhalskanker
- Purulente infecties in de vagina, baarmoederhals of baarmoeder
- Onbehandelde baarmoederafwijking
- Diffuse intravasale stolling
- Een operatieplaats waar het hulpmiddel de bloeding niet effectief kan beheersen

WAARSCHUWINGEN

- Dit hulpmiddel is bedoeld als tijdelijk middel om hemostase te verkrijgen in gevallen waarbij conservatieve behandeling van postpartumbloedingen uit de baarmoeder is geïndiceerd.
- De Bakri-postpartumballon is geïndiceerd voor gebruik in geval van een primaire postpartumhemorragie binnen 24 uur na de bevalling.
- Het hulpmiddel mag niet meer dan 24 uur in het lichaam verblijven.
- De ballon moet worden gevuld met een steriele vloeistof zoals steriel water, steriel fysiologisch zout of ringerlactaat. De ballon mag nooit worden gevuld met lucht, kooldioxide of welk ander gas dan ook.
- Het maximale vulvolume is 500 mL. Zorg dat de ballon niet overvuld wordt. Overvullen van de ballon kan ertoe leiden dat de ballon tot in de vagina verschuift.
- Patiëntes bij wie dit hulpmiddel wordt gebruikt, moeten nauwgezet worden gemonitord op tekenen van verhoogd bloedverlies en/of diffuse intravasale stolling (DIS). In dergelijke gevallen moet urgente interventie volgens het ziekenhuisprotocol worden geboden.
- Er zijn geen klinische gegevens beschikbaar ter ondersteuning van het gebruik van dit hulpmiddel bij DIS.
- Het monitoren van de patiënte is een integraal onderdeel van de behandeling van postpartumbloedingen. Tekenen van verslechtering of niet-verbetering van de toestand moeten leiden tot agressiever behandeling van de baarmoederbloeding bij de patiënte.
- De urineproductie van de patiënte moet worden gemonitord terwijl de Bakri-postpartumballon in gebruik is.

VOORZORGSMAATREGELEN

- Dit product is bestemd voor gebruik door artsen met een opleiding in en ervaring met verloskundige en gynaecologische technieken.
- Vermijd overmatige kracht bij het inbrengen van de ballon in de baarmoeder.

GEBRUIKSAANWIJZING

BELANGRIJK: Vóór de transvaginale of transabdominale plaatsing van de Bakri-postpartumballon moet de baarmoeder vrij zijn van alle placentafragmenten en moet de patiënte worden geëvalueerd om er zeker van te zijn dat de geslachtsorganen geen rijtwonden of trauma vertonen en dat de oorsprong van de bloeding niet arterieel is.

Transvaginale plaatsing

1. Bepaal het volume van de baarmoeder door direct onderzoek of echografisch onderzoek.
2. Breng het ballongedeelte van de katheter in de baarmoeder in en zorg daarbij dat de gehele ballon voorbij het baarmoederhalskanaal en het ostium internum is ingebracht.
3. Plaats nu een Foley-verblijfsblaaskatheter, indien deze nog niet is geplaatst, om de urineproductie op te vangen en te monitoren.

Transabdominale plaatsing, na keizersnede

1. Bepaal het volume van de baarmoeder door direct onderzoek.
2. Breng van bovenaf, door de keizersnede, de tamponnadeballon in de baarmoeder en de baarmoederhals in, met de vulpoort het eerst.

NB: Verwijder de afsluitkraan om het plaatsen van de ballon te vergemakkelijken en bevestig opnieuw voordat de ballon wordt gevuld.

3. Laat een assistent de schacht van de ballon door het vaginale kanaal trekken totdat de basis van de geleegde ballon in contact komt met het ostium internum.
4. Sluit de incisie volgens de normale procedure en let er daarbij goed op dat u de ballon tijdens het hechten niet aanprikt.

NB: Controleer of alle componenten van het product intact zijn en de hysterotomie stevig gehecht is alvorens de ballon te vullen. Indien klinisch relevant kan het abdomen na het vullen van de ballon openblijven om de uitzetting van de baarmoeder nauwgezet te bewaken en de sluiting van de hysterotomie te bevestigen.

NB: Indien klinisch relevant kan een B-Lynch-compressiehechting worden gebruikt in combinatie met de Bakri-postpartumballon.

De ballon vullen

Met spuit

WAARSCHUWING: Vul de ballon altijd met een steriele vloeistof. Vul de ballon nooit met lucht, kooldioxide of welk ander gas dan ook.

WAARSCHUWING: Het maximale vulvolume is 500 mL. Zorg dat de ballon niet overvuld wordt. Overvullen van de ballon kan ertoe leiden dat de ballon tot in de vagina verschuift.

NB: Om de ballon tot het gewenste volume te vullen, verdient het aanbeveling het vooraf bepaalde vloeistofvolume in een aparte houder te gieten, in plaats van de hoeveelheid in de ballon ingespoten vloeistof te verifiëren aan de hand van de schaalverdeling van de spuit.

1. Plaats nu een Foley-verblijfsblaaskatheter, indien deze nog niet is geplaatst, om de urineproductie op te vangen en te monitoren.
2. Gebruik de meegeleverde spuit om de ballon via de afsluitkraan tot het vooraf bepaalde volume te vullen.
3. Nadat de ballon is gevuld tot het vooraf bepaalde volume, controleert u via echografisch onderzoek of de ballon correct is geplaatst. **NB: Zie Afb. 1 voor correcte plaatsing.**
4. Indien gewenst kan trekkracht op de ballonschacht worden uitgeoefend. Om de spanning te handhaven, maakt u de ballonschacht aan het been van de patiënte vast of bevestigt u de schacht aan een gewicht van maximaal 500 g.

NB: Om verschuiving van de ballon in de vagina te voorkomen, kan tegendruk worden uitgeoefend door het vaginale kanaal op te vullen met vaginaal gaas dat met jodium of antibiotica is doordrenkt.

5. Sluit de drainagepoort aan op een vloeistofopvangzak om de hemostase te monitoren.

NB: Om de hemostase afdoende te monitoren, kunnen de drainagepoort en de slang met steriel isotoon fysiologisch zout worden doorgespoeld zodat ze vrij van stolsels zijn.

6. Monitor de patiënte continu op tekenen van verhoogd bloedverlies en baarmoederkrampen.

De ballon vullen

Met componenten voor snelle instillatie

Zie **Afb. 2-8** aan het begin van dit boekje.

NB: Nadat de ballon met het vooraf bepaalde volume is gevuld, moet via echografisch onderzoek worden gecontroleerd of hij correct is geplaatst.

De ballon verwijderen

NB: Het tijdstip waarop de ballon wordt verwijderd, moet worden bepaald door de behandelend arts na evaluatie van de patiënte wanneer de bloeding beheerst is en de patiënte is gestabiliseerd. De ballon mag eerder worden verwijderd bij vaststelling van hemostase door de arts. De maximale verblijfsduur is 24 uur.

1. Verlicht de spanning op de ballonschacht.
2. Verwijder eventueel vaginaal opvulgaas.
3. Gebruik een geschikte spuit om de inhoud van de ballon te aspireren totdat de ballon helemaal leeg is. De vloeistof kan stapsgewijs worden verwijderd zodat de patiënte periodiek kan worden geobserveerd.

NB: In urgente gevallen kan de katheterschacht worden doorgeknipt om het legen van de ballon te versnellen.

4. Trek de ballon zachtjes uit de baarmoeder en het vaginale kanaal terug en voer de ballon af.
5. Monitor de patiënte op tekenen van bloedverlies.

WIJZE VAN LEVERING

Wordt steriel (gesteriliseerd met ethyleenoxide) in gemakkelijk open te trekken verpakkingen geleverd. Bestemd voor eenmalig gebruik. Steriel indien de verpakking ongeopend en onbeschadigd is. Gebruik het product niet indien er twijfel bestaat over de steriliteit van het product. Koel, donker en droog bewaren. Vermijd langdurige blootstelling aan licht. Inspecteer het product wanneer u het uit de verpakking haalt om te controleren of het niet beschadigd is.

LITERATUUR

Deze gebruiksaanwijzing is gebaseerd op de ervaringen van artsen en/of hun publicaties. Neem contact op met de plaatselijke verkoopvertegenwoordiger van Cook voor informatie over beschikbare literatuur.

NORSK

BAKRI-POSTPARTUMBALLONG

FORSIKTIG: I henhold til amerikansk lovgivning skal dette instrumentet bare selges av eller forskrives av en lege (eller en autorisert behandler).

BESKRIVELSE AV ANORDNINGEN

Bakri-postpartumballongen er et ballongkateter i silikon med et maksimalt fyllevolum på 500 mL. Komponentene for hurtig instillasjon inkluderer polymerslanger med IV-posefeste og treveisventil.

TILTENKT BRUK

Dette instrumentet er beregnet for å gi midlertidig kontroll, eller reduksjon, av blødning i livmoren etter fødsel når konservativ behandling er garantert.

KONTRAINDIKASJONER

- Arteriell blødning som krever kirurgisk inngripen eller angiografisk embolisering

- Tilfeller som indikerer hysterektomi
- Graviditet
- Livmorhalskreft
- Purulente infeksjoner i skjede, livmorhals eller livmor
- Ubehandlet uterusanomali
- Disseminert intravaskulær koagulasjon
- Et kirurgisk område som vil hindre instrumentet i å kontrollere blødningen på en effektiv måte

ADVARSLER

- Dette instrumentet er ment å være en midlertidig metode for å oppnå hemostase i tilfeller som krever konservativ behandling av blødning i livmoren etter fødsel.
- Bakri-postpartumballong er beregnet for bruk ved primær blødning etter fødsel innen 24 timer etter forløsning.
- Instrumentet skal ikke være lagt inn i mer enn 24 timer.
- Ballongen skal fylles med en steril væske, for eksempel sterilt vann, steril saltoppløsning eller Ringers løsning. Ballongen må aldri fylles med luft, karbondioksid eller noen annen gass.
- Maksimal fylling er 500 mL. Fyll ikke ballongen for mye. Hvis ballongen fylles for mye, kan ballongen bli forskjøvet inn i skjeden.
- Pasienter som bruker dette instrumentet, skal overvåkes nøye for tegn på økt blødning og/eller disseminert intravaskulær koagulasjon (DIC). I slike tilfeller bør sykehusets nødprosedyrer følges.
- Det finnes ingen kliniske data som støtter bruken av dette instrumentet ved tilfeller av DIC.
- Pasientovervåking er en viktig del av behandlingen av blødning etter fødsel. Tegn på forverret eller ikke forbedret tilstand bør føre til en mer aggressiv behandling og håndtering av den uterine blødningen hos pasienten.
- Pasienturinvolum skal overvåkes mens Bakri-postpartumballong er i bruk.

FORHOLDSREGLER

- Dette produktet er tiltenkt for bruk av leger som er opplært i og har erfaring med obstetrikk og gynekologiske teknikker.
- Unngå bruk av for mye makt når du setter inn ballongen i livmoren.

BRUKSANVISNING

VIKTIG: Før transvaginal eller transabdominal plassering av Bakri-postpartumballongen, må livmoren være fri for alle placenta-fragmenter og pasienten må evalueres for å sikre at det ikke er noen laserasjoner eller traumer i genitaltraktus og at blødningskilden ikke er arteriell.

Transvaginal plassering

1. Fastsett livmorvolum ved manuell undersøkelse eller ultralyd.
2. Sett ballongdelen av kateteret inn i livmoren og sørg for at hele ballongen settes inn forbi livmorshalskanalen og den interne åpningen.
3. Hvis det ikke allerede er lagt inn et Foley-kateter i urinblæren for oppsamling og overvåking av urinstrømmen, bør dette gjøres nå.

Transabdominal plassering, etter keisersnitt

1. Fastsett livmorvolum ved direkte undersøkelse.
2. Før tamponeringsballongen, ovenfra via keisersnittet, med fylleporten først gjennom livmor og cervix.

MERKNAD: Fjern stoppekranen for å lette plassering, og sett den på igjen før ballongen fylles.

3. La en assistent trekke skaftet til ballongen gjennom skjeden helt til enden av den tomme ballongen kommer i kontakt med den interne livmorshalsåpningen.
4. Lukk snittet i henhold til normal prosedyre, og påse at det ikke stikkes hull på ballongen under sutureringen.

MERKNAD: Kontroller at alle produktkomponentene er intakte og at hysterotomien er sikkert suturert før ballongen fylles. Hvis det er klinisk relevant, kan abdomen være åpen når ballongen fylles, for å overvåke distensjonen av livmoren nøye og bekrefte hysterotomilukkingen.

MERKNAD: Hvis det er klinisk relevant, kan en B-Lynch-kompresjonssutur brukes sammen med Bakri-postpartumballongen.

Ballonginflasjon

Med sprøyte

ADVARSEL: Fyll alltid ballongen med en steril væske. Ballongen skal aldri fylles med luft, karbondioksid eller andre gasser.

ADVARSEL: Maksimal fylling er 500 mL. Fyll ikke ballongen for mye. Hvis ballongen fylles for mye, kan ballongen bli forskjøvet inn i skjeden.

MERKNAD: Sørg for at ballongen er fylt til ønsket volum. Når du skal verifisere mengden væske som skal fylles i ballongen, anbefales det å plassere det forhåndsbestemte volumet med væske i en egen beholder i stedet for å bruke flere fylte sprøyter.

1. Hvis det ikke allerede er lagt inn et Foley-kateter i urinblæren for oppsamling og overvåking av urinstrømmen, bør dette gjøres nå.
2. Bruk vedlagt sprøyte, og fyll ballongen til det forhåndsbestemte volumet gjennom stoppekranen.
3. Når ballongen er fylt til det forhåndsbestemte volumet, bekreft plassering ved hjelp av ultralyd.
   MERKNAD: Se fig. 1 for riktig plassering.
4. Hvis ønskelig, kan det brukes traksjon på ballongskaftet. Opprettholdstrammingen ved å feste ballongskaftet til pasientens ben eller til en vekt som ikke overstiger 500 gram.

MERKNAD: For å unngå at ballongen forflyttes til skjeden kan det brukes mottrykk ved å pakke skjeden med vaginal gas fuktet med jod eller antibiotika.

5. Koble tømmeporten til en væskeoppsamlingspose for å overvåke hemostasen.

MERKNAD: For å overvåke hemostasen tilstrekkelig kan ballongens tømmeport og slanger skylles fri for klumper med steril isotonisk saltoppløsning.

6. Overvåk pasienten kontinuerlig for tegn på økt blødning og krampetrekninger i livmoren.

Ballonginflasjon

Med komponenter for hurtig instillasjon

Se **fig. 2–8** foran i dette heftet.

MERKNAD: Ultralyd skal brukes til å bekrefte riktig plassering av ballongen når ballongen er fylt til det forhåndsbestemte volumet.

Fjerning av ballongen

MERKNAD: Tidspunktet for fjerning av ballongen skal bestemmes av behandlende lege etter evaluering av pasienten når blødningen har blitt kontrollert og pasienten har blitt stabilisert. Ballongen kan fjernes tidligere, etter legens bestemmelse av hemostasen. Maksimal tid for innlegging er 24 timer.

1. Fjern strammingen fra ballongskaftet.
2. Fjern eventuelle tamponader fra skjeden.
3. Bruk en egnet sprøyte og aspirer innholdet i ballongen til den er helt tømt. Væsken kan fjernes trinnvis, slik at pasienten kan observeres periodemessig.

MERKNAD: I en nødsituasjon kan kateterskaftet kuttes for å muliggjøre hurtigere tømming.

4. Trekk ballongen forsiktig ut av livmoren og skjeden, og kast den.
5. Overvåk pasienten for tegn på blødning.

LEVERINGSFORM

Leveres sterilisert med etylenoksidgass i peel-open-innpakninger. Kun til engangsbruk. Steril hvis pakningen ikke er åpnet eller skadet. Bruk ikke produktet hvis du er i tvil om det er sterilt. Oppbevares på et mørkt, tørt og kjølig sted. Må ikke utsettes for lys i lengre perioder. Etter utpakking må du kontrollere at det ikke har oppstått skader på produktet.

REFERANSE

Denne bruksanvisningen er basert på legers erfaring og (eller) deres publiserte litteratur. Henvend deg til Cooks salgsrepresentant hvis du vil ha informasjon om tilgjengelig litteratur.

POLSKI

BALON POPORODOWY BAKRIEGO

PRZESTROGA: Zgodnie z prawem federalnym Stanów Zjednoczonych sprzedaż opisywanego urządzenia może być prowadzona wyłącznie przez lekarza lub na zlecenie lekarza (bądź uprawnionej osoby posiadającej odpowiednie zezwolenie).

OPIS URZĄDZENIA

Balon poporodowy Bakriego jest silikonowym cewnikiem balonowym o maksymalnej objętości napełniania 500 mL. Elementy do szybkiego zakroplenia obejmują polimerowy wężyk, kolec do worka infuzyjnego i zawór trójdrożny.

PRZEZNACZENIE URZĄDZENIA

Urządzenie to jest przeznaczone do zapewnienia czasowej kontroli lub zredukowania poporodowego krwotoku macicznego w przypadkach uzasadnionego postępowania zachowawczego.

PRZECIWWSKAZANIA

- Krwotok tętniczy wymagający postępowania chirurgicznego lub embolizacji angiograficznej
- Przypadki, w których wskazana jest histerektomia
- Ciąża
- Rak szyjki macicy
- Ropne zakażenia pochwy, szyjki macicy lub macicy
- Nieleczona anomalia macicy
- Rozsiane wykrzepianie wewnątrznaczyniowe
- Lokalizacja chirurgiczna uniemożliwiająca skuteczną kontrolę krwawienia za pomocą tego urządzenia

OSTRZEŻENIA

- Niniejsze urządzenie jest zaprojektowane jako tymczasowy środek do zapewnienia hemostazy w przypadkach poporodowego krwotoku macicznego, gdzie wskazane jest postępowanie zachowawcze.
- Balon poporodowy Bakriego jest przeznaczony do użycia w przypadku pierwotnego krwotoku poporodowego w ciągu 24 godzin od porodu.
- Urządzenia nie należy pozostawiać w miejscu na dłużej niż 24 godziny.
- Balon należy napełniać sterylnym płynem, takim jak woda jałowa, jałowa sól fizjologiczna lub roztwór Ringera z dodatkiem mleczanu. Nigdy nie wolno napełniać balonu powietrzem, dwutlenkiem węgla ani żadnym innym gazem.
- Maksymalna objętość napełnienia wynosi 500 mL. Nie należy nadmiernie wypełniać balonu. Nadmierne napełnienie balonu może spowodować jego przemieszczenie do pochwy.
- Pacjentki, u których zastosowano urządzenie, powinny być ściśle monitorowane pod kątem objawów nasilania się krwotoku i/lub rozsianego wykrzepiania wewnątrznaczyniowego (DIC). W takich przypadkach należy wdrożyć procedurę ratunkową zgodnie z protokołem szpitalnym.
- Brak danych klinicznych uzasadniających zastosowanie tego urządzenia w przypadku DIC.
- Monitorowanie pacjentek jest integralną częścią postępowania w przypadkach krwotoków poporodowych. Objawy pogorszania się lub braku poprawy powinny prowadzić do zastosowania bardziej agresywnego leczenia i postępowania u pacjentek z krwawieniem macicznym.
- Podczas stosowania balonu poporodowego Bakriego u pacjentek należy prowadzić monitorowanie diurezy.

ŚRODKI OSTROŻNOŚCI

- Produkt ten jest przeznaczony do użytku przez lekarzy przeszkolonych i doświadczonych w stosowaniu technik położniczych i ginekologicznych.
- Unikać nadmiernej siły przy wprowadzaniu balonu do jamy macicy.

INSTRUKCJA UŻYCIA

WAŻNE: Przed umieszczeniem przezpochwowym lub przezbrzusznym balonu poporodowego Bakriego macica powinna być oczyszczona ze wszystkich fragmentów łożyska; należy również przeprowadzić kontrolę pacjentki, aby upewnić się, że nie nastąpiło rozerwanie lub uraz dróg rodnych, i że źródłem krwawienia nie jest tętnica.

Umieszczanie przezpochwowe

1. Określić objętość macicy w badaniu bezpośrednim lub badaniem ultrasonograficznym.
2. Wprowadzić balonową część cewnika do jamy macicy upewniając się, że cały balon przeszedł przez kanał szyjki i ujście wewnętrzne.
3. Teraz założyć cewnik pęcherzowy Foleya, o ile nie został wcześniej założony, w celu zbierania moczu i monitorowania diurezy.

Umieszczanie przezbrzuszne, po cięciu cesarskim

1. Określić objętość macicy w badaniu bezpośrednim.
2. Od góry, z dostępu przez nacięcie do cięcia cesarskiego, wsunąć balon do tamponady, portem do napełniania wprzód, przez macicę i szyjkę.

UWAGA: Kranik można odłączyć dla ułatwienia umieszczania i ponownie przyłączyć przed napełnieniem balonu.

3. Poprosić asystenta o przeciągnięcie trzonu balonu przez kanał pochwy, aż do zetknięcia podstawy pustego balonu z ujściem wewnętrznym szyjki.
4. Zamknąć nacięcie zgodnie z normalną procedurą uważając, aby nie przebić balonu przy zakładaniu szwów.

UWAGA: Przed napełnieniem balonu sprawdzić, czy wszystkie elementy wyrobu są nienaruszone oraz czy nacięcie macicy zostało należycie zszyte. Jeżeli jest to klinicznie uzasadnione, brzuch może pozostać otwarty po napełnieniu balonu, aby ściśle monitorować rozszerzenie macicy i potwierdzić zamknięcie nacięcia macicy.

UWAGA: Jeżeli jest to klinicznie uzasadnione, można zastosować szew uciskowy B-Lyncha w połączeniu z balonem poporodowym Bakriego.

Wypełnianie balonu

Przy pomocy strzykawki

OSTRZEŻENIE: Balon napełniać zawsze sterylnym płynem. Nie wolno napełniać balonu powietrzem, dwutlenkiem węgla ani żadnym innym gazem.

OSTRZEŻENIE: Maksymalna objętość napełnienia wynosi 500 mL. Nie należy nadmiernie wypełniać balonu. Nadmierne napełnienie balonu może spowodować jego przemieszczenie do pochwy.

UWAGA: Dla zapewnienia napełnienia balonu do żądanej objętości zaleca się, aby określona wcześniej objętość płynu została wlana do osobnego naczynia, nie zaleca się ustalania ilości płynu podanego do balonu tylko na podstawie napełnienia według liczby strzykawek.

1. Teraz założyć cewnik pęcherzowy Foleya, o ile nie został wcześniej założony, w celu zbierania moczu i monitorowania diurezy.
2. Za pomocą dołączonej strzykawki rozpocząć napełnianie balonu do określonej wcześniej objętości przez kranik.
3. Po napełnieniu balonu do określonej wcześniej objętości potwierdzić jego umieszczenie za pomocą ultrasonografii. **UWAGA: Poprawne umieszczenie przedstawiono na rys. 1.**
4. Jeśli wymagane można zastosować naprężenie trzonu balonu. Aby utrzymać naprężenie, zamocować trzon balonu do nogi pacjentki lub przymocować ciężarek nieprzekraczający 500 g.

UWAGA: Aby zapobiec przemieszczeniu balonu w pochwie, można zastosować przeciwciśnienie poprzez uszczelnienie kanału pochwy za pomocą tamponu dopochwowego z gazy, nasączonego jodyną lub antybiotykiem.

5. Podłączyć port drenujący do worka na zbiórkę płynu w celu monitorowania hemostazy.

UWAGA: W celu odpowiedniego monitorowania hemostazy, port drenujący balonu i przewody można przepłukać jałową, izotoniczną solą fizjologiczną, aby wyczyścić je z zakrzepów.

6. Monitorować pacjentkę w sposób ciągły pod kątem wystąpienia objawów nasilenia krwotoku i skurczów macicy.

Wypełnianie balonu

Przy pomocy komponentów do szybkiego napełniania

Patrz **rys. 2-8**, na początku tej broszury.

UWAGA: Po napełnieniu balonu do określonej wcześniej objętości, potwierdzić jego poprawne umieszczenie za pomocą ultrasonografii.

Usuwanie balonu

UWAGA: Czas usunięcia balonu powinien ustalić lekarz prowadzający na podstawie oceny pacjentki, po opanowaniu krwawienia i ustabilizowaniu pacjentki. Balon można usunąć wcześniej, jeżeli lekarz ustali, że nastąpiła hemostaza. Maksymalny czas pozostawienia balonu w miejscu wynosi 24 godziny.

1. Usunąć naprężenie z trzonu balonu.
2. Usunąć wszelkie tampony dopochwowe.
3. Za pomocą odpowiedniej strzykawki zaaspirować zawartość balonu do momentu jego całkowitego opróżnienia. Płyn można usuwać stopniowo, co pozwoli na okresową obserwację pacjentki.

UWAGA: W przypadku nagłej potrzeby można odciąć trzon cewnika, aby ułatwić szybsze opróżnianie balonu.

4. Delikatnie wycofać balon z jamy macicy i kanału pochwy, i wyrzucić.
5. Monitorować pacjentkę pod kątem objawów krwawienia.

SPOSÓB DOSTARCZENIA

Produkt wyjałowiony tlenkiem etylenu; dostarczany w rozrywalnych opakowaniach. Urządzenie jest przeznaczone do jednorazowego użytku. Urządzenie zachowuje jałowość, jeśli opakowanie nie jest otwarte ani uszkodzone. Jeśli jałowość budzi wątpliwości, nie należy używać produktu. Przechowywać w ciemnym, suchym i chłodnym miejscu. Unikać przedłużonej ekspozycji na światło. Po wyjęciu z opakowania sprawdzić produkt, aby upewnić się, że nie doszło do uszkodzenia.

PIŚMIENNICTWO

Niniejszą instrukcję użycia opracowano na podstawie doświadczeń lekarzy i (lub) ich publikacji. W celu uzyskania informacji na temat dostępnego piśmiennictwa należy się zwrócić do lokalnego przedstawiciela handlowego firmy Cook.

PORTUGUÊS

BALÃO PÓS-PARTO BAKRI

ATENÇÃO: A lei federal dos EUA restringe a venda deste dispositivo a um médico ou um profissional de saúde licenciado ou mediante prescrição de um destes profissionais.

DESCRIÇÃO DO DISPOSITIVO

O Balão Pós-Parto Bakri é um cateter de balão de silicone com um volume de máximo de enchimento de 500 mL. Os componentes de instilação rápida incluem tubagem de polímero com um espigão de saco IV e uma válvula de três vias.

UTILIZAÇÃO PREVISTA

Este dispositivo destina-se a proporcionar controlo temporário ou redução da hemorragia uterina pós-parto quando se necessita de tratamento conservador.

CONTRA-INDICAÇÕES

- Hemorragia arterial que requer exploração cirúrgica ou embolização angiográfica
- Casos indicadores de histerectomia
- Gravidez
- Cancro do colo do útero
- Infeções purulentas da vagina, colo do útero ou útero
- Anomalia uterina não tratada
- Coagulação intravascular disseminada
- Um local cirúrgico que impediria que o dispositivo controlasse eficazmente a hemorragia

ADVERTÊNCIAS

- Este dispositivo destina-se a funcionar como um meio temporário de estabelecimento da hemóstase em casos indicadores de tratamento conservador da hemorragia uterina pós-parto.
- O balão pós-parto Bakri está indicado para utilização em caso de hemorragia pós-parto primária no período de 24 horas após o parto.
- O dispositivo não deve ser deixado no interior do organismo por mais de 24 horas.
- O balão deve ser enchido com um líquido estéril como, por exemplo, água estéril, soro fisiológico estéril ou solução de Ringer com lactato. O balão nunca deve ser enchido com ar, dióxido de carbono ou qualquer outro gás.
- O enchimento máximo corresponde a 500 mL. Não encha excessivamente o balão. O enchimento excessivo do balão pode provocar a deslocação do balão para a vagina.
- As doentes nas quais este dispositivo está a ser utilizado devem ser monitorizadas de perto para deteção de sinais de agravamento da hemorragia e/ou de coagulação intravascular disseminada (CID). Nesses casos, é necessário seguir a intervenção de emergência de acordo com o protocolo hospitalar.
- Não existem dados clínicos que fundamentem a utilização deste dispositivo no contexto da CID.
- A monitorização da doente constitui uma parte integral do controlo da hemorragia no pós-parto. Os sinais de deterioração ou ausência de melhoria do estado devem conduzir a um tratamento e controlo mais agressivos da hemorragia uterina da doente.
- O débito urinário da doente deve ser monitorizado durante a utilização do balão pós-parto Bakri.

PRECAUÇÕES

- Este produto destina-se a utilização por médicos com formação e experiência em técnicas obstétricas e ginecológicas.
- Evite exercer força excessiva ao inserir o balão no útero.

INSTRUÇÕES DE UTILIZAÇÃO

IMPORTANTE: Antes da colocação transvaginal ou transabdominal do balão pós-parto Bakri, o útero não deve apresentar quaisquer fragmentos de placenta, a doente deve ser avaliada por forma a garantir que não há lacerações ou traumatismo no trato genital e que a origem da hemorragia não é arterial.

Colocação transvaginal

1. Determine o volume uterino por exame direto ou exame ecográfico.
2. Insira a parte do balão do cateter no útero e certifique-se de que o balão fica completamente inserido para lá do canal cervical e do óstio interno.
3. Caso ainda não se encontre inserido, coloque nesta altura um cateter Foley permanente na bexiga para colher e monitorizar o débito urinário.

Colocação transabdominal, pós-cesariana

1. Determine o volume uterino por exame direto.
2. A partir de cima, através do acesso da incisão da cesariana, faça passar o balão de tamponamento, com o orifício de enchimento primeiro, através do útero e do colo do útero.

NOTA: Remova a torneira de passagem para auxiliar na colocação e fixação antes de encher o balão.

3. Peça a um assistente para puxar a haste do balão através do canal vaginal até a base do balão esvaziado ficar em contacto com o óstio cervical interno.
4. Feche a incisão de acordo com o procedimento normal, tomando o devido cuidado para evitar perfurar o balão durante a sutura.

NOTA: Antes de encher o balão, certifique-se de que todos os componentes do produto estão intactos e de que a histerotomia está suturada em segurança. Se for clinicamente relevante, o abdómen pode permanecer aberto aquando do enchimento do balão para assim se monitorizar atentamente a distensão uterina e confirmar o fecho da histerotomia.

NOTA: Se for clinicamente relevante, pode utilizar-se uma sutura de compressão B-Lynch em conjunto com o balão pós-parto Bakri.

Enchimento do balão

Com seringa

ADVERTÊNCIA: Encha sempre o balão com líquido estéril. Nunca encha o balão com ar, dióxido de carbono ou qualquer outro gás.

ADVERTÊNCIA: O enchimento máximo corresponde a 500 mL. Não encha excessivamente o balão. O enchimento excessivo do balão pode provocar a deslocação do balão para a vagina.

NOTA: Para garantir que o balão é enchido até ao volume pretendido, recomenda-se a colocação do volume predeterminado do líquido num recipiente separado, em vez de se basear numa contagem da seringa para verificar a quantidade de líquido que foi instilada no balão.

1. Caso ainda não se encontre inserido, coloque nesta altura um cateter Foley permanente na bexiga para colher e monitorizar o débito urinário.
2. Utilizando a seringa fornecida, comece a encher o balão até ao volume predeterminado através da torneira de passagem.
3. Depois de o balão ter sido enchido até ao volume predeterminado, confirme a colocação por meios ecográficos. **NOTA: Consulte a colocação correta na Fig. 1.**
4. Se desejar, pode aplicar tração na haste do balão. Para manter a tensão, fixe a haste do balão à perna da doente ou prenda-a a um peso que não exceda 500 g.

NOTA: Para evitar a deslocação do balão para a vagina, pode aplicar uma contrapressão enchendo o canal vaginal com gaze vaginal embebida em iodo ou antibiótico.

5. Ligue a porta de drenagem a um saco de recolha de líquido para monitorizar a hemóstase.

NOTA: Para monitorizar adequadamente a hemostase, pode irrigar o orifício e a tubagem de drenagem do balão com soro fisiológico isotónico para eliminar coágulos.

6. Monitorize continuamente a doente em relação a sinais de aumento da hemorragia e cólicas uterinas.

Enchimento do balão

Com componentes de instilação rápida

Consulte as **Figs. 2-8**, na parte da frente deste folheto.

NOTA: Deve realizar-se uma ecografia para confirmar a colocação correta do balão depois de este ser enchido até ao volume predeterminado.

Remoção do balão

NOTA: O momento da remoção do balão deve ser determinado pelo médico assistente aquando da avaliação da doente depois de a hemorragia estar controlada e a doente estabilizada. O balão pode ser removido antes, assim que o médico determinar a hemostase. O tempo de permanência máximo é de 24 horas.

1. Elimine a tensão da haste do balão.
2. Retire qualquer gaze vaginal.
3. Com uma seringa adequada, aspire o conteúdo do balão até ficar totalmente esvaziado. O líquido pode ser removido incrementalmente de modo a permitir observar a doente com regularidade.

NOTA: Em caso de emergência, a haste do cateter pode ser cortada para facilitar um esvaziamento mais rápido.

4. Retire cuidadosamente o balão do útero e do canal vaginal e elimine-o.
5. Monitorize a doente para a deteção de sinais de hemorragia.

APRESENTAÇÃO

Fornecido esterilizado pelo gás óxido de etileno em embalagens de abertura fácil. Destina-se a uma única utilização. Estéril desde que a embalagem não esteja aberta nem danificada. Se tiver alguma dúvida quanto à esterilidade do produto, não o utilize. Guarde num local protegido da luz, seco e fresco. Evite a exposição prolongada à luz. Depois de retirar o produto da embalagem, inspecione-o para se certificar de que não ocorreram danos.

REFERÊNCIA

Estas instruções de utilização baseiam-se na experiência de médicos e/ou na literatura publicada por médicos. Consulte o representante local de vendas da Cook para obter informações sobre a literatura disponível.

SVENSKA

BAKRI POSTPARTUMBALLONG

VAR FÖRSIKTIG: Enligt federal lagstiftning i USA får denna produkt endast säljas av eller på ordination från en läkare (eller korrekt legitimerad praktiker).

PRODUKTBESKRIVNING

Bakri postpartumballong är en ballongkateter av silikon med en högsta fyllnadsvolym på 500 mL. Komponenterna för snabb instillation inkluderar en polymerslang med en spetsanslutning för infusionspåse och en trevägsventil.

AVSEDD ANVÄNDNING

Denna anordning är avsedd att ge tillfällig kontroll över eller reduktion av uterusblödning postpartum när konservativ hantering är motiverad.

KONTRAINDIKATIONER

- Arteriell blödning som kräver kirurgisk undersökning eller angiografisk embolisering
- Fall som indikerar hysterektomi
- Graviditet
- Livmoderhalscancer
- Infektioner med varbildningar i vagina, cervix eller uterus
- Obehandlad uterusanomali
- Spridd intravaskulär koagulation
- Ett operationsställe som skulle hindra anordningen från att hålla blödningen under kontroll på ett effektivt sätt

VARNINGAR

- Denna anordning är avsedd som ett sätt att tillfälligt upprätta hemostas i fall som indikerar konservativ hantering av uterusblödning postpartum.

- Bakri postpartumballong är indicerad för användning vid primär postpartumblödning inom 24 timmar efter förlossningen.
- Anordningen får inte lämnas kvar i mer än 24 timmar.
- Ballongen ska fyllas med en steril vätska, t.ex. sterilt vatten, steril koksaltlösning eller lakterad Ringerlösning. Ballongen får aldrig fyllas med luft, koldioxid eller någon annan gas.
- Högsta fyllningsvolym är 500 mL. Ballongen får inte överfyllas. Överfyllning av ballongen kan leda till att ballongen rubbas in i vaginan.
- Patienter som denna anordning används på ska övervakas noga för tecken på förvärrad blödning och/eller spridd intravaskulär koagulation (DIC). I sådana fall ska akut intervention enligt sjukhusets rutiner utföras.
- Det finns inga kliniska data som stödjer användning av denna anordning vid DIC.
- Patientövervakning är en ingående del i hanteringen av postpartumblödningar. Tecken på att tillståndet förvärras eller inte förbättras ska leda till en mer aggressiv behandling och hantering av patientens uterusblödning.
- Patientens urinavgång ska övervakas medan Bakri postpartumballong används.

FÖRSIKTIGHETSÅTGÄRDER

- Denna produkt är avsedd att användas av läkare med utbildning i och erfarenhet av obstetrik och gynekologiska tekniker.
- Undvik alltför stor kraft när ballongen förs in i livmodern.

BRUKSANVISNING

VIKTIGT: Före transvaginal eller transabdominal placering av Bakri postpartumballong ska uterus vara helt fri från placentafragment och patienten ska undersökas för att säkerställa att det inte förekommer några lacerationer eller trauman i genitalvägarna och att källan till blödningen inte är arteriell.

Transvaginal placering

1. Fastställ uterus volym genom direkt undersökning eller ultraljudsundersökning.
2. För in ballongdelen av katetern i uterus och se till att hela ballongen förs in förbi cervixkanalen och den inre livmodermunnen.
3. Placera nu en inneliggande Foley-kateter i urinblåsan om det inte redan finns en på plats för att samla upp och övervaka urinavgången.

Transabdominell placering efter kejsarsnitt

1. Fastställ uterus volym genom direkt undersökning.
2. För in tamponadballongen med fyllningsporten först uppifrån genom kejsarsnittet och genom uterus och cervix.

OBS! Avlägsna infusionskranen för att underlätta placeringen och sätt tillbaka innan ballongen fylls.

3. Låt en assistent dra ballongskaftet genom den vaginala kanalen tills den tömda ballongbasen kommer i kontakt med den inre livmodermunnen.
4. Förslut snittet på normalt sätt, och var försiktig så att ballongen inte punkteras när du syr.

OBS! Säkerställ att alla produktkomponenter är oskadade och att hysterotomin har suturerats på ett säkert sätt före fyllning av ballongen. Om det är kliniskt relevant kan buken lämnas öppen vid fyllningen av ballongen för att nära övervaka utspänningen av uterus och bekräfta förslutningen av hysterotomin.

OBS! Om det är kliniskt relevant kan en kompressionssutur av typen B-Lynch användas i kombination med Bakri postpartumballong.

Ballongfyllning

Med spruta

VARNING: Fyll alltid ballongen med steril vätska. Den får aldrig fyllas med luft, koldioxid eller någon annan gas.

VARNING: Högsta fyllningsvolym är 500 mL. Ballongen får inte överfyllas. Överfyllning av ballongen kan leda till att ballongen rubbas in i vaginan.

OBS! För att säkerställa att ballongen fylls till önskad volym rekommenderas att den i förväg fastställda vätskevolymen placeras i en separat behållare, istället för att förlita sig på markeringarna på sprutan för att verifiera vilken vätskemängd som har fyllts i ballongen.

1. Placera nu en inneliggande Foley-kateter i urinblåsan om det inte redan finns en på plats för att samla upp och övervaka urinavgången.
2. Använd medföljande spruta och börja fylla ballongen med den i förväg fastställda volymen genom injektionskranen.
3. Så snart ballongen har fyllts till den i förväg fastställda volymen ska dess placering kontrolleras med ultraljud. **OBS! Se figur 1 för korrekt placering.**
4. Om så önskas kan traktion tillämpas på ballongskaftet. För att bibehålla denna spänning ska ballongskaftet fästas vid patientens ben eller vid en vikt på högst 500 g.

OBS! För att förhindra att ballongen placeras fel i vaginan kan ett mottryck appliceras genom att packa den vaginala kanalen med vaginal gasväv som blötlagts i jod eller antibiotika.

5. Anslut dräneringsporten till en vätskeuppsamlingspåse för att övervaka hemostasen.

OBS! För fullgod övervakning av hemostas kan koagel spolas ut ur ballongdränageporten och slangarna med steril isotonisk koksaltlösning.

6. Övervaka patienten kontinuerligt för tecken på ökad blödning och uteruskramper.

Ballongfyllning

Med komponenter för snabb instillation

Se **figurerna 2-8**, i broschyrens främre del.

OBS! Ultraljud ska användas för att bekräfta korrekt placering av ballongen så snart ballongen har fyllts till den i förväg fastställda volymen.

Avlägsnande av ballongen

OBS! Tidpunkten för avlägsnande av ballongen ska fastställas av den behandlande klinikern vid bedömning av patienten efter att blödningen har kunnat kontrolleras och patienten har stabiliserats. Ballongen kan avlägsnas tidigare, i samband med att klinikern fastställer hemostas. Längsta kvarliggningstid är 24 timmar.

1. Avlägsna spänningen från ballongskaftet.
2. Avlägsna eventuell fyllning från vaginan.
3. Använd lämplig spruta och aspirera innehållet i ballongen tills denna har tömts helt. Vätskan kan avlägsnas stegvis för att möjliggöra regelbunden observation av patienten.

OBS! I en nödsituation kan kateterskaftet kapas för att underlätta snabbare tömning.

4. Dra försiktigt ut ballongen ur livmodern och den vaginala kanalen och kassera den.
5. Övervaka patienten för tecken på blödning.

LEVERANSFORM

Levereras i etylenoxidgassteriliserade "peel-open"-förpackningar. Avsedd för engångsbruk. Steril såvida förpackningen är oöppnad och oskadad. Använd inte produkten om det är tveksamt att produkten är steril. Förvaras mörkt, torrt och svalt. Undvik långvarig exponering för ljus. Undersök produkten vid uppackningen för att säkerställa att den inte är skadad.

REFERENS

Denna bruksanvisning är baserad på erfarenheter från läkare och (eller) deras publicerade litteratur. Kontakta din lokala Cook-återförsäljare för information om tillgänglig litteratur.

If symbol appears on product label, X = quantity per box
Pokud je symbol uveden na označení výrobku, X = množství v krabici
Hvis symbolet vises på produktetiketten, er X = antal pr. æske
Sofern das Symbol auf dem Verpackungsetikett erscheint: X = Anzahl pro Karton
Εάν εμφανίζεται κάποιο σύμβολο στην ετικέτα του προϊόντος, X = ποσότητα ανά κουτί
Si el símbolo aparece en la etiqueta del producto, X = cantidad por caja
Si le symbole est visible sur l'étiquette du produit, X = quantité par boîte
Ha ez a szimbólum szerepel a termék címkéjén, akkor X a dobozonkénti mennyiség
Se questo simbolo compare sull'etichetta del prodotto, X = quantità per scatola
Als dit symbool op het productetiket staat: X = hoeveelheid per doos
Hvis symbolet vises på produktetiketten, X = antall per eske
Jeżeli symbol występuje na etykiecie produktu, X oznacza ilość sztuk w kartonie
Se o símbolo aparecer no rótulo do produto, X = quantidade por caixa
Om symbolen finns på produktetiketten, X = antal per förpackning

CE
0088

MANUFACTURER
COOK INCORPORATED
750 Daniels Way
Bloomington, IN 47404 U.S.A.

www.cookmedical.com

EC REPRESENTATIVE
COOK IRELAND LTD.
O'Halloran Road
National Technology Park
Limerick, Ireland

2016-10
T_J-SOSR_REV2

Hello Reginald,

Confirming receipt! We will respond by end of our day today.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

<image001.png>

<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 10:41 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov
Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)
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Ph: 240-402-6152
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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 28, 2020 1:10 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

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From: Cindy Domecus <domecusconsulting@comcast.net>
Sent: Thursday, August 27, 2020 6:36 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R[redacted] (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

Thank you for sending the Word version of the 510(k) Summary. We have reviewed the responses to our August 26th interactive requests and have the following requests for revisions to the labeling. **If possible, please provide the revised documents by COB today, but no later than 9 am EDT on Friday, August 28th.**

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Cc: K201199@docs.fda.gov
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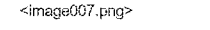

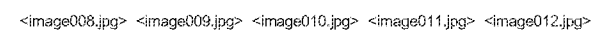

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Sent: Thursday, August 27, 2020 12:50 AM
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Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
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(b)(4) Deficiencies

From: Nandy, Poulomi (CDRH)
To: Cindy Domecus
Subject: RE: (b)(4) Deficiencies
Date: Friday, April 17, 2020 1:55:00 PM

Hi Cindy,

(b)(4) Deficiencies

Thanks,
Poulomi.

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Monday, April 6, 2020 10:53 AM
To: Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov>
Subject: Re: (b)(4) Deficiencies

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Apr 6, 2020, at 7:52 AM, Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov> wrote:

Hi Cindy,

(b)(4) Deficiencies

Thanks,
Poulomi.

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Monday, April 6, 2020 10:49 AM
To: Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov>
Subject: Re: (b)(4) Deficiencies
System

Hello Poulomi,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Mar 17, 2020, at 5:48 PM, Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov> wrote:

Hi Cindy,

(b)(4) Deficiencies

Thanks,
Poulomi.

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Tuesday, March 17, 2020 8:46 PM
To: Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov>
Subject: (b)(4) Deficiencies
(b)(4) Deficiencies

Hello Poulomi,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks much Poulomi. We hope that you and your colleagues and loved ones are quite well.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: June 30, 2020
See PRA Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
July 27, 2020	(b)(4)	

SECTION A TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Request for Feedback
☐ Original Submission	☐ Regular (180 day)	☐ Original PDP	☐ Original Submission:	☐ Pre-Submission
☐ Premarket Report	☐ Special	☐ Notice of Completion	☐ Traditional	☐ Informational Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Submision Issue Meeting
☐ Amendment	☐ 30-day Supplement		☐ Abbreviated (Complete section I, Page 5)	☐ Day 100 Meeting
☐ Report	☐ 30-day Notice		☒ Additional Information	☐ Agreement Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Determination Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Study Risk Determination
	☐ Amendment to PMA & HDE Supplement			☐ Other *(specify):*
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☒ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
☐ Amendment	☐ Amendment	☐ Additional Information	☐ Additional Information	☐ Other *(describe submission):*
☐ Supplement	☐ Supplement			
	☐ Report			
	☐ Report Amendment			

Have you used or cited Standards in your submission? ☒ Yes ☐ No *(If Yes, please complete Section I, Page 5)*

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Alydia Health	N/A		
Division Name *(if applicable)*	**Phone Number** *(including area code)*		
	650-275-3772		
Street Address	**FAX Number** *(including area code)*		
3495 Edison Way			
City	**State / Province**	**ZIP/Postal Code**	**Country**
Menlo Park	CA	94025	U.S.
Contact Name			
Colby Holtshouse			
Contact Title	**Contact E-mail Address**		
Interim CEO	colby@alydiahealth.com		

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Domecus Consulting Services LLC			
Division Name *(if applicable)*	**Phone Number** *(including area code)*		
	650-343-4813		
Street Address	**FAX Number** *(including area code)*		
1171 Barroilhet Drive	650-343-7822		
City	**State / Province**	**ZIP Code**	**Country**
Hillsborough	CA	94010	U.S.
Contact Name			
Cindy Domecus, R.A.C.			
Contact Title	**Contact E-mail Address**		
Principal	DomecusConsulting@comcast.net		

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ New Device
- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Process change:
  - ☐ Manufacturing ☐ Packaging
  - ☐ Sterilization
  - ☐ Other *(specify below)*

- ☐ Response to FDA correspondence:

- ☐ Change in design, component, or specification:
  - ☐ Software / Hardware
  - ☐ Color Additive
  - ☐ Material
  - ☐ Specifications
  - ☐ Other *(specify below)*

- ☐ Labeling change:
  - ☐ Indications
  - ☐ Instructions
  - ☐ Performance Characteristics
  - ☐ Shelf Life
  - ☐ Trade Name
  - ☐ Other *(specify below)*

- ☐ Location change:
  - ☐ Manufacturer
  - ☐ Sterilizer
  - ☐ Packager

- ☐ Report Submission:
  - ☐ Annual or Periodic
  - ☐ Post-approval Study
  - ☐ Adverse Reaction
  - ☐ Device Defect
  - ☐ Amendment

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify)*:

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - ☐ Correspondent / Applicant
  - ☐ Design / Device
  - ☐ Informed Consent
  - ☐ Manufacturer
  - ☐ Manufacturing Process
  - ☐ Protocol - Feasibility
  - ☐ Protocol - Other
  - ☐ Sponsor

- ☐ Report submission:
  - ☐ Current Investigator
  - ☐ Annual Progress Report
  - ☐ Site Waiver Report
  - ☐ Final

- ☐ Response to FDA Letter Concerning:
  - ☐ Conditional Approval
  - ☐ Deemed Approved
  - ☐ Deficient Final Report
  - ☐ Deficient Progress Report
  - ☐ Deficient Investigator Report
  - ☐ Disapproval
  - ☐ Request Extension of Time to Respond to FDA
  - ☐ Request Meeting
  - ☐ Request Hearing

- ☐ Other Reason *(specify)*:

SECTION D3 REASON FOR SUBMISSION - 510(k)

- ☒ New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☐ Other Reason *(specify)*:

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	OQY	2		3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☐ 510 (k) summary attached

☐ 510 (k) statement

Information on devices to which substantial equivalence is claimed *(if known)*

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K170622	1	Bakri® Postpartum Balloon	1	Cook Inc.
2		2		2	
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Vacuum-induced Hemorrhage Control

	Trade or Proprietary or Model Name for This Device		Model Number
1	Jada® System	1	
2		2	
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions *(regardless of outcome)*

1 (b)(4)		4	5	6	
7	8	9	10	11	12

Data Included in Submission

☒ Laboratory Testing ☒ Animal Trials ☒ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
OQY	884.4530	☐ Class I ☒ Class II
Classification Panel		☐ Class III ☐ Unclassified
Obstetrics/Gynecology		

Indications *(from labeling)*

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

Note: Submission of the information entered in Section H does not affect the need to submit device establishment registration.	FDA Document Number *(if known)*

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

(b)(4)

(b)(4)

☐ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Manufacturer ☐ Contract Sterilizer ☐ Repackager / Relabeler		
Company / Institution Name		Establishment Registration Number		
Division Name *(if applicable)*		Phone Number *(including area code)*		
Street Address		FAX Number *(including area code)*		
City		State / Province	ZIP Code	Country
Contact Name	Contact Title	Contact E-mail Address		

SECTION I — UTILIZATION OF STANDARDS

Note: Complete this section if your application or submission cites standards or includes a *"Declaration of Conformity to a Recognized Standard"* statement.

	Standards No.	Standards Organization	Standards Title	Version	Date
1	11137-2	ISO	Sterilization of Health Care Products -- Radiation -- Part 2: Establishing the Sterilization Dose	Third Edition 2013-06-01	04/04/2016
2	10993-1	ISO	Biological Evaluation Of Medical Devices - Part 1: Evaluation And Testing Within A Risk Management Process	Fifth Edition, 2018-08	01/14/2019
3	11607-1	ANSI/AAMI/ ISO	Packaging For Terminally Sterilized Medical Devices – Part 1: Requirements For Materials, Sterile Barrier Systems And Packaging [Including Amendment 1 (2014)]	2006/R2010	01/27/2015
4	F-1980	ASTM	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices	2016	12/23/2016
5	D4169	ASTM	Standard Practice for Performance Testing of Shipping Containers and Systems	2016	12/23/2016
6	14971	ISO	Medical Devices—Application of Risk Management to Medical Devices	Third Edition 2019-12	12/23/2019
7	111607-2	ISO	Packaging For Terminally Sterilized Medical Devices – Part 2: Validation Requirements For Forming, Sealing And Assembly Processes [Including Amendment 1 (2014)]	First Edition 2006-04-15	01/27/2015

Please include any additional standards to be cited on a separate page.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF ADDRESS BELOW.

The burden time for this collection of information is estimated to average 0.5 hour per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
1350 Piccard Drive, Room 400
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

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(b)(4) Protocol

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Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

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Exhibit D: Redlined copy of revised Jada System Instructions for Use

(b)(4) Draft Manual

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SECTION 20: PERFORMANCE DATA - NONCLINICAL

There is no device-specific guidance document, special controls document or requirements in a device-specific classification regulation regarding performance data that is applicable to the subject device.

A. Summary of Bench Testing Performed

(b)(4)

Table 20-2 provides a summary of the additional bench testing conducted in support of 510(k) clearance. Full test protocols and reports and associated test methods (TMs) for this suite of tests are provided in **Exhibits 20.A-20.N** and include the following: 1) Test performed, 2) Objective of the test, 3) Description of test methods, 4) Pass/Fail Criteria, 5) Data Analysis Plan, and 6) Test Results.

Tables 20-1 and 20-2 contain component names that are consistent throughout this submission. Different names for some of these components have been used in the past for testing and for engineering descriptions. Following is a list of the current component names and potential synonyms used in the actual test reports and engineering descriptions.

Tube: bilumen tube, main body
Cervical Seal: balloon, occlusion balloon, vacuum seal, seal
Vacuum Connector: vacuum port, connection tube
Intrauterine Loop: distal loop
Loop Tube: drain tube
Vacuum Pore: drainage hole
Seal Valve: inflation tube, inflation port

Table 20-1. Summary of Bench Testing Submitted in (b)(4)

Test	Test Method	Result	Doc Reference
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Discussion and Conclusions

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Summary of Animal Testing Performed

(b)(4) Testing

B. Explanation of How Nonclinical Data Support Finding of Substantial Equivalence

The nonclinical performance data summarized above and in the corresponding exhibits support a demonstration that the Jada System is safe and effective for its intended use and does not raise different questions of safety or effectiveness as compared to the predicate device.

D. Literature

There is no literature cited in this 510(k) that pertains to substantial equivalence. Any literature cited is for background purposes only.

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Alydia HEALTH

July 27, 2020

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: K201199/S001; Response to July 2, 2020 Hold Letter
Jada® System

Attn: Poulomi Nandy, Ph.D.
Microbiologist, Obstetrical and Reproductive Health Devices Team
DHT3B: Division of Reproductive and Urology Devices
OHT3: Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors

Dear Dr. Nandy and 510(k) Review Team,

This supplement to the above referenced 510(k) is being submitted to respond to FDA's requests for additional information identified in its Hold Letter of July 2, 2020. We believe that the responses provided herein adequately address all of FDA's requests and we look forward to addressing any further questions FDA may have upon its review of our responses.

A hard copy of the signed cover letter and one eCopy of the entire 510(k) supplement are provided herein. The eCopy was prepared in accordance with FDA's December 16, 2019 guidance titled "eCopy Program for Medical Device Submissions, Guidance for Industry and Food and Drug Administration Staff."

Alydia Health considers the information described in this 510(k) supplement and all related exhibits to be confidential commercial information and therefore exempt from public disclosure. We request that this notification and its contents be treated as confidential in accordance with 21 CFR § 807.95.

Please direct any questions or requests for additional information to me at the below numbers or by electronic mail at: DomecusConsulting@comcast.net. We thank the FDA review team for its continued review of our application.

Sincerely,

(b)(6)

Cindy Domecus, R.A.C. (US & EU)
Principal, Domecus Consulting Services LLC
Regulatory Consultant to Alydia Health
Office: 650-343-4813 I Mobile: (b)(6) I Fax: 650-343-7822

Enclosure: One paper copy of signed cover letter and one eCopy of entire 510(k) supplement

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SECTION 16: SHELF LIFE

The proposed shelf-life for the Jada System is 4 years. Below is a summary of the methods used to establish that the device packaging will maintain a sterile barrier for the entirety of the proposed shelf-life and that device performance is maintained for the entirety of the proposed shelf-life, based on FDA's April 1991 guidance, "Shelf Life of Medical Devices".

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Clinical Evaluation Report: InPress Postpartum Hemorrhage Vacuum Device

Prepared for:
InPress Technologies, Inc.
955 Morro Street
San Luis Obispo, CA 93401 USA

Prepared by:

(b)(4)

November 19, 2015

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From: Colden, Kelly
To: Avery, Reginald
Subject: RE: Request for information for Jada System (K201199/S001)
Date: Tuesday, August 25, 2020 12:14:34 PM
Attachments: image001.png
image003.png

Reggie,

(b)(5)

Thanks,

Kelly

Kelly Colden MD, MPH
Medical Officer
Obstetrical and Reproductive Health Devices Team
Division of Reproductive, Gynecology, and Urology Devices (DHT3B)
FDA/CDRH/OPEQ/OHT3

WO 66, 2660B
Silver Spring, MD 20993
Phone: 240-402-5341
kelly.colden@fda.hhs.gov

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Sent: Monday, August 24, 2020 5:45 AM
To: Colden, Kelly <Kelly.Colden@fda.hhs.gov>
Subject: FW: Request for information for Jada System (K201199/S001)

(b)(5)

Thanks,
Reggie

Reginald Avery, Ph.D.
Biomedical Engineer
Obstetrical and Reproductive Health Devices Team
Division of Reproductive, Gynecology and Urology Devices (DHT3B)

OHT3 | OPEQ | CDRH | FDA
White Oak, Bldg. 66, Rm. 2647
Tel: 240-402-6152
Reginald.Avery@fda.hhs.gov

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <domecusconsulting@comcast.net>
Sent: Saturday, August 22, 2020 10:07 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: Request for information for Jada System (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Thank you for your continued reivew of our file.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? **If possible, please provide a response by noon on Tuesday,**

August 25, 2020.

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

SECTION 8: CLASS III CERTIFICATION

The subject device is a Class II device per 21 CFR 884.4530, so this element of FDA's 510(k) Acceptance Checklist is not applicable.

Hello,

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received:
https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <domecusconsulting@comcast.net>
Sent: Thursday, August 27, 2020 6:36 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343 4813 (office)
(b)(6) (cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
DHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 10:41 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) cell)

On Aug 27, 2020, at 4:47 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

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Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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CLINICAL STUDY REPORT

APPENDIX 9.5

List of Study Monitors

Name	Affiliation
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Exhibit A: Clean copy of revised Jada System Instructions for Use

(b)(4) Draft Manual

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CLINICAL STUDY REPORT

APPENDIX 9.3

List of Investigators and Affiliated Sites

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(b)(4) Testing

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SECTION 21: PERFORMANCE DATA – CLINICAL

There is no device-specific guidance document, special controls document or requirements in a device-specific classification regulation regarding performance data that is applicable to the subject device.

This submission is supported by the following clinical performance data:

1. Pilot study in Indonesia
2. Cases enrolled under earlier version of pivotal study protocol in Uganda
3. PEARLE IDE Pivotal Study in the U.S.

The clinical performance data from each of these studies is summarized below. The clinical study reports for the pilot and pivotal studies are provided in **Exhibit 21.A and 21.B,** respectively.

A. Pilot Study: Indonesia

A First-in-Human (FIH) feasibility investigational study with Ethics Committee oversight was conducted at two clinical sites in Indonesia. The purpose of the study was to demonstrate the placement, function, and operation of the Jada System to meet its intended use.

Ten women were enrolled between July 2014 and February 2015. None of the subjects presented with a retained placenta, uterine lacerations, uterine scarring, or for any conditions other than atonic postpartum hemorrhage. The Jada System was successfully placed and activated in all ten subjects. A vacuum force of 70 mmHg - 90 mmHg was used for treatment. The average time from placement of the Jada to removal was 152.0 ± 111.7 minutes (range 60-390 minutes).

Bleeding was controlled within two minutes for all ten subjects. Evaluation of the primary clinical data safety endpoints determined that: 1) no safety issues were observed relative to the placement, insertion, or removal of the Jada, 2) there were no complications related to delayed arrest of blood loss, 3) there was no damage to the uterus, cervix, or vagina, and 4) no uterine inversion or folding events were observed during the Jada procedure.

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(b)(4) . Alydia Health also revised the Site Selection and Analysis Cohorts sections of the v2.5 protocol to reflect inclusion of U.S. sites only and its monitoring procedures to include a requirement that the site have readily available access to blood product supply (G150265/S015).

Provided below is a summary of the data collected from this site in Uganda under Protocol Revision 2.4.

- Thirteen (13) subjects were enrolled at the clinical trial site at St. Francis Hospital Nsambya, in Kampala, Uganda.
- 24 devices were shipped to the site in Uganda, 11 of which were returned at site close out.
- The site address and IRB information are as follows:

St. Francis Hospital Nsambya Nsambya Road Kampala, Uganda	IRB Chairperson: Professor Ignatius Kakande St. Francis Hospital Nsambya Research Ethics Committee St. Francis Hospital Nsambya PO Box 7146, Nsambya Road Kampala, Uganda Date of IRB approval: 08 September 2017 Date of IRB closure: 28 August 2018	PIs: Dr. Othiniel Musana & Dr. Daniel Zaake

- Jada was effective at treating the PPH in all 13 subjects, even in the three cases in which the subjects were enrolled with estimated blood loss (EBL) at study entry higher than allowed per study inclusion criterion; hemorrhage was controlled in each subject but two subjects subsequently died due to lack of blood product supply for transfusion to treat their severe blood loss.
- A summary of the adverse events reported at this site are provided in **Table 21-1**.

(b)(4) Clinical Studies

C. PEARLE IDE Pivotal Study: United States

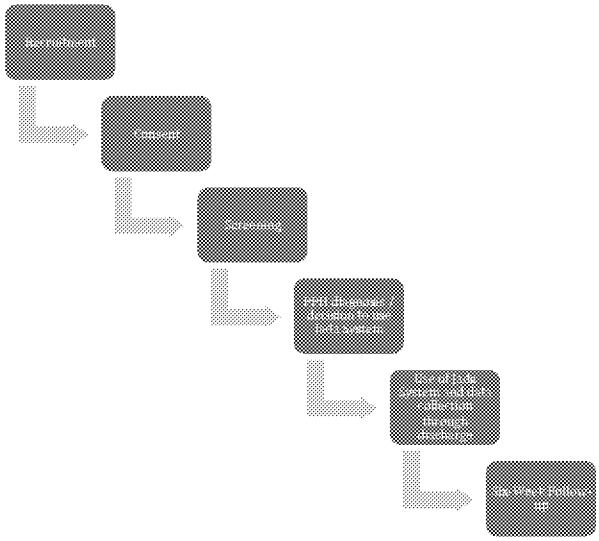
A synopsis of the study design is provided in **Table 21-3** and a summary of the results follows the study synopsis. The full clinical study report is provided in **Exhibit 21.B** and includes the study objective, study design, study endpoints, pre-defined pass/fail criteria, results, and conclusions.

Study Design Summary

Table 21-3. PEARLE IDE Pivotal Study Synopsis

Title:	Prospective, Single Arm, Pivotal Clinical Trial Designed to Assess the Safety and Effectiveness of the Jada System In Treating Primary Postpartum Hemorrhage ("PPH")
Short Title:	PEARLE Study
Design:	Prospective, single-arm, literature-controlled, multi-center study
Purpose:	Evaluate the safety and effectiveness of the Jada System in the control and reduction of primary postpartum hemorrhage.
Inclusion Criteria:	1. Adult Female, 18 years of age or older at time of consent. 2. Able to understand and provide informed consent to participate in the study. 3. Diagnosis of PPH with suspected atony within 24 hours after vaginal or c-section delivery. 4. EBL, to be determined when investigator is ready to have the Jada peel pack opened: Vaginal delivery: 500 – 1500 mL EBL or C-section delivery: 1000 – 1500 mL EBL 5. Failed first-line intervention of uterotonics and uterine massage/bimanual uterine massage to stop bleeding. *Note: Uterotonic administration may continue concomitant with and post Jada use, as long as such use does not exceed the maximum dose of the drug.*
Exclusion Criteria:	1. EBL >1500 mL, to be determined when investigator is ready to have the Jada peel pack opened. 2. Delivery at a gestational age < 34 weeks. 3. For C-sections: Cervix < 3 cm dilated before use of Jada. 4. PPH that the investigator determines to require more aggressive treatment, including any of the following: a) hysterectomy; b) b-lynch suture; c) uterine artery embolization or ligation; d) hypogastric ligation. 5. Known uterine anomaly. 6. Ongoing intrauterine pregnancy. 7. Placenta abnormality including any of the following: a) known placenta accreta;

	b) retained placenta with known risk factors for placenta accreta (e.g. history of prior uterine surgery, including prior c-section and placenta previa); c) retained placenta without easy manual removal. 8. Known uterine rupture. 9. Unresolved uterine inversion. 10. Subject has undergone intrauterine balloon therapy or uterine packing for tamponade treatment of this PPH prior to use of the Jada System. 11. Current cervical cancer. 12. Current purulent infection of vagina, cervix, uterus. 13. Diagnosis of coagulopathy.
Duration of Study:	It is expected to take approximately 12-18 months to enroll, treat, and follow-up all 107 subjects.
Primary Safety Endpoint:	Incidence, severity and seriousness of device-related Adverse Events (AEs).
Primary Effectiveness Endpoint:	Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use. Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy. Note: Continuation of the administration of uterotonics concomitant with and post Jada System use is standard of care and does not constitute failure of the primary effectiveness endpoint.
Statistical Analysis Plan Summary:	The primary effectiveness objective of this Pivotal Study is to show that the observed Treatment Success Rate is not worse than the rate reported in the literature. The study is considered a success when the lower bound of the two-sided Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success is greater than or equal to 73.4%.

Study Flowchart:	

Study Results Summary

The primary endpoint was overwhelmingly met, with 96.2% (with a lower bound 95% confidence limit of 90.4%), and 99% of subjects in the mITT and PP Cohorts ($p<0.001$), respectively, achieving the pre-defined criterion for success, non-inferiority to the 82.0% treatment success rate of the Bakri Balloon in the meta-analysis. The lower bound 95% confidence limit in the mITT is 90.4%, and in the PP was 94.4%, non-overlapping with the confidence intervals measured on the Bakri Balloon success rate (95% CI: 73.4% to 89.2%).

The secondary effectiveness endpoints were also overwhelmingly positive. Bleeding was controlled in 3 minutes (median) in both the mITT and PP populations. The rate at which no further surgical intervention was required and no further non-surgical intervention was required after Jada was very high. The rate of blood transfusion (36.5% in the mITT Cohort and 34% in the PP Cohort) and rate with 4 or more units PRBCs (4.8% in the mITT Cohort and 4.1% in the PP Cohort) was expected in this patient population with postpartum hemorrhage treated at U.S. hospitals with ready access to these resources.

(b)(4)

(b)(4) Clinical Studies

Explanation of How the Clinical Data Support Finding of Substantial Equivalence

The clinical performance data support the safety and effectiveness of the Jada System and confirm that the technological differences between the subject and predicate device do not raise different questions of safety and effectiveness. Therefore, the clinical performance data support a finding of substantial equivalence.

Literature

The clinical report includes references for information purposes, but the references are not related to the demonstration of substantial equivalence.

SECTION 11: VOLUNTARY CONSENSUS STANDARDS

This submission utilizes FDA-recognized voluntary consensus standards. Each is addressed below.

A. FDA-Recognized Consensus Standards

In consultation with FDA Guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices" issued September 14, 2018, Alydia Health declares conformance with the following consensus standards for the Jada System, JADA-1001 (Product Code OQY, 21 CFR § 884.4530):

Standard Designation Number and Date	Standard Developing Organization	Title of Standard	FDA Recognition Number
11137-2 Third Edition 2013-06-01	ISO	Sterilization of Health Care Products -- Radiation -- Part 2: Establishing the Sterilization Dose	14-409
10993-1 Fifth Edition, 2018-08	ISO	Biological Evaluation Of Medical Devices - Part 1: Evaluation And Testing Within A Risk Management Process	2-258 (Partial recognition)
11607-1:2006/ R2010	ANSI/AAMI/ ISO	Packaging For Terminally Sterilized Medical Devices – Part 1: Requirements For Materials, Sterile Barrier Systems And Packaging [Including Amendment 1 (2014)]	14-454
11607-2 First Edition 2006-04-15	ISO	Packaging For Terminally Sterilized Medical Devices – Part 2: Validation Requirements For Forming, Sealing And Assembly Processes [Including Amendment 1 (2014)]	14-455
F-1980-16	ASTM	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices	14-497
D4169-16	ASTM	Standard Practice for Performance Testing of Shipping Containers and Systems	14-499
14971 Third Edition 2019-12	ISO	Medical Devices—Application of Risk Management to Medical Devices	5-125

I hereby attest that, as required by the risk analysis, all verification activities were performed by the designated individuals and the results of those activities demonstrated that the predetermined acceptance criteria were met. Additionally, the Alydia Health, Inc. contract manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.

(b)(6)

May 1, 2020

Andy Uchida
Date

Vice President of R&D and Manufacturing
3495 Edison Way
Menlo Park, CA 94025

B. Non-FDA-Recognized Consensus Standards

This section of the Acceptance Checklist is not applicable, as no non-FDA-recognized consensus standards were utilized.

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The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 183, OCTOBER 2017 *(Replaces Practice Bulletin Number 76, October 2006)*

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics in collaboration with Laurence E. Shields, MD; Dena Goffman, MD; and Aaron B. Caughey, MD, PhD.

Postpartum Hemorrhage

Maternal hemorrhage, *defined as a cumulative blood loss of greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process, remains the leading cause of maternal mortality worldwide (1). Additional important secondary sequelae from hemorrhage exist and include adult respiratory distress syndrome, shock, disseminated intravascular coagulation, acute renal failure, loss of fertility, and pituitary necrosis (Sheehan syndrome).*

Hemorrhage that leads to blood transfusion is the leading cause of severe maternal morbidity in the United States closely followed by disseminated intravascular coagulation (2). In the United States, the rate of postpartum hemorrhage increased 26% between 1994 and 2006 primarily because of increased rates of atony (3). In contrast, maternal mortality from postpartum obstetric hemorrhage has decreased since the late 1980s and accounted for slightly more than 10% of maternal mortalities (approximately 1.7 deaths per 100,000 live births) in 2009 (2, 4). This observed decrease in mortality is associated with increasing rates of transfusion and peripartum hysterectomy (2–4).

The purpose of this Practice Bulletin is to discuss the risk factors for postpartum hemorrhage as well as its evaluation, prevention, and management. In addition, this document will encourage obstetrician–gynecologists and other obstetric care providers to play key roles in implementing standardized bundles of care (eg, policies, guidelines, and algorithms) for the management of postpartum hemorrhage.

Background

The American College of Obstetricians and Gynecologists' (ACOG) reVITALize program defines *postpartum hemorrhage* as cumulative blood loss greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process (includes intrapartum loss) regardless of route of delivery (5). This is in contrast to the more traditional definitions of postpartum hemorrhage as an estimated blood loss in excess of 500 mL after a vaginal birth or a loss of greater than 1,000 mL after a cesarean birth (6). This new classification is likely to reduce the number of individuals labeled with postpartum hemorrhage. However, despite this new characterization, a blood loss greater than 500 mL in a vaginal delivery should be considered abnormal and should serve as an indication for the health care provider to investigate the increased blood deficit. Although visually estimated blood loss is considered inaccurate, use of an educational process, with limited instruction on estimating blood loss, has been shown to improve the accuracy of such estimates (7). Historically, a decrease in hematocrit of 10% had been proposed as an alternative marker to define postpartum hemorrhage; however, determinations of hemoglobin or hematocrit concentrations are often delayed, may not reflect current hematologic status, and are not clinically useful in the setting of acute postpartum hemorrhage (8).

In postpartum women, it is important to recognize that the signs or symptoms of considerable blood loss (eg, tachycardia and hypotension) often do not present or do not present until blood loss is substantial (9). Therefore, in a patient with tachycardia and hypotension, the obstetrician–gynecologist or other obstetric care provider should be concerned that considerable blood loss, usually

representing 25% of the woman's total blood volume (or approximately 1,500 mL or more), has occurred (10). Thus, earlier recognition of postpartum hemorrhage (eg, before deterioration in vital signs) should be the goal in order to improve outcomes.

Differential Diagnosis

The initial management of any patient with obstetric hemorrhage requires that the obstetrician–gynecologist or other obstetric care provider first identify the source of bleeding (uterine, cervical, vaginal, periurethral, periclitoral, perineal, perianal, or rectal). This can be quickly done with a careful physical examination. After the anatomic site is identified, it is important to identify the cause because treatment may vary. The most common etiologies (see Box 1) are broken into primary or secondary causes. Primary postpartum hemorrhage occurs within the first 24 hours of birth, whereas *secondary postpartum hemorrhage* is defined as excessive bleeding that occurs more than 24 hours after delivery and up to 12 weeks postpartum (11, 12).

When evaluating a patient who is bleeding, it may be helpful to consider "the 4 Ts" mnemonic device—tone, trauma, tissue, and thrombin (13). Abnormal uterine tone (uterine atony) is estimated to cause 70–80% of postpartum hemorrhage and usually should be suspected first as the etiology of postpartum hemorrhage (14). Recommended interventions for uterine atony include uterine massage, bimanual compression, and uterotonic drugs (15). Maternal trauma is indicated by lacerations, expanding hematomas, or uterine rupture. Retention of placental tissue can be readily diagnosed with manual examination or bedside ultrasonography of the uterine cavity and is addressed with manual removal or uterine curettage. Thrombin is a reminder to evaluate the patient's coagulation status and if abnormal to correct with replacement of clotting factors, fibrinogen, or other factor replacement sources (see sections on Transfusion Therapy and Massive Transfusion). It is important to identify the most likely diagnosis or diagnoses to initiate appropriate interventions. These diagnoses are outlined individually in the Clinical Considerations and Recommendations section.

Box 1. Etiology of Postpartum Hemorrhage

Primary:

- Uterine atony
- Lacerations
- Retained placenta
- Abnormally adherent placenta (accreta)
- Defects of coagulation (eg, disseminated intravascular coagulation)*
- Uterine inversion

Secondary:

- Subinvolution of the placental site
- Retained products of conception
- Infection
- Inherited coagulation defects (eg, factor deficiency such as von Willebrand)

*These include inherited coagulation defects as well as acute coagulopathies that may develop from events such as amniotic fluid embolism, placental abruption, or severe preeclampsia.

Risk Factors

Because obstetric hemorrhage is unpredictable, relatively common, and leads to severe morbidity and mortality, all obstetric unit members, including the physicians, midwives, and nurses who provide obstetric care, should be prepared to manage women who experience it. A number of well-established risk factors such as prolonged labor or chorioamnionitis are associated with postpartum hemorrhage (Table 1). However, many women without these risk factors can experience a postpartum hemorrhage (16). State and national organizations have suggested that a maternal risk assessment should be conducted antenatally and at the time of admission and continuously modified as other risk factors develop during labor or the postpartum period (17).

Risk assessment tools are readily available (18, 19) and have been shown to identify 60–85% of patients who will experience a significant obstetric hemorrhage (17, 20, 21). An example of this type of assessment tool is outlined in Table 2. However, a validation study of this tool among a retrospective cohort of more than 10,000 women showed that although the tool correctly identified more than 80% of patients with severe postpartum hemorrhage, more than 40% of women who did not experience hemorrhage were placed into the high-risk group giving the tool a specificity of just below 60% (20). Additionally, approximately 1% of women in the low-risk group experienced a severe postpartum hemorrhage, which indicates that the clinical value for identifying patients through risk assessment is low. These findings reinforce the need for diligent surveillance in all patients, including those initially thought to be at low risk.

Prevention

Many organizations have recommended active management of the third stage of labor as a method to reduce

the incidence of postpartum hemorrhage (22–24). The three components of active management are as follows: 1) oxytocin administration, 2) uterine massage, and 3) umbilical cord traction (25). Prophylactic oxytocin, by dilute intravenous infusion (bolus dose of 10 units), or intramuscular injection (10 units), remains the most effective medication with the fewest adverse effects (26). Oxytocin plus methylergonovine or oxytocin in combination with misoprostol appears to be no more effective than oxytocin used alone for prophylaxis (26, 27). The timing of oxytocin administration—after delayed umbilical cord clamping, with delivery of the anterior shoulder,

Table 1. Antenatal and Intrapartum Risk Factors for Postpartum Hemorrhage

Etiology	Primary Problem	Risk Factors, Signs
Abnormalities of uterine contraction—atony	Atonic uterus	Prolonged use of oxytocin High parity Chorioamnionitis General anesthesia
	Over-distended uterus	Twins or multiple gestation Polyhydramnios Macrosomia
	Fibroid uterus	Multiple uterine fibroids
	Uterine inversion	Excessive umbilical cord traction Short umbilical cord Fundal implantation of the placenta
Genital tract trauma	Episiotomy Cervical, vaginal, and perineal lacerations Uterine rupture	Operative vaginal delivery Precipitous delivery
Retained placental tissue	Retained placenta Placenta accreta	Succenturiate placenta Previous uterine surgery Incomplete placenta at delivery
Abnormalities of coagulation	Preeclampsia Inherited clotting factor deficiency (von Willebrand, hemophilia) Severe infection Amniotic fluid embolism Excessive crystalloid replacement Therapeutic anticoagulation	Abnormal bruising Petechia Fetal death Placental abruption Fever, sepsis Hemorrhage Current thromboembolism treatment

Modified from New South Wales Ministry of Health. Maternity—prevention, early recognition and management of postpartum haemorrhage (PPH). Policy Directive. North Sydney: NSW Ministry of Health; 2010. Available at: http://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2010_064.pdf. Retrieved July 24, 2017. Copyright 2017.

Table 2. Example of Risk Assessment Tool

Low Risk	Medium Risk	High Risk
Singleton pregnancy	Prior cesarean or uterine surgery	Previa, accreta, increta, percreta
Less than four previous deliveries	More than four previous deliveries	HCT <30
Unscarred uterus	Multiple gestation	Bleeding at admission
Absence of postpartum hemorrhage history	Large uterine fibroids	Known coagulation defect
	Chorioamnionitis	History of postpartum hemorrhage
	Magnesium sulfate use	Abnormal vital signs (tachycardia and hypotension)
	Prolonged use of oxytocin	

Abbreviation: HCT, hematocrit.

Modified from Lyndon A, Lagrew D, Shields L, Main E, Cape V, editors. Improving health care response to obstetric hemorrhage version 2.0. A California quality improvement toolkit. Stanford (CA): California Maternal Quality Care Collaborative; Sacramento (CA): California Department of Public Health; 2015.

or with placental delivery—has not been adequately studied or found to be associated with a difference in the risk of hemorrhage (28). Specifically, delaying oxytocin until after delayed umbilical cord clamping has not been found to increase the risk of hemorrhage (29). The World Health Organization, ACOG, American Academy of Family Physicians, and Association of Women's Health, Obstetric and Neonatal Nurses recommend administering uterotonics (usually oxytocin) after all births for the prevention of postpartum hemorrhage (13, 22, 24). Therefore, all obstetric care facilities should have guidelines for the routine administration of uterotonics in the immediate postpartum period.

Although the number of well-conducted studies is limited, one small study found that the use of uterine massage was associated with reduced postpartum blood loss and reduced need for additional uterotonic agents (30); however, a Cochrane review found no statistical differences and found the evidence inconclusive (31). Furthermore, neither early umbilical cord clamping nor umbilical cord traction have been shown to have a significant effect on the incidence or volume of postpartum hemorrhage (32). Additionally, in a Cochrane review, two trials examining nipple stimulation or breastfeeding did not demonstrate a difference in postpartum hemorrhage (33, 34).

Techniques for Management

Management may vary greatly among patients and depends on the etiology and available treatment options. In general, management of postpartum hemorrhage should use a multidisciplinary and multifaceted approach that involves maintaining hemodynamic stability while simultaneously identifying and treating the cause of blood loss. Treatment options for postpartum hemorrhage because of uterine atony include administration of uterotonics or pharmacologic agents, tamponade of the uterus (eg, intrauterine balloons), surgical techniques to control the bleeding (eg, the B-Lynch procedure), embolization of pelvic arteries or, ultimately, hysterectomy. Generally, less invasive methods should be tried initially if possible; however, if unsuccessful, more invasive measures may be required. More specific guidance for these management approaches is delineated later in the document.

Systematic approaches to postpartum hemorrhage based on algorithms have been created, and these approaches have been used more widely at individual hospitals and in health systems (19, 35, 36). These approaches employ a multidisciplinary (eg, obstetrics, nursing, anesthesia, transfusion medicine), multifaceted, stepwise approach to the detection and management of postpartum hemorrhage. The approaches are aimed at treating cases early and consistently to reduce severe maternal morbidity and mortality as well as to identify the need for more aggressive interventions (such as hysterectomy or other surgeries) and intensive care unit admissions. Although it does appear that hemorrhage is treated earlier with such approaches, evidence regarding maternal outcomes, such as severe maternal morbidity or intensive care unit admission, is inconsistent (12).

Facilities With Limited Resources

Many hospitals that provide maternal services are located in rural or small communities. In the United States, obstetric services are provided in 50% of critical access hospitals and 92% of rural hospitals (37). Because these centers typically do not have the same resources as most urban centers, developing a comprehensive plan for dealing with obstetric emergencies such as postpartum hemorrhage is important. In particular, these small centers should consider establishing guidelines regarding appropriate case selection to triage or transfer patients to higher-level centers. Additionally, assessing available resources and developing a comprehensive plan for evaluating and managing obstetric hemorrhage are important for reducing morbidity. For more information see Obstetric Care Consensus No. 2, *Levels of Maternal Care* (38).

Clinical Considerations and Recommendations

▶ ***What should be considered in the initial evaluation and management of a patient with excessive bleeding in the immediate postpartum period?***

When postpartum bleeding exceeds expected volumes (500 mL in a vaginal delivery or 1,000 mL in a cesarean delivery), a careful and thorough evaluation should be undertaken. A rapid physical examination of the uterus, cervix, vagina, vulva, and perineum can often identify the etiology (sometimes multiple sources) of the postpartum hemorrhage. Obstetrician–gynecologists and other obstetric care providers should be familiar with algorithms for the diagnosis and management of postpartum hemorrhage (18, 39) and, ideally, these should be posted on labor and delivery units (see For More Information). The most common etiologies include uterine atony, genital tract lacerations, retained placental tissue and, less commonly, placental abruption, coagulopathy (acquired or inherited), amniotic fluid embolism, placenta accreta, or uterine inversion.

Uterine Atony

Because uterine atony causes 70–80% of cases of postpartum hemorrhage, it remains the single most common cause, and its incidence appears to be increasing (14, 21, 40). At the time of delivery, risk factors include, but are not limited to, prolonged labor, induction of labor, prolonged use of oxytocin, chorioamnionitis, multiple gestation, polyhydramnios, and uterine leiomyomas (see Table 1 and Table 2).

In the setting of postpartum hemorrhage, identification of a soft, poorly contracted (boggy) uterus suggests atony as a causative factor. When atony is suspected, the bladder should be emptied and a bimanual pelvic examination conducted, any intrauterine clots should be removed, and uterine massage should be performed. In addition to oxytocin, a second uterotonic agent is required in 3–25% of cases of postpartum hemorrhage (15). Supplemental uterotonics that are most commonly administered include methylergonovine, 15-methyl prostaglandin $F_{2\alpha}$, or misoprostol. As discussed in a 2015 systematic review, there is a lack of evidence that suggests which specific additional uterotonics are the most effective (12). Treatment of refractory atony may require the use of secondary methods such as uterine tamponade with an intrauterine tamponade balloon or compression sutures (41, 42).

Occasionally, the fundus is firm and contracted down, but the lower uterine segment is dilated and atonic. In this setting, the usual approach is to manually remove any clots and to use bimanual compression to reduce the blood loss while waiting for the uterotonic agents to work. Treatment with the intrauterine tamponade balloon can be considered if there is persistent lower uterine segment atony.

Obstetric Trauma

Genital tract lacerations are the most common complications of obstetric trauma. Although such lacerations are predominantly venous bleeding, they can be the primary source of a postpartum hemorrhage. Rapid identification and repair of cervical lacerations, lacerations complicated by arterial bleeding, and high vaginal lacerations should be performed. Similarly, distal vaginal, vulvar, periclitoral, and perineal lacerations should be repaired if contributing significantly to blood loss. If a uterine artery laceration is suspected, interventional radiology or surgical exploration and ligation should be considered. Repair may require assistance from anesthesia and transfer to a well-equipped operating room.

Genital tract hematomas (labial, vaginal, broad ligament, or retroperitoneal) also can lead to significant blood loss and should be suspected in the setting of a precipitous uncontrolled delivery or an operative vaginal delivery. Labial, rectal, pelvic pressure or pain, or vital sign deterioration may be the only symptoms of genital tract hematomas and may not be recognized until hours after delivery. Once identified, most genital tract hematomas can be managed conservatively. However, rapid progressive enlargement of the hematoma, particularly in the setting of abnormal vital signs, indicates a need for incision and drainage. One reason that opening a hematoma is reserved for only the most severe cases is that often a single bleeding source is not identified when a hematoma is incised. Exploration with suturing or packing may be needed to achieve hemostasis. Arterial embolization is another option for management of a hematoma and should be considered as a possibility before opening the hematoma.

Deterioration of maternal vital signs without obvious bleeding should alert the obstetric team that there may be intraperitoneal or retroperitoneal bleeding. In this setting, resuscitative measures, diagnostic imaging, and surgical intervention or an interventional radiology procedure should not be delayed.

Retained Placenta

Detailed visual inspection of the placenta for completeness should be conducted after all deliveries. Even when the placenta appears intact, there may be additional remaining products of conception (eg, succenturiate lobe) within the uterine cavity. Manual removal of the placenta, prior uterine surgery, or other risk factors for morbidly adherent placenta should raise suspicion for retained placental tissue or placenta accreta. Ultrasonography or intrauterine manual examination is usually used to diagnose retained placental tissue. Retained placental tissue is unlikely when ultrasonography reveals a normal endometrial stripe. However, although ultrasonographic images of retained placental tissue can be inconsistent, detection of an echogenic mass within the uterus is highly suspicious. When a retained placenta is identified, the first step is to attempt manual removal of the tissue. If a woman has adequate regional analgesia, assessment of the uterine cavity may be performed. If manual extraction fails, either a "banjo" curette or large oval forceps (Sopher or Bierer) can be used for removal. Because of the concern for uterine perforation in the postpartum uterus and to ensure removal of all tissue, ultrasound guidance may be used. If the placental tissue is adherent to the uterine wall, there should be increased suspicion for placenta accreta, particularly in the presence of risk factors for placenta accreta. Management of placenta accreta is discussed later in the document.

Acute Coagulopathy

An acute coagulopathy can complicate postpartum hemorrhage and, in such a setting, two specific etiologies beyond massive blood loss alone should be considered: 1) placental abruption and 2) amniotic fluid embolism. Placental abruption often is associated with uterine atony secondary to extravasation of blood into the myometrium (Couvelaire uterus), and disseminated intravascular coagulation and hypofibrinogenemia are known complications. Placental abruption usually presents as a combination of vaginal bleeding, frequent uterine contractions (tachysystole), and pain (43). The classic contraction pattern includes high-frequency, low-amplitude contractions. Placental abruption is responsible for 17% of cases that require massive transfusion (44).

Amniotic fluid embolism is a rare, unpredictable, unpreventable, and devastating obstetric emergency signaled by a triad of hemodynamic and respiratory compromise in addition to strictly defined disseminated intravascular coagulation (45). Given the profound coagulopathy, postpartum hemorrhage is almost always seen with amniotic fluid embolism. Coagulopathy and the resultant hemorrhage should be managed with aggressive volume replacement and initiation of a massive transfusion protocol (discussed later in this document).

▶ *What are the medical and surgical approaches for the management of postpartum hemorrhage?*

When treating postpartum hemorrhage, it is necessary to balance the use of less invasive management techniques with the need to control the bleeding and achieve hemostasis. Treatment is based upon the etiology for the postpartum hemorrhage. Although hemorrhage etiologies such as lacerations and accreta have specific treatment approaches, the evidence evaluating these approaches is almost nonexistent. However, there is a wide range of approaches to treat postpartum hemorrhage in the setting of atony, which is the most common cause. Thus, this section will focus on the evidence underlying the different approaches to treat postpartum hemorrhage. Generally, in the treatment of postpartum hemorrhage, less invasive methods should be used initially if possible, but if unsuccessful, preservation of life may require more aggressive interventions, including hysterectomy. Few randomized controlled trials that examine the management of postpartum hemorrhage have been conducted, so management decisions usually are based on observational studies and clinical judgment.

Medical Management

Uterotonic agents should be the first-line treatment for postpartum hemorrhage caused by uterine atony. The specific agent selected, outside of recognized contraindications, is at the health care provider's discretion because none has been shown to have greater efficacy than others for the treatment of uterine atony (12). Common medical agents (eg, oxytocin, methylergonovine, 15-methyl prostaglandin $F_{2\alpha}$, and misoprostol) and their doses are outlined in Table 3. It is common for multiple uterotonic agents to be used, assuming there are no contraindications, and without adequate uterine response and ongoing hemorrhage, they should be used in rapid succession (15). When uterotonics fail to adequately control postpartum hemorrhage, prompt escalation to other interventions (such as tamponade or surgical techniques) and escalation of intensity of care and support personnel are indicated.

Tranexamic Acid

Tranexamic acid is an antifibrinolytic agent that can be given intravenously or orally. A large, randomized, international trial, the WOMAN trial, compared 1 g of intravenous tranexamic acid to placebo in the setting of postpartum hemorrhage (46). Although the composite primary endpoint of hysterectomy or death from all causes was not reduced with tranexamic acid treatment, a significant reduction of mortality in the subgroup of death from obstetric hemorrhage was noted (1.5% versus 1.9%, P=.045 for tranexamic acid compared to placebo, respectively). When the treatment was given within 3 hours of birth, the mortality rates from obstetric hemorrhage were 1.2% versus 1.7% comparing tranexamic acid to placebo (P=.008). Tranexamic acid has been shown in a number of small studies to modestly reduce obstetric blood loss when given prophylactically and as part of treatment for postpartum hemorrhage (47, 48). Additionally, the risk of thrombosis appears to not be different from controls when used in surgeries (49, 50), and the risk of thrombosis was not higher in women who received tranexamic acid as part of the WOMAN trial. At this time, data are insufficient to recommend the use of tranexamic acid as prophylaxis against postpartum hemorrhage outside of the context of research. Although the generalizability of the WOMAN trial and the degree of effect in the United States is uncertain, given the mortality reduction findings, tranexamic acid should be considered in the setting of obstetric hemorrhage when initial medical therapy fails. Earlier use is likely to be superior to delayed treatment, given that in the stratified analysis it appeared that the benefit was primarily in women treated sooner than 3 hours from the time of delivery. For those clinicians unfamiliar with tranexamic acid, it should be used in consultation with a local or regional expert in massive hemorrhage and specifically incorporated into management guidelines.

Table 3. Acute Medical Management of Postpartum Hemorrhage

Drug*	Dose and Route	Frequency	Contraindications	Adverse Effects
Oxytocin	IV: 10–40 units per 500–1,000 mL as continuous infusion or IM: 10 units	Continuous	Rare, hypersensitivity to medication	Usually none. Nausea, vomiting, hyponatremia with prolonged dosing. Hypotension can result from IV push, which is not recommended.
Methylergonovine	IM: 0.2 mg	Every 2–4 h	Hypertension, preeclampsia, cardiovascular disease, hypersensitivity to drug	Nausea, vomiting, severe hypertension particularly when given IV, which is not recommended
15-methyl $PGF_{2\alpha}$	IM: 0.25 mg Intramyometrial: 0.25 mg	Every 15–90 min, eight doses maximum	Asthma. Relative contraindication for hypertension, active hepatic, pulmonary, or cardiac disease	Nausea, vomiting, diarrhea, fever (transient), headache, chills, shivering hypertension, bronchospasm
Misoprostol	600–1,000 micrograms oral, sublingual, or rectal	One time	Rare, hypersensitivity to medication or to prostaglandins	Nausea, vomiting, diarrhea shivering, fever (transient), headache

Abbreviations: IV, intravenously; IM, intramuscularly; PG, prostaglandin.

*All agents can cause nausea and vomiting.

Modified from Lyndon A, Lagrew D, Shields L, Main E, Cape V, editors. Improving health care response to obstetric hemorrhage version 2.0. A California quality improvement toolkit. Stamford (CA): California Maternal Quality Care Collaborative; Sacramento (CA): California Department of Public Health; 2015.

Tamponade Techniques

When uterotonics and bimanual uterine massage fail to sustain uterine contractions and satisfactorily control hemorrhage, the use of compression (including manual compression), intrauterine tamponade or packing can be effective in decreasing hemorrhage secondary to uterine atony (Table 4). Although the evidence that compares these approaches is poor or absent, it is important for institutions to adopt an approach and train personnel in this approach. For example, the California Maternal Quality Care Collaborative recommends the use of an intrauterine balloon for tamponade after uterotonics have failed.

Evidence for the benefits of use of intrauterine balloon tamponade is limited; however, in one study, 86% of women who had balloon tamponade did not require further procedures or surgeries (12, 51). Similarly, a summary of studies showed that 75% of patients did not need further treatment after intrauterine balloon tamponade (12). In some refractory cases, intrauterine tamponade and uterine compression sutures (described later) may be used together (52).

If a balloon tamponade system is not available, the uterus may be packed with gauze. This requires careful layering of the material back and forth from one uterine cornu to the other repeatedly using a sponge stick, and ending with extension of the gauze through the cervical os. To avoid leaving gauze in the uterus at time of removal, it can be carefully counted and tied together. Similarly, multiple large Foley catheters (which were common before the development of commercial intrauterine tamponade devices) can still be used, but the challenge is placing multiple devices and keeping

Table 4. Tamponade Techniques for Postpartum Hemorrhage

Technique	Comment
Commercially available intrauterine balloon tamponade devices	Inserted transcervically or through cesarean incision; has an exit port for blood drainage
- Bakri Balloon	Inflated with 300–500 mL of saline
- ebb uterine tamponade system	Double Balloon: maximum recommended fill volumes are 750 mL for the uterine balloon and 300 mL for the vaginal balloon.
Foley catheter	Insert one or more 60 mL bulbs and fill with 60 mL of saline.
Uterine packing	4-inch gauze, can be soaked with 5,000 units of thrombin in 5 mL of saline then insert from one cornua to the other with ring forceps.

careful count of them. In cases where compression, or intrauterine tamponade, or both, fail to adequately control hemorrhage, they may be used to temporize while planning to move to uterine artery embolization (UAE) or hysterectomy.

Uterine Artery Embolization

Candidates for UAE typically are hemodynamically stable, appear to have persistent slow bleeding and have failed less invasive therapy (uterotonic agents, uterine massage, uterine compression, and manual removal of any clots) (12). When successful, UAE also has the benefit of a woman retaining her uterus and, potentially, future fertility. Fluoroscopic identification of bleeding vessels allows embolization with absorbable gelatin sponges, coils, or microparticles. Studies (n=15) have shown that UAE for postpartum hemorrhage has a median success rate of 89%, ranging from 58% to 98% (12). Moreover, one of the largest series (114 UAE procedures) reported a success rate greater than 80%, with 15% requiring subsequent hysterectomy (53). The risk of significant harm (uterine necrosis, deep vein thrombosis, or peripheral neuropathy) appears to be low (less than 5%) based on reports from small case series (12). After UAE, infertility has been reported in up to 43% of women (12). Other studies have reported that in women who have had a UAE, subsequent pregnancy complications such as preterm birth (5–15%) and fetal growth restriction (7%) appear to be similar to the general obstetric population (12, 54).

Surgical Management

Vascular Ligation

When less invasive approaches such as uterotonic agents (with or without tamponade measures) or UAE fail to control bleeding in the setting of postpartum hemorrhage, exploratory laparotomy is indicated. In the setting of a vaginal delivery, it is common to use a midline vertical abdominal incision to optimize exposure and reduce risk of surgical bleeding. In the setting of cesarean birth, the existing surgical incision may be used. Several techniques are available to control bleeding with limited evidence for each (12). The general aim of vascular ligation in the setting of atony is to diminish the pulse pressure of blood flowing to the uterus. A common first approach is bilateral uterine artery ligation (O'Leary sutures), which commonly accomplishes this goal of reducing blood flow to the uterus, and is quickly and easily performed (55, 56). Similarly, to further diminish blood flow to the uterus, sutures also can be placed across the vessels within the utero–ovarian ligaments. Reports from case series indicate that, when used as a second-line approach to postpartum hemorrhage, the median success of vascular ligation is 92% (12).

However, because these less invasive vascular techniques appear to be effective, it appears that internal iliac (hypogastric) artery ligation is performed less frequently than in the past. The procedure has been found to be considerably less successful than originally thought (57) and because practitioners have become less familiar with this technique (which requires a retroperitoneal approach) it is rarely used today.

Uterine Compression Sutures

Although there are no good-quality studies that provide evidence for the success of uterine compression sutures, the B-Lynch technique probably is the most common uterine compression technique for atony (42); however, other techniques, such as Cho and Hayman, have been described (42, 58–61). The effectiveness of uterine compression sutures as a secondary treatment for uterine atony unresponsive to medical management appears to be approximately 60–75%, with none of the techniques shown to be superior to another (12, 62, 63). B-lynch sutures are placed from the cervix to fundus and provide physical compression of the uterus. A large suture (eg, a number 1 chromic suture) should be used to prevent breaking and the suture should be rapidly absorbed to prevent risk of bowel herniation through a persistent loop of suture after uterine involution. Physicians should be familiar with the technique and it could be helpful to have diagrams available on labor and delivery for quick reference such as those available in the Alliance for Innovation on Maternal Health Obstetric Hemorrhage Bundle (64) (see For More Information). Direct comparisons between compression sutures and uterine balloons have been described in small case series and suggest they have similar effectiveness (65). Uterine necrosis after placement of compression sutures has been reported; however, the exact incidence is not clear because of the small number of patients in case reports and series.

Hysterectomy

When more conservative therapies have failed, hysterectomy is considered the definitive treatment and is not only associated with permanent sterility but also potential surgical complications. For example, six small studies have shown that bladder injuries range from 6% to 12% and ureteral injuries range from 0.4% to 41% (12). There are inadequate studies that compared hysterectomy to other management approaches. Additionally, there is inadequate evidence examining different surgical approaches to hysterectomy (eg, total hysterectomy versus supracervical hysterectomy). Therefore, in the

setting of an emergent postpartum hysterectomy, the surgical approach felt to be the fastest and safest should be used.

▶ *What are the clinical considerations for placenta accreta not diagnosed before delivery?*

Placenta accreta is a life-threatening condition in which either a portion of or the entire placenta invades into the myometrium and fails to separate from the uterine wall during the third stage of labor (66). The risk factors that have the most significant effect appear to be a history of prior uterine surgery, particularly prior cesarean delivery, and placenta previa (67, 68). One multicenter study of more than 30,000 patients who had cesarean deliveries without labor found that the risk of placenta accreta increased with the number of cesarean deliveries (ie, 0.2%, 0.3%, 0.6%, 2.1%, 2.3%, and 6.7% for women experiencing their first through sixth cesarean deliveries, respectively) (68). Therefore, in the presence of placenta previa and a history of cesarean delivery, the obstetrician–gynecologist should have a high clinical suspicion for placenta accreta. The risk was far higher in women with placenta previa with 3%, 11%, 40%, 61%, and 67% of such women with their first through fifth or more cesarean deliveries having a placenta accreta. When diagnosed antenatally, an organized, multidisciplinary management and delivery plan should be developed. Preparations will include establishing a delivery date and assembling an experienced team (including surgical, anesthesiology, blood bank, nursing, and neonatal intensive care unit personnel) and relevant resources (including an operating room and equipment) (66).

In the setting of postpartum hemorrhage and a vaginal delivery, accreta should be strongly suspected if the placenta does not detach easily, and there should be no further attempt to manually remove the placenta in the delivery room. The patient should be moved to an operating room, if not already there, for further assessment. The patient should be counseled about the likely need for hysterectomy and blood transfusion. In the operating room, the extent (eg, area and depth) of the abnormal attachment can be assessed to determine the plan (eg, curettage, wedge resection, medical management, or hysterectomy). If there is ongoing hemorrhage and likely accreta is diagnosed, plans for a prompt hysterectomy should be underway. Adequate intravenous access with at least two large bore intravenous lines should be obtained. Blood products (including red blood cells, fresh frozen plasma, platelets, and cryoprecipitate) should be made readily available while the local blood bank is alerted that additional blood products may be needed. Once the diagnosis of suspected accreta is made, other specialties such as urology, surgery, or interventional radiology should be notified in case additional support is needed.

Uterine conserving options may work in the setting of a small focal accreta; however, in most cases with ongoing bleeding, abdominal hysterectomy will be needed. Attempts at uterine conservation have been recently reviewed (69) and were associated with a 40% risk of emergency hysterectomy, and 42% of women in this setting suffered major morbidity. The risk of an abnormally adherent placenta in a subsequent pregnancy appears to be approximately 20% in a review of 407 patients (70). Thus, an attempt to conserve the uterus in the presence of a focal accreta may be considered for women with a strong desire to retain fertility and a clear understanding of the significant risks of this approach; however, without control of ongoing bleeding, hysterectomy should be the surgical plan.

▶ *What is the management approach for hemorrhage caused by a ruptured uterus?*

Uterine rupture can occur at the site of a previous cesarean delivery or other surgical procedure that involves the uterine wall, from intrauterine manipulation or trauma, from congenital malformation (small uterine horn), or it can occur spontaneously, particularly in the setting of abnormal labor (71–73). Surgical repair is required, with the specific approach tailored to reconstruct the uterus, if possible. Care depends on the extent and site of rupture, the patient's current clinical condition, and her desire for future childbearing. For example, rupture of a previous cesarean delivery scar often can be managed by revision of the edges of the prior incision followed by primary closure. In addition to the myometrial disruption, consideration should be given to neighboring structures, such as the broad ligament, parametrial vessels, ureters, and bladder. Although the patient may wish to avoid hysterectomy, this procedure may be necessary in a life-threatening situation. Supportive care with intravenous fluids, uterotonic medications, and blood transfusion will depend on the degree of blood loss and the patient's hemodynamic status.

▶ *What is the management approach for an inverted uterus?*

Uterine inversion (when the uterine corpus descends to, and sometimes completely through, the uterine cervix) can be associated with marked hemorrhage and cardiovascular collapse. It is relatively rare with an incidence of 1 in 3,700 to 20,000 at vaginal delivery and 1 in 1,860

at cesarean delivery (74, 75). Uterine inversion in a prior pregnancy leads to an increased risk in a subsequent pregnancy (1 per 26 subsequent deliveries) although it is still relatively uncommon (74). Upon bimanual examination, the finding of a firm mass at or below the cervix, coupled with the absence of identification of the uterine corpus on abdominal examination, suggests inversion. If the inversion occurs before placental separation, detachment or removal of the placenta is generally not undertaken before replacement of the uterus because, presumably, this could lead to additional hemorrhage (76).

Manual replacement of the uterine corpus involves placing the palm of the hand or a closed fist against the fundus (now inverted and lowermost at or through the cervix), as if holding a tennis ball, with the fingertips exerting upward pressure circumferentially (77). To restore normal anatomy, relaxation of the uterus may be necessary. Terbutaline, magnesium sulfate, halogenated general anesthetics, and nitroglycerin have all been used for uterine relaxation without clear evidence supporting any one approach as superior to the others (78). Manual replacement with or without uterine relaxants usually is successful with the large majority being successfully replaced in one small series (76). In the unusual circumstance in which it is not, laparotomy is required. Two procedures have been reported to return the uterine corpus to the abdominal cavity. The Huntington procedure involves progressive upward traction on the inverted corpus using Babcock or Allis forceps (79). The Haultain procedure involves incising the cervix posteriorly, which allows for digital repositioning of the inverted corpus, with subsequent repair of the incision (80).

Supportive measures and treatment of the associated hemorrhage should be employed while the inversion is corrected. In the setting of recurrent uterine inversion, the use of intrauterine tamponade balloons has been reported to prevent recurrent uterine inversion as well as the accompanying hemorrhage in a number of case reports (81–84). The use of uterine compression sutures for prevention of acute recurrence also has been successful in a limited number of case reports (59, 85).

▶ *What is the management approach for secondary or delayed postpartum hemorrhage?*

Secondary postpartum hemorrhage, defined as excessive bleeding that occurs more than 24 hours after delivery and up to 12 weeks postpartum, occurs in approximately 1% of pregnancies (11). In the event of secondary hemorrhage, a number of specific etiologies should be considered. Uterine atony (perhaps secondary to retained products of conception) with or without infection contributes to secondary hemorrhage. Ultrasound evaluation can help identify intrauterine tissue. Endometritis should be strongly suspected in the presence of uterine tenderness and a low grade fever. Secondary postpartum hemorrhage also may be the first indication of bleeding disorders such as von Willebrand disease.

Treatment should be focused on the etiology of the hemorrhage and may include uterotonic agents and antibiotics, but if these fail to resolve the problem or if retained products of conception are suspected, uterine curettage may be necessary. If treating endometritis, broad antibiotic coverage with clindamycin and gentamicin is a common choice, although other combinations also are used (86). Often the volume of tissue removed by curettage is relatively small, yet bleeding usually subsides promptly. Concurrent ultrasound assessment at the time of curettage can help prevent uterine perforation. Patients should be counseled about the possibility of hysterectomy before initiating any operative procedure.

▶ *What is best practice for blood product replacement during and after a postpartum hemorrhage?*

The Timing of Transfusion Therapy

Initiation of transfusion therapy generally is based on estimated blood deficit and ongoing blood loss. However, in the setting of postpartum hemorrhage, acute changes in hemoglobin or hematocrit will not accurately reflect blood loss. As noted previously, maternal vital signs typically do not change drastically until significant blood loss has occurred (10). Inadequate early resuscitation and hypoperfusion may lead to lactic acidosis, systemic inflammatory response syndrome with accompanying multiorgan dysfunction, and coagulopathy (87). In women with ongoing bleeding that equates to the blood loss of 1,500 mL or more or in women with abnormal vital signs (tachycardia and hypotension), immediate preparation for transfusion should be made (18, 19, 39). Because such a large blood loss includes depletion of coagulation factors, it is common for such patients to develop a consumptive coagulopathy, commonly labeled as disseminated intravascular coagulation, and the patients will require platelets and coagulation factors in addition to packed red blood cells.

Transfusion and Massive Obstetric Hemorrhage

Massive transfusion usually is defined as a transfusion of 10 or more units of packed red blood cells within

24 hours, transfusion of 4 units of packed red blood cells within 1 hour when ongoing need for more blood is anticipated, or replacement of a complete blood volume (87). Despite the low quality of evidence regarding the benefit of massive transfusion for early postpartum hemorrhage (12), massive transfusion protocols should be part of a comprehensive management plan for treatment of postpartum hemorrhage in settings with adequate blood banking.

Recommendations for optimal blood product replacement therapy and timing of transfusion in obstetric patients have been primarily limited to consensus opinion (18), protocols adapted from trauma literature (88, 89), and a few clinical reports (19, 39, 90–92). All recommend the use of multicomponent therapy with fixed ratios of packed red blood cells, fresh or thawed plasma, platelets, and cryoprecipitate. When a massive transfusion protocol is needed, fixed ratios of packed red blood cells, fresh frozen plasma, and platelets should be used. The recommended initial transfusion ratio for packed red blood cells:fresh frozen plasma:platelets has been in the range of 1:1:1 and is designed to mimic replacement of whole blood. In a recent survey, more than 80% of institutions reported using the 1:1 red blood cell:plasma ratio (93). These recommendations are different from protocols that have previously suggested ratios such as 4:4:1 or 6:4:1 and are related to how a unit of platelets is defined (18). What is more important than the actual ratio is that there is a specific protocol for multicomponent therapy in place at each institution. In women with suspected disseminated intravascular coagulation (ie, consumptive coagulopathy, or low fibrinogen, or both) administration of cryoprecipitate also should be considered. Findings of critically low fibrinogen should be particularly anticipated in the setting of placental abruption or amniotic fluid embolism, and early use of cryoprecipitate is commonly included as part of the resuscitation.

Although smaller hospitals may not have all blood products, every obstetric unit should have a comprehensive maternal hemorrhage emergency management plan that includes protocols for accessing packed red blood cells. In emergency situations, type specific or type O Rh-negative blood also should be readily available. Physicians should be familiar with their hospitals' protocol and recommendations for use of combination blood component therapy. No specific hemorrhage protocol has been proved to be more effective than another; therefore, each hospital will need to address its specific resources and make modifications specific to its unique setting. For examples of algorithms, see For More Information.

It is also important to establish approaches to address situations in which patients decline various treatment approaches. For example, refusal of blood products is common in patients who are Jehovah's Witnesses. This subset of patients has between a 44-fold to 130-fold higher risk of maternal mortality from obstetric hemorrhage because of refusal of blood products (94, 95). Because this population may accept some blood products, a predelivery directive that can be used in the event of a severe postpartum hemorrhage can be discussed with the patient during the prenatal period (18, 96). Greater detail on this issue is outlined in Committee Opinion No. 664, Refusal of Medically Recommended Treatment During Pregnancy.

Although transfusion is often lifesaving in obstetrics, usage of blood products, particularly in the setting of massive transfusion, is not without risk. Massive transfusion is associated with hyperkalemia from packed red blood cells and citrate (used as a preservative in stored blood products) toxicity that will typically worsen hypocalcemia. The combination of acidosis, hypocalcemia, and hypothermia all contribute to worsening coagulopathy and increased morbidity (87, 97). Overzealous resuscitation with crystalloid also can be associated with dilution-related coagulopathy and can contribute to pulmonary edema (98). Other complications include transfusion febrile nonhemolytic reactions (0.8 per 1,000 units transfused), acute hemolytic transfusion reaction (0.19 per 1,000 units transfused), and acute transfusion reactions related lung injury (TRALI, 0.1 per 1,000 units transfused) (99). Transfusion-associated infections (eg, hepatitis, human immunodeficiency virus, West Nile virus, Chagas disease, malaria, and Lyme disease) are relatively rare (less than 1/100,000–1,000,000) (100).

Other Related Therapies

Cell Salvage

Intraoperative cell salvage—also known as autologous blood transfusion—has been shown to be effective and safe in obstetric patients. Limitations are primarily related to availability of appropriate staff and equipment. In certain settings where significant blood loss is anticipated, such as placenta previa and placenta accreta, having this tool available may reduce the need for or volume of allogeneic blood transfusion. Early concerns related to amniotic fluid contamination have been dispelled with higher quality filtering techniques (101). There is some concern for anti-D isoimmunization, and appropriate testing and treatment with anti-D immunoglobulin is necessary (102, 103). However, because the large majority of postpartum hemorrhage events are unpredictable, cell salvage is rarely available or used.

Prothrombin Complex and Fibrinogen Concentrates

Prothrombin complex concentrates (PCCs) are human plasma-derived concentrates of vitamin K-dependent clotting factors. They are the first-line treatment modality for the urgent reversal of acquired coagulation factor deficiency induced by vitamin-K antagonists (eg, warfarin) (104). Different preparations of PCCs are available that contain three factors (factors II, IX, and X) or four factors (factors II, VII, IX, and X). Fibrinogen concentrates are approved for the treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency. Data regarding the use of PCC and fibrinogen concentrates in the setting of postpartum hemorrhage and disseminated intravascular coagulation are limited. Thus, these should be used only after multiple rounds of the standard massive transfusion agents and in consultation with a local or regional expert in massive hemorrhage.

Recombinant Factor VII

Factor VII is a vitamin K-dependent serine protease with a pivotal role in coagulation. The only U.S. Food and Drug Administration-approved indication for recombinant factor VII is for treatment of patients with hemophilia A and B. The role of recombinant factor VII in primary postpartum hemorrhage is controversial (105, 106). It has been reported to significantly improve hemostasis in hemorrhaging obstetric patients, but also may result in life-threatening thrombosis (107) estimated to be in the range of 2–9% (12). Use of recombinant factor VII is not considered first-line therapy and should be reserved for extenuating circumstances after multiple rounds of the standard massive transfusion agents and in consultation with a local or regional expert in massive hemorrhage.

▶ *What is the best approach to managing anemia in the nonacute postpartum period once the postpartum hemorrhage has been treated?*

After a patient has been stabilized posthemorrhage, the degree of anemia is sometimes not apparent until the patient receives her routine postpartum laboratory results the following day or has symptoms of dizziness or lightheadedness when she begins to ambulate. At this point a decision to treat using a transfusion of packed red blood cells (PRBCs), supplement oral iron, or intravenous iron will need to be made. The degree of ongoing blood loss (lochia), risk of subsequent blood loss, and patient symptoms should all be considered when deciding on the best approach to treatment. It is common practice to offer a transfusion of PRBCs to symptomatic women with a hemoglobin value less than 7 g/dL (hematocrit less than 20%) (108). Alternatively, the management of women with hemoglobin values less than 7 g/dL who are asymptomatic and hemodynamically stable should be individualized between transfusion, oral iron supplementation, or intravenous iron therapy. Each is designed to replace red cell mass, but at differing rates. Although transfusions historically were initiated with 2 units of PRBCs, the most recent recommendation from the American Association of Blood Banks for a stable patient is to begin with 1 unit and reassess (108).

When a blood transfusion is not necessary, but supplemental iron is indicated, the use of intravenous iron (ferrous sucrose) has been compared to oral iron for postpartum anemia in a few small randomized controlled trials. (109–112). Two of these studies have shown significant improvement in hemoglobin levels on posttreatment day 14 from intravenous iron, but these differences were modest. In absolute terms, there was a smaller increase in hemoglobin of 1.4–1.5 g/dL in those receiving oral iron as compared with 2.0–3.8 g/dL in those receiving intravenous iron (109, 111). At posttreatment day 40–42 none of the studies demonstrated a difference in hemoglobin level or any other clinical outcomes between oral or intravenous iron.

▶ *Which systems-level interventions are effective in improving the management of postpartum hemorrhage?*

Using a standardized, multistage evaluation and response protocol has been associated with earlier intervention and resolution of maternal hemorrhage at an earlier stage of hemorrhage (19, 35). However, studies have not consistently demonstrated improvement in maternal outcomes, including severe morbidity or mortality (19, 35, 36). In the 2015 Agency for Health Research and Quality systematic review, there was no consistent evidence for benefit in severe postpartum hemorrhage, transfusion, hysterectomy, intensive care unit admission, or mortality from standardized protocols (12). Despite this lack of consistent evidence, numerous organizations recommend that an organized, multidisciplinary approach be taken in order to reduce the morbidity and mortality from postpartum hemorrhage, and a quality improvement approach to this leading cause of maternal morbidity and mortality appears appropriate. Thus, all obstetric facilities should have a standardized hospital-wide process in place for management of obstetric hemorrhage. Obstetrician–gynecologists and other obstetric care providers should work with their institutions to ensure the existence of a designated multidisciplinary response team, a staged postpartum hemorrhage protocol that includes guidelines

for escalation of care, and a functioning massive transfusion protocol.

Every obstetric unit should have an organized, systematic obstetric hemorrhage response that coordinates care among all critical personnel. Hospitals should consider adopting a system to implement key elements in four categories: 1) *readiness* to respond to a maternal hemorrhage, 2) *recognition and prevention* measures in place for all patients, 3) *a multidisciplinary response* to excessive maternal bleeding, and 4) a systems-based quality improvement process to improve responsiveness through *reporting and system learning*. The Council on Patient Safety in Women's Healthcare has endorsed a system and further details can be found on the For More Information web page. Education, drills, and review of team protocol compliance are needed to ensure everyone remains proficient with the treatment algorithm and tools at each facility.

Multidisciplinary simulation-based team training, including postpartum hemorrhage scenarios, have been associated with improved safety culture and outcomes in obstetrics (113–115). Hemorrhage drills have been used for multiple purposes, including the following: identify management pitfalls (116), improve confidence and competence in skills (117), pilot and modify checklists (118), identify and correct systems issues (119, 120), familiarize staff with management algorithms, and ensure timely management of hemorrhage (19). Although one standardized approach for drills, simulation, and team training has not been established, there are several recommended tools and techniques that can be incorporated into unit-based improvement strategies (121, 122).

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on good and consistent scientific evidence (Level A):

- All obstetric care facilities should have guidelines for the routine administration of uterotonics in the immediate postpartum period.
- Uterotonic agents should be the first-line treatment for postpartum hemorrhage caused by uterine atony. The specific agent selected, outside of recognized contraindications, is at the health care provider's discretion because none has been shown to have greater efficacy than others for the treatment of uterine atony.

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

- When uterotonics fail to adequately control postpartum hemorrhage, prompt escalation to other interventions (such as tamponade or surgical techniques) and escalation of intensity of care and support personnel are indicated.
- Given the mortality reduction findings, tranexamic acid should be considered in the setting of obstetric hemorrhage when initial medical therapy fails.
- Obstetrician–gynecologists and other obstetric care providers should work with their institutions to ensure the existence of a designated multidisciplinary response team, a staged postpartum hemorrhage protocol that includes guidelines for escalation of care, and a functioning massive transfusion protocol.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- Management of postpartum hemorrhage should use a multidisciplinary and multifaceted approach that involves maintaining hemodynamic stability while simultaneously identifying and treating the cause of blood loss.
- Generally, in the treatment of postpartum hemorrhage, less invasive methods should be used initially if possible, but if unsuccessful, preservation of life may require more aggressive interventions including hysterectomy.
- When a massive transfusion protocol is needed, fixed ratios of packed red blood cells, fresh frozen plasma, and platelets should be used.
- Hospitals should consider adopting a system to implement key elements in four categories: 1) *readiness* to respond to a maternal hemorrhage, 2) *recognition and prevention* measures in place for all patients, 3) *a multidisciplinary response* to excessive maternal bleeding, and 4) a systems-based quality improvement process to improve responsiveness through *reporting and system learning*.

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view

these resources at www.acog.org/More-Info/Postpartum Hemorrhage.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's website, or the content of the resource. These resources may change without notice.

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and June 2017. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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Clinical Investigation Report	
Title of Clinical Investigation	PEARLE: Prospective, Single Arm, Pivotal Clinical Trial Designed to Assess the Safety and Effectiveness of the Jada® System In Treating Primary Postpartum Hemorrhage ("PPH")
Study Indications for Use	The Jada System is intended to provide control or reduction of postpartum uterine bleeding when conservative management is warranted.
Name of Device and Model Number	Jada® System PN-1002
Study Design	Prospective, single-arm, literature-controlled, multi-center clinical study
Development Phase	Pivotal trial
Sponsor Name and Contact Information	Alydia Health, Inc. 3495 Edison Way Menlo Park, CA 94025 Kathryn Wine, MPH Vice President of Clinical Operations kathryn@alydiahealth.com (415) 990-4104
CIP Identification	CIP-01, PPH-02
Principal Investigator	Mary D'Alton, MD – Overall Study PI Obstetrician and Gynecologist in Chief and Chair of Department of Obstetrics and Gynecology NewYork-Presbyterian / Columbia University Irving Medical Center
Monitoring and Data Management	(b)(4)
Statisticians	
ISO Standard	ISO 14155
Final Data Lock	April 30, 2020
Report Version	(b)(4) – August 26, 2020

(b)(4) Clinical Studies

(b)(4) Clinical Studies

1. SUMMARY

1.1. Title of the Clinical Investigation

PEARLE: Prospective, Single Arm, Pivotal Clinical Trial Designed to Assess the Safety and Effectiveness of the Jada System In Treating Primary Postpartum Hemorrhage ("PPH")

1.2. Introduction

The Jada System ("Jada") was developed to treat abnormal postpartum uterine bleeding and hemorrhage related to atony of the uterus. The PEARLE study was designed to evaluate the safety and effectiveness of the Jada System for this purpose and was conducted under an approved IDE (G150265) from the U.S. Food and Drug Administration (FDA).

Mary D'Alton, MD, served as the Principal Investigator for the study. Additional investigators and their sites are listed in **Tables 01 and 02** below; each investigator's curriculum vitae (CV) is on file at Alydia Health.

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Table 01: Study Sites and Investigators.

Site Number*	Site Name Site Investigators
04	Site Name: University of Texas Medical Branch (Galveston, TX) Investigator Names: (b)(4)
05	Site Name: University of Utah (Salt Lake City, UT) Investigator Names: (b)(4)
06	Site Name: NewYork-Presbyterian / Queens (Flushing, NY) Investigator Names: (b)(4)
07	Site Name: NewYork-Presbyterian / Columbia University Irving Medical Center (New York, NY) Investigator Names: (b)(4)

Site Number*	Site Name Site Investigators
08	Site Name: Rutgers University / Robert Woods Johnson Hospital (New Brunswick, NJ) Investigator Names: (b)(4)
09	Site Name: Northwestern University Investigator Name: (b)(4)
11	Site Name: University of Alabama (Birmingham, AL) Investigator Names: (b)(4)
12	Site Name: University of Virginia (Charlottesville, VA) Investigator Names: (b)(4)
14	Site Name: University of Texas Health Science Center / McGovern School of Medicine (Houston, TX) Investigator Name: (b)(4)

Site Number*	Site Name Site Investigators
16	Site Name: The Ohio State University (Columbus, OH) Investigator Names: (b)(4)
17	Site Name: MetroHealth (Cleveland, OH) Investigator Names: (b)(4)
19	Site Name: MedStar Washington Hospital (Washington, D.C.) Investigator Names: (b)(4)

Site Number*	Site Name Site Investigators
20	Site Name: University of Pittsburgh Medical Center / Magee Women's Hospital (Pittsburgh, PA) Investigator Names: (b)(4)
21	Site Name: Indiana University (Indianapolis, IN) Investigator Names: (b)(4)
22	Site Name: Geisinger Medical Center (Danville, PA) Investigator Names: (b)(4)

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Table 02: Terminated Study Sites and Investigators.

Site Number*	Site Name Site Investigators
(b)(4)	

1.3. Purpose of the Clinical Investigation

The purpose of the PEARLE study was to evaluate the safety and effectiveness of the Jada System to treat abnormal postpartum uterine bleeding and hemorrhage. It was conducted in order to support a 510(k) submission to FDA for the Jada System (b)(4) (b)(4)

1.4. Description of the Clinical Investigation Population

Subjects were identified and recruited from inpatient and outpatient facilities affiliated with or at twelve (12) U.S. study sites out of a total of fifteen (15) active sites at the time of final enrollment described in **Table 01**. Three (3) sites of the active fifteen (15) did not enroll any subjects but did consent potential subjects for participation (b)(4) (b)(4). Per the study protocol, subjects were considered "enrolled" only after they both signed the consent form and met all study entrance criteria (b)(4)

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Enrolled subjects were between the ages of 19 and 51 who had recently had a vaginal or Cesarean-section delivery and were diagnosed with abnormal postpartum uterine bleeding or hemorrhage due to uterine atony. Prior to enrollment, subjects were consented to the study using IRB-approved materials (b)(4)

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the consented patients, one hundred seven (107) women were enrolled in the study.

1.5. Clinical Investigation Method Used

The study was a prospective, single-arm, literature-controlled, multi-center treatment study where each enrolled subject was treated with the Jada System. A subject was considered enrolled once she had provided written informed consent and met all study eligibility criteria, and if the appropriate study personnel were present, Jada treatment was attempted. To avoid consenting during a time of duress, informed consent was required prior to a diagnosis of postpartum hemorrhage.

The primary effectiveness endpoint was as follows:

"Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada use is standard of care as long as such use does not exceed the maximum dose of the drug and does not constitute failure of the primary effectiveness endpoint."

Secondary effectiveness endpoints were as follows:

1. Time to control hemorrhage, defined as the time from turning on the vacuum source until the time the *first* of any of the following occurs:
    - there is no blood being collected in the tubing or canister, or
    - the blood loss is observed as leveled off in the canister, or
    - blood loss is at a rate of < 500 mL in 24 hours.
2. Rate of surgical intervention required to control PPH after Jada use.
3. Rate of non-surgical intervention required to control PPH after Jada use.
4. Assessment of device usability as reported by the clinician using a dedicated data collection form.
5. Rate of blood product transfusion required after Jada use, and number of transfusion units when administered.

The primary safety endpoint was the incidence, severity and seriousness of device-related adverse events.

1.6. Background

Postpartum hemorrhage (PPH), or excessive blood loss after childbirth, is the leading cause of maternal mortality. PPH is responsible for over a quarter of maternal deaths worldwide[1]; is the leading cause of global maternal mortality, (b)(4)

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1.7. Results of the Clinical Investigation

For the primary study endpoint, 94.3% of the Intent to Treat (ITT) Cohort met the success criterion (lower bound of the 95% confidence interval was 88.1%). The success rate in the modified Intent to Treat (mITT) was 96.2% (lower bound of the 95% confidence interval was 90.4%),and 99% of the Per Protocol (PP) Cohort met the success criterion (lower bound of the 95% CI was 94.4%).

The secondary endpoints are summarized below:

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[1] Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, Gülmezoglu AM, Temmerman M, Alkema L. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014 Jun;2(6):e323-33. doi:10.1016/S2214-109X(14)70227-X. Review. PubMed PMID: 25103301.

[2] CDC: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-mortality-surveillance-system.htm

[3] Marshall AL et al. "The impact of postpartum hemorrhage on hospital length of stay and inpatient mortality: a National Inpatient Sample-based analysis." Ampo J Obstet Gynecol 2017;217:344.e1-6.

[4] CDC: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-mortality-surveillance-system.htm

1. Time to PPH control was fast with Jada use. The median time to hemorrhage control was 3 minutes after vacuum connection in the ITT Cohort.

2. The need for surgical intervention after use of Jada was rare, with only 3 of 106 (2.8%) subjects requiring surgical intervention in the ITT Cohort.

3. The need for non-surgical intervention after use of Jada was rare, with 2 of 106 (1.9%) subjects requiring non-surgical intervention in the ITT Cohort.

4. The Device Usability was notably positive on all measurements.

5. The rate of blood product transfusion was 37.7% and the rate at which subjects received four or more units of packed red blood cells was 4.7% in the ITT Cohort. Transfusions are expected in a study of this patient population conducted in the US where blood and blood products are universally available.

There were no unanticipated adverse device effects reported in the study. There were no adverse events deemed “definitely related” to the Jada System or the study procedure. Of the reported adverse events, there were eight (8) events adjudicated by the Independent Medical Monitor deemed “possibly related” to the Jada System or the study procedure. Of these, three (3) were of moderate severity and five (5) were of mild severity. The three (3) moderate events also met the definition of serious. They were cases of endometritis, a known risk of long labor, vaginal exam, and PPH. The remaining related events were deemed non-serious.

1.8. Conclusion

The comparator was a literature control; a meta-analysis of the Bakri Balloon. Based on a random effects model used in the meta-analysis, the estimated pooled proportion of subjects who reached control of uterine hemorrhage following Bakri balloon treatments was 82.0% (95% CI: 73.4% to 89.2%). Based on the observed success rate in the ITT Cohort of 94.3% (with a lower bound 95% confidence limit of 88.1%), the Jada treatment success rate is non-inferior to the treatment success rate of the Bakri Balloon. These results demonstrate the effectiveness of the Jada System in treating postpartum hemorrhage and abnormal postpartum uterine bleeding. The success rate in the mITT Cohort is 96.2% (with a lower bound 95% confidence limit of 90.4%). The confidence intervals for the mITT Cohort and the Bakri comparator do not overlap -- the lower bound of the Jada confidence interval is higher than the upper bound of the Bakri confidence interval.

Safety results demonstrated that the Jada System is safe for its intended use with a low rate of adverse events, none of which were deemed definitely related to the use of the Device. All secondary endpoints also support safety and effectiveness where the use of Jada stopped abnormal postpartum uterine bleeding/PPH quickly without need for surgical or non-surgical intervention in almost all cases, usability ratings were high across all measurements and the transfusion rate was not unexpected given this was a study of women experiencing abnormal postpartum uterine bleeding/PPH.

1.9. Date of the Clinical Investigation Initiation

The first subject was enrolled on February 9, 2018.

1.10. Date of the Clinical Investigation Completion

The last subject was treated with Jada on January 26, 2020 and the last subject completed study-required follow-up at 6 weeks postpartum on March 25, 2020.

2. INTRODUCTION

2.1. Background of Clinical Condition

Postpartum hemorrhage (PPH), or excessive blood loss after childbirth, is the leading cause of maternal mortality. PPH is responsible for over a quarter of maternal deaths worldwide[5]. In Africa and Asia, where most maternal deaths occur, PPH accounts for more than 30% of all maternal deaths. It is estimated that PPH afflicts 6% of women giving birth[6]. Africa has the highest rate of PPH, with a prevalence of 10.5% of women giving birth[7]. Even developed countries are challenged by this life-threatening complication of childbirth, causing 10.6% of maternal deaths in the United Kingdom, and 12% of maternal deaths in the United States[8].

Primary PPH, which is PPH that occurs within 24 hours after the birth of the baby, is the most common form of major obstetric hemorrhage. Severe primary PPH is commonly defined as loss of more than 1500 mL of blood within 24 hours after the birth of a baby. Blood loss of more than 1500 mL is usually considered life threatening and triggers a full complement of emergency measures to achieve resuscitation and hemostasis. As such, bleeding above 1500 mL was excluded from the study.

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[5] Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, Gülmezoglu AM, Temmerman M, Alkema L. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014 Jun;2(6):e323-33. doi:10.1016/S2214-109X(14)70227-X. Review. PubMed PMID: 25103301.

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[9] CDC: https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-mortality-surveillance-system.htm

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[10] ProPublica series: Lost Mothers, Maternal Care and Preventable Deaths, 2017-2019. https://www.propublica.org/series/lost-mothers

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[12] https://safehealthcareforeverywoman.org/aim-program/

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[19] Glover P. Blood loss at delivery: how accurate is your estimation? Aust Midwifery [Internet]. 2003 Jun [cited 2014 Dec 23];16(2):21–4.

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2.3. Jada System

The Jada System is a new option for the treatment of abnormal postpartum uterine bleeding and hemorrhage. The Jada System was developed for the purpose of using of gentle vacuum to control abnormal postpartum uterine bleeding and hemorrhage. Vacuum offers the potential to control bleeding faster, with a high degree of safety and effectiveness, using a mechanism that encourages the natural postpartum physiological response of uterine contraction, rather than a mechanism that pushes outwards, against the natural uterine contraction.

3. INVESTIGATIONAL DEVICE AND METHODS

3.1. Investigational Device

3.1.1. Investigational Device Description

The Jada System is a 41cm long intrauterine device made of silicone. The device consists of an elliptical Intrauterine Loop on the distal end of the Tube. The Tube is collared by a donut-shaped Cervical Seal and terminates on the proximal end with a Vacuum Connector for attachment to a sterile vacuum tubing (see **Figure 01**). The Intrauterine Loop has twenty Vacuum Pores directed towards the interior of the Intrauterine Loop. The outer surface of the Intrauterine Loop is covered by a Shield, which overhangs the Vacuum Pores to protect tissue from vacuum and to prevent the Vacuum Pores from plugging with tissue and blood clots. The Tube has a Seal Valve that can be attached to a sterile syringe, allowing the Cervical Seal to be filled with and emptied of sterile fluid. The various portions of the device are soft enough to reduce the chance of injury or perforation, but firm enough for easy insertion and smooth function without kinking. The Jada System is designed to attach to sterile vacuum tubing and a regulated vacuum source with an in-line graduated vacuum collection canister.

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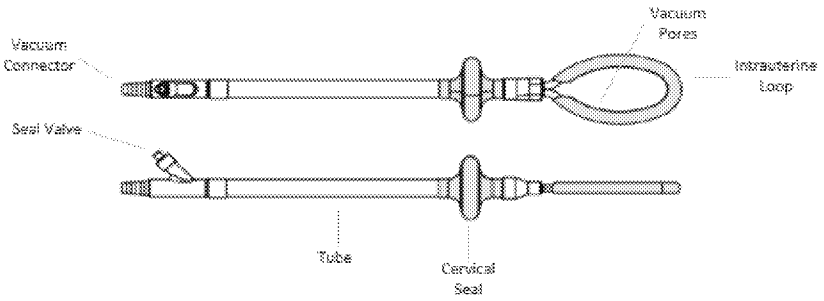

Figure 01: Jada System.

For convenience at the time of enrollment, the Jada System and the Instructions for Use (IFU) were provided within a kit (see **Figure 02**) that also included the following components:
1. Sterile vacuum tubing;
2. Sterile saline;
3. Sterile 60 mL syringe;
4. Data collection sheet for the case; and
5. Quick Reference Guide.

Figure 02: Jada System Kit for PEARLE Study.

3.1.2. Operating Parameters

The Jada System is inserted into a woman's uterus transvaginally after vaginal deliveries or after the hysterotomy is closed following c-section deliveries.

During insertion, the Intrauterine Loop is introduced in the uterine cavity. The Cervical Seal is positioned in the upper vagina, against the external cervical os. Per the Jada System IFU, the Jada positioning can be confirmed via ultrasound if needed, or it can be manually felt or visually confirmed. The Cervical Seal is filled with sterile fluid using a sterile 60 mL syringe to ensure

that a vacuum can be achieved in the uterine cavity. The Vacuum Connector can then be connected to sterile tubing, regulated vacuum source, and in-line graduated vacuum collection canister. See **Figure 03**.

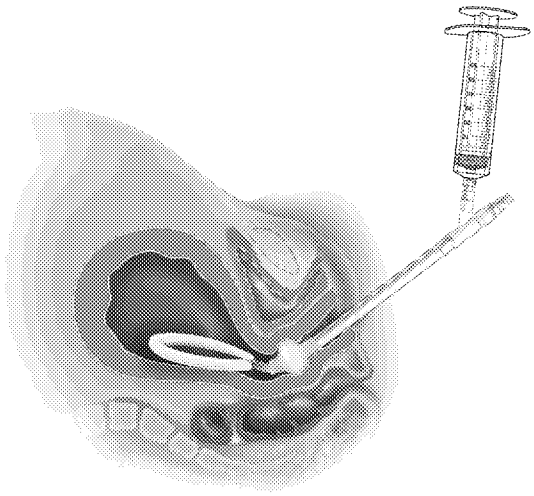

Figure 03: Jada positioning.

Once the vacuum is connected, residual blood and clots can be evacuated with applied suction through the vacuum tube. After any residual blood or clots are suctioned, the continued application of vacuum within the uterine cavity causes the uterus to collapse upon itself, **Figure 04**. The collapse of the uterine walls and accompanying movement of the uterine fundus downward can often be palpated over the abdomen by the user. Additionally, the clear Tube of the device allows for visualization of the flow of evacuated fluids and air providing further confirmation of device function. This is an important safety feature, as the blood evacuation is measurable by the level in the graduated vacuum canister, making it possible to evaluate cessation of hemorrhage and any recurrence of bleeding. Additional instructions on the use of the device are detailed in the Instructions for Use, **Appendix 9.2**

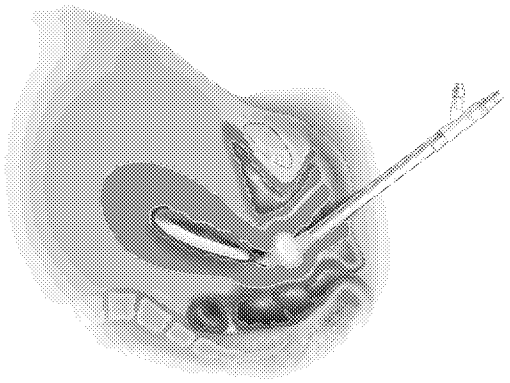

Figure 04: Vacuum within the uterine cavity causing uterine collapse.

3.1.3. Intended Use of the Investigational Device

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3.1.4. Changes to the Investigational Device during the Clinical Investigation

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4. CLINICAL INVESTIGATION PLAN (CIP)

4.1. Clinical Investigation Objectives and Hypothesis

A meta-analysis of the published clinical literature regarding the Bakri device was conducted to provide a numerical estimate of the overall Treatment Success Rate for that device. Based on a random effects model, the estimated pooled proportion of subjects who reached hemostasis (i.e., control of uterine hemorrhaging) following treatment with the Bakri Balloon was 82.0% (95% CI: 73.4% to 89.2%).

The primary effectiveness objective of this pivotal study was to show that the observed Treatment Success Rate is not worse than the Treatment Success Rate reported in the literature for the Bakri device. Based on a random effects model, the estimated pooled proportion of subjects who reached hemostasis (i.e., control of uterine hemorrhage) following Bakri Balloon treatments was 82% (95% CI: 73.4% to 89.2%). By this definition, the study was to be considered a success if the lower bound of the two-sided Exact Clopper-Pearson mid-p 95% Confidence Interval for the Study Treatment Success was greater than or equal to 73.4%.

4.2. Clinical Investigation Design

4.2.1. Type of Clinical Investigation

PEARLE is a prospective, single-arm, literature-controlled, multi-center study. It is the pivotal trial of the Jada System.

4.2.2. Clinical Investigation Endpoints

4.2.2.1. Safety Endpoints

Primary Safety Endpoint: Incidence, severity and seriousness of device-related adverse events.

4.2.2.2. Primary Effectiveness Endpoint

Primary Effectiveness Endpoint: Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second line or surgical intervention to control uterine hemorrhage after the use of the Jada System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada use is standard of care as long as such use does not exceed the maximum dose of the drug and does not constitute failure of the primary effectiveness endpoint.

4.2.2.3. Secondary Effectiveness Endpoints

1. Time to control hemorrhage, defined as the time from turning on the vacuum source until the time the *first* of any of the following occurs:
   - there is no blood being collected in the tubing or canister, or
   - the blood loss is observed as leveled off in the canister, or
   - blood loss is at a rate of < 500 mL in 24 hours.
2. Rate of surgical intervention required to control PPH after Jada use.
3. Rate of non-surgical intervention required to control PPH after Jada use.
4. Assessment of device usability as reported by the clinician using a dedicated data collection form.
5. Rate of blood product transfusion required after Jada use, and number of transfusion units when administered.

4.2.2.4. Additional Analyses

Analysis of the primary safety and effectiveness endpoints was repeated for two subgroups of subjects: subjects with vaginal delivery and subjects with surgical delivery by c-section.

4.2.2.5. Poolability

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4.2.2.6. Lost to Follow-Up

Data on subjects who were lost to follow-up were maintained and analyzed up to the point at which they discontinued.

4.2.2.7. Dropout mechanism and analysis

None of the subjects withdrew from the study prior to completing the assessment of Treatment Success.

4.3. Ethical Considerations

Several precautionary measures were built into the investigational protocol to protect the study subjects and to detect any potential adverse effects. Inclusion/exclusion criteria were identified to help ensure that any study subject who would be at undue risk was not enrolled in the study. Also, study subjects were observed during and following the intervention to assure that any acute adverse events were detected in a timely manner so that proper medical treatment could be initiated. Subjects were followed until 6 weeks post-treatment in order to capture other possible intervention-related adverse events that did not manifest immediately. In addition, safeguards were noted in the study protocol with respect to the informed consent process.

The study protocol included the following principles of informed consent:

"As stated by US FDA,[37] *'To many, the term informed consent is mistakenly viewed as synonymous with obtaining a subject's signature on the consent form. FDA believes that obtaining a subject's oral or written informed consent is only part of the consent process. Informed consent involves providing a potential subject with adequate information to allow for an informed decision about participation in the clinical investigation, facilitating the potential subject's comprehension of the information, providing adequate opportunity for the potential subject to ask questions and to consider whether to participate, obtaining the potential subject's voluntary agreement to participate, and continuing to provide information as the clinical investigation progresses or as the subject or situation requires. To be effective, the process must provide sufficient opportunity for the subject to consider whether to participate. (21 CFR 50.20.) FDA considers this to include allowing sufficient time for subjects to consider the information and providing time and opportunity for the subjects to ask questions and have those questions answered. The Investigator (or other study staff who are conducting the informed consent interview) and the subject should exchange information and discuss the contents of the*

[37] Informed Consent Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors, Draft issued July 2014

informed consent document. This process must occur under circumstances that minimize the possibility of coercion or undue influence.'"

In addition, the protocol stated that upon determination of subject eligibility (preliminary completion of study entry criteria), the patient would have the opportunity to discuss any risks, benefits, alternative therapies, and the study requirements with the investigator or their designee prior to signing the informed consent document. Signed informed consent was required from each study subject prior to use of the investigational device.

Given the potential for duress, the timing for obtaining informed consent from women undergoing labor and delivery raised unique considerations in this study. As such, considerations and requirements for timing of obtaining informed consent were included in the study protocol and are described below.

Informed consent for this study was permitted to be obtained during several different phases of interaction with the patient:

Phase 1: At any antenatal obstetrical office visit prior to the onset of labor

Phase 2: After hospital admission, but before the onset of labor, including the following:

- Women making an antenatal visit at the hospital
- Women admitted for labor induction
- Women with ruptured membranes, but who were not in labor

Phase 3: After the onset of labor, **but before the diagnosis of PPH**

In all 3 phases, the patient was provided adequate time to review the informed consent form and consider whether or not to participate.

During Phase 3, there is an increased likelihood that the woman would be under periods of duress. As such, the following safeguards were applied to informed consent that was obtained during Phase 3.

Informed consent was not obtained when any of the following applied:

1. The patient had been diagnosed with PPH.
2. The patient had arterial bleeding requiring surgical exploration or angiographic embolization.
3. The patient required immediate life-saving hysterectomy.
4. The patient was in the second stage of labor.
5. The patient was experiencing a contraction.
6. The patient was experiencing pain or discomfort that prevents a lucid discussion of the elements of the informed consent form.
7. The patient was undergoing a gynecological examination.
8. The patient was distracted by the placement or adjustment of fetal or labor monitoring devices.
9. The patient was undergoing administration of an epidural regional anesthetic or spinal anesthetic.

10. The study investigator believed that the patient's level of mental and/or physical stress prevented a lucid discussion of the elements of the informed consent form.

Patients were informed by the investigator or investigator's designee that they were free to refuse participation in this research study. If they elected to participate, it was made clear that they were permitted to withdraw from the study at any time without prejudicing further care.

The investigator or the investigator's designee informed patients that their medical records were subject to review by the sponsor and appropriate regulatory bodies. They were informed that this information would be used during the analysis of the results of the clinical study, but the patients' identities would be confidential.

The investigator or their designee explained the conditions of the study, giving the patient sufficient time to ask questions and to consider whether or not they wanted to participate. If the patient agreed to participate, then they were given an IRB-approved consent form for signature and date. A copy of the consent form was required to be given to the patient. The original consent forms were kept by the investigator and were subject to review by the sponsor or a representative of the sponsor, and by the appropriate regulatory bodies. The template for the informed consent form was reviewed by FDA during the IDE submission and supplement process.

When the patient signed the informed consent form (and was admitted for delivery), the site placed a PEARLE Consent ID bracelet on their wrist to indicate that they had been consented. The study team member dedicated to the completion of documentation at each case was required to document clearly that informed consent had been obtained prior to each enrollment and that the subject was wearing the specific PEARLE study consent bracelet. An example of the brightly colored PEARLE Consent ID bracelet is shown in **Figure 05**.

Figure 05: PEARLE consent ID bracelet.

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4.4. Data Quality Assurance

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4.5. Subject Population

The following were the inclusion and exclusion criteria followed for the study.

4.5.1. Inclusion and Exclusion Criteria

Inclusion Criteria

1. Adult Female, 18 years of age or older at time of consent.
2. Able to understand and provide informed consent to participate in the study.
3. Diagnosis of PPH with suspected atony within 24 hours after vaginal or c-section delivery.
4. EBL, to be determined when investigator is ready to have the Jada peel pack opened:
   Vaginal delivery: 500 – 1500 mL EBL or;
   c-section delivery: 1000 – 1500 mL EBL.
5. Failed first-line intervention of uterotonics and uterine massage/bimanual uterine massage to stop bleeding.

Note: Uterotonic administration may continue concomitant with and post Jada use, as long as such use does not exceed the maximum dose of the drug.

Exclusion Criteria

1. EBL >1500 mL, to be determined when investigator is ready to have the Jada peel pack opened.

2. Delivery at a gestational age < 34 weeks.
3. For c-sections: Cervix < 3 cm dilated before use of Jada.
4. PPH that the investigator determines to require more aggressive treatment, including any of the following:
   a) hysterectomy;
   b) b-lynch suture;
   c) uterine artery embolization or ligation;
   d) hypogastric ligation.
5. Known uterine anomaly.
6. Ongoing intrauterine pregnancy.
7. Placenta abnormality including any of the following:
   a) known placenta accreta;
   b) retained placenta with known risk factors for placenta accreta (e.g. history of prior uterine surgery, including prior c-section and placenta previa);
   c) retained placenta without easy manual removal.
8. Known uterine rupture.
9. Unresolved uterine inversion.
10. Subject has undergone intrauterine balloon therapy or uterine packing for tamponade treatment of this PPH prior to use of the Jada System.
11. Current cervical cancer.
12. Current purulent infection of vagina, cervix, uterus.
13. Diagnosis of coagulopathy.

4.5.2. Sample Size

The study was designed to enroll up to 107 subjects to ensure that 96 subjects were evaluable for the analysis of the primary effectiveness endpoint. The actual enrollment was 107. Sites were expected to enroll a minimum of 5 subjects. Actual enrollment from participating sites was between 1 and 29 subjects. Site enrollment was capped at 30% of the total expected enrollment, such that no site was permitted to enroll more than 32 subjects.

4.6. Treatment and Treatment Schedule

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4.7. Concomitant Medications

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4.8. Duration of Follow-Up

Subjects enrolled in the trial were followed with one postpartum visit at 6 weeks. This visit was consistent with timing for standard postpartum follow-up and included a pelvic exam and an evaluation of any adverse events. If the subject was unable to return for her normal 6-week visit, a call was acceptable per the protocol, given that women were at home with newborns. In this

case, the subject was called and interviewed for possible adverse events from the time of discharge through this single follow-up point.

Any ongoing AEs were followed until they resolved or were not expected to change. The protocol required that subjects be referred to the primary care physician for any ongoing medical issue continuing beyond the completion of the study.

4.9. Statistical Analysis

4.9.1. Clinical Investigation Hypothesis and Sample Size Justification

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4.9.2. Statistical Analysis Methods

Safety was evaluated by analyzing all adverse events for device or procedure relatedness, seriousness, severity, and if related, whether or not they were anticipated.

Up to 20 study sites were allowed to enroll a total of up to 107 subjects in the study to ensure that 96 subjects were evaluable for the analysis of the primary effectiveness endpoint.

Different groups of subjects, or Analysis Cohorts, were identified depending on the type and extent of analysis being performed.

Only subjects from study sites located within the United States and study sites located outside the U.S. (O.U.S.) that were enrolled under the 2.6 version of the protocol were planned to be included in the analyses. However, no O.U.S. sites participated under version 2.6 of the study protocol. Therefore, the analysis and data presentations are from U.S. sites only.

4.9.2.1. Screening Cohort

All subjects who were consented and screened for the study were included in the Screening Cohort. Subjects excluded during the procedure from receiving Jada treatment for non-device related reasons were included in this Cohort. Only an accounting of the numbers of subjects screened in the study, plus the reasons given for subjects not enrolled in the study, were performed on this Cohort.

4.9.2.2. Safety/Intent to Treat (ITT) Cohort

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4.9.2.3. Modified ITT (mITT) Cohort

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4.9.2.4. Per-Protocol (PP) Cohort

(b)(4)

4.9.3. Cohort for Primary and Secondary Effectiveness Endpoints

Analyses of all primary and secondary effectiveness endpoints were conducted for the ITT, mITT Cohort and the PP Cohort. Study success was based on the ITT Cohort.

4.9.4. Cohort for Safety Endpoints

Analyses for all safety-related endpoints were performed using the Safety/ITT Cohort.

4.9.5. Methods

Categorical data were summarized using frequency tables, presenting the subject counts and relative percentages.

Continuous variables were summarized by the mean, standard deviation, median, minimum and maximum. Within-subject changes (Change-from-Baseline) were analyzed parametrically using the Paired t-test when the differences are normally distributed, or non-parametrically using the Sign-Rank Test when the differences are not normally distributed.

The SAS system statistical package was used to perform all analyses. Exact confidence intervals were generated for estimates of proportions. Asymptotic confidence intervals were generated for estimates of means. The p-values of all tests are reported without any correction for the multiplicity of tests performed.

5. RESULTS

5.1. Clinical Investigation Initiation Date

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5.3. Disposition of Investigational Devices

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Site No.	Site Name	Total # Subjects Enrolled	Total # Devices Delivered to Site	Total # Devices Used	Total # Devices Unused and Transferred to PEARLE ACCESS Study (Continued Access Study)	Total # Unused and Returned
02	St. Mary's Hospital, St. Louis University	(b)(4)				

Site No.	Site Name	Total # Subjects Enrolled	Total # Devices Delivered to Site	Total # Devices Used	Total # Devices Unused and Transferred to PEARLE ACCESS Study (Continued Access Study)	Total # Unused and Returned
04	University of Texas Medical Branch					
05	University of Utah					
06	NewYork Presbyterian/ Queens					
07	NewYork-Presbyterian/ Columbia University Irving Medical Center					
08	Rutgers University / Robert Woods Johnson Hospital					
09	Northwestern University					
10	SSM Health St. Mary's Hospital					
11	University of Alabama - Birmingham					
12	University of Virginia Health System					
14	University of Texas Health Science Center / McGovern School of Medicine					
16	The Ohio State University					
17	MetroHealth / Case Western					
19	MedStar Washington Hospital					
20	University of Pittsburgh					

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Site No.	Site Name	Total # Subjects Enrolled	Total # Devices Delivered to Site	Total # Devices Used	Total # Devices Unused and Transferred to PEARLE ACCESS Study (Continued Access Study)	Total # Unused and Returned
	Medical Center / Magee Women's Hospital					
21	Indiana University					
22	Geisinger Medical Center					
	TOTAL					

(b)(4)

5.4. Disposition of Subjects and Analysis Cohorts

A total of 107 subjects were enrolled in the study at 12 investigational centers. **Table 04** shows the subject enrollment by investigational center.**Table 04: Enrollment by investigational site.**

Site ID	Investigational Center Name	Number of Subjects Enrolled
02*	St. Mary's Hospital, St. Louis University	(b)(4)
04	University of Texas Medical Branch	
05	University of Utah	
06	NewYork-Presbyterian / Queens	
07	NewYork-Presbyterian/ Columbia University Irving Medical Center	
08	Rutgers University / Robert Woods Johnson Hospital	
09**	Northwestern University	
10*	SSM Health St. Mary's Hospital	
11	University of Alabama / Birmingham	
12	University of Virginia	
14**	University of Texas Health Science Center / McGovern School of Medicine	
16	The Ohio State University	
17	MetroHealth / Case Western	
19	MedStar Washington Hospital	
20	University of Pittsburgh Medical Center / Magee Women's Hospital	
21**	Indiana University	
22	Geisinger Medical Center	
	Total	

*Two (2) centers were terminated without enrollment.

(b)(4) Clinical Studies

(b)(4) Clinical Studies

5.6. Subject Demographics and Obstetrical History

Table 07 summarizes the demographics and obstetrical history characteristics of the enrolled subjects. The median maternal age was 29.2 years with an age range of 19.3 to 51.6 years at time of consent. The majority of subjects (57%) had race reported as "White" with the next most common race reported as "Black or African American" (24.3%). Fifteen percent (15%) of subjects were Hispanic. A majority of subjects enrolled had a high BMI, with 91.6% of subjects classified in the categories of "Pre-obesity" to "Obese Class III." Approximately one-third of all subjects had no prior pregnancies (32.7%) while about one-quarter had three or more prior pregnancies (24.3%). About half of the study subjects had no prior vaginal deliveries (50.5%), and 91.6% of subjects had no prior c-sections.

Over one-third of subjects (36.4%) had anemia at their admission for the study-related delivery while 9.3% were described at baseline as "chronically anemic". PPH had occurred for 8.4% of enrolled subjects following a prior delivery.

Table 07: Subject demographics and obstetrical and medical history.

Subject demographics and obstetrical and medical history	Enrollment Cohort (N=107)
Age (years)	
Mean	29.7
SD	5.54
Median	29.2
Min, Max	19.3, 51.6
Ethnicity	
Hispanic	15.0% (16/107)
Non-Hispanic	82.2% (88/107)
Other	0.9% (1/107)
Refused	1.9% (2/107)
Race	
American Indian/Alaskan Native	0.9% (1/107)
Asian	8.4% (9/107)
Black or African American	24.3% (26/107)
Native Hawaiian or Pacific Islander	0.0% (0/107)
White	57.0% (61/107)
Other	7.5% (8/107)
Refused	1.9% (2/107)

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(b)(4) Clinical Studies

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Table 18: Adverse Events possibly related to device or procedure.

Subject ID	Detail	Event Description	Relatedness to Device	Relatedness to Procedure	Type of Delivery

(b)(6) Patient Data

(b)(6) Patient Data

5.11.2. Adverse Events

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Table 19: Adverse Events

		Safety / ITT Cohort (N=106)			
		Possibly related to procedure or device		Not related	
		n (%)	# events	n (%)	# events

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(b)(4) Clinical Studies

(b)(6) Patient Data

5.12. Effectiveness Results

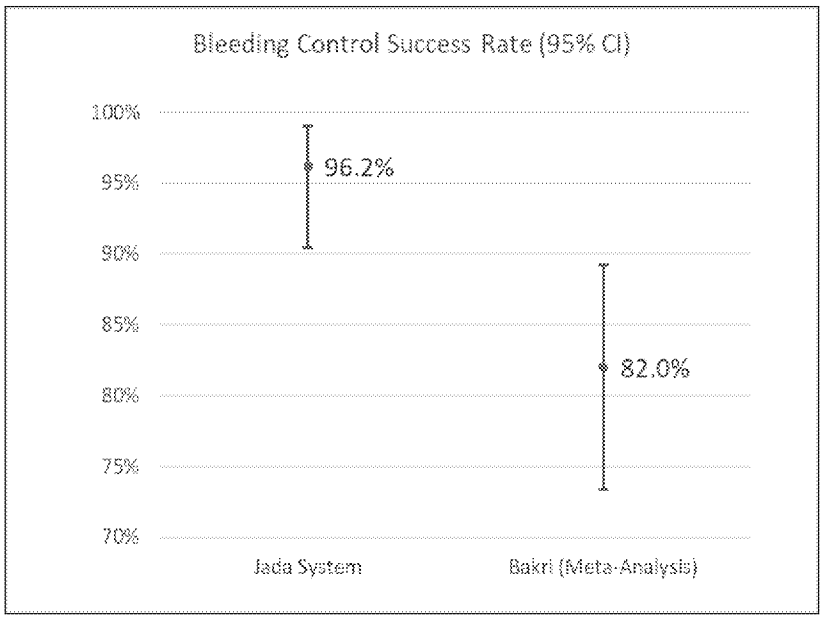
5.12.1. Primary Endpoint

The analysis of effectiveness was based on the 106 subjects in the Safety/ITT Cohort. Results from the 104 subjects in the mITT Cohort and 97 subjects in the PP Cohort are also presented. The primary effectiveness outcome is presented in **Table 21.** The treatment success rate in the Safety/ITT Cohort was 94.3% (100/106) (p<0.001), with a lower bound 95% confidence limit of 88.1%. Based on this observed success rate, the Jada treatment success rate is non-inferior to the treatment success rate of the Bakri Balloon in the meta-analysis, which was 82.0% (95% CI: 73.4% to 89.2%). The confidence intervals for the mITT and PP Cohorts do not overlap with the Bakri comparator -- the lower bound of the mITT Jada confidence interval shown in **Figure 07** is higher than the upper bound of the Bakri confidence interval.

Table 21: Primary effectiveness outcome.

Analysis Data set	N	Treatment Success	95% Confidence Limit (2-sided)	*P* value
Safety/ITT	106	94.3% (100/106)	88.1%, 97.9%	<0.001
mITT	104	96.2% (100/104)	90.4%, 98.9%	<0.001
PP	97	99.0% (96/97)	94.4%, 100%	<0.001

Figure 07: mITT Jada success rate compared to meta-analysis of Bakri.



The cases that met the criteria for failure per the pre-defined criteria are described in **Appendix 9.7**.

5.12.2. Poolability

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(b)(4) Clinical Studies

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Table 27. Summary of non-surgical interventions after Jada treatment.

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Table 28. Summary of surgical interventions after Jada treatment.

	Safety/ITT (N=106)		mITT (N=104)		PP (N=97)	
	% (n/N)	95% Confidence Interval	% (n/N)	95% Confidence Interval	% (n/N)	95% Confidence Interval
Surgical treatment	(b)(4)					
B-Lynch added to Jada						
B-Lynch followed by hysterectomy						
Hysterectomy						

5.13.3. Device Usability

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(b)(4) Clinical Studies

6. CONCLUSIONS

The Jada System offers significant potential to improve outcomes for women experiencing abnormal postpartum uterine bleeding or hemorrhage. In study subjects described above, and consistent with the initial clinical experience in Indonesia and Uganda, use of Jada has been shown to be effective in controlling uterine bleeding within minutes, with only rare need for

further intervention to control bleeding, and with no adverse events definitely related to the device or procedure. The investigators also reported high ratings for ease of use with the Jada System. Finally, the Jada System offers additional value due to its unique mechanism of action, and its ability to provide observable confirmation of bleeding control, allowing for changes in patient management, if needed, on a more urgent basis.

6.1.1. Safety and Performance Results and Other Endpoints

The primary endpoint was overwhelmingly met, in the Safety/ITT Cohort with 94.3% (lower bound 95% confidence limit of 88.1%), achieving the pre-defined criterion for success of non-inferiority ($p<0.001$) to the 82.0% (95% CI: 73.4% to 89.2%) treatment success rate of the Bakri Balloon in the meta-analysis. The treatment success rate in the mITT Cohort was 96.2% (lower bound 95% confidence limit is 90.4%), and in the PP treatment success was 99% (lower bound confidence limit is 94.4%), where both mITT Cohort and PP Cohort show non-overlapping confidence intervals as measured against the Bakri Balloon success rate.

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7. ETHICS

7.1. Confirmation that the CIP and Amendments were Reviewed by the IRBs

The protocol and amendments were reviewed by IRBs for participating sites prior to performance of study activities described in the protocol / amendment. FDA approval of IDE supplements related to the amendments was also obtained prior to implementation of the protocol amendments.

7.2. List of IRBs/ECs consulted

The list of IRBs that reviewed the study is included in **Appendix 9.6**.

8. INVESTIGATORS AND ADMINISTRATIVE STRUCTURE OF CLINICAL INVESTIGATION

8.1. Brief Description of the Organization of the Clinical Investigation

Mary D'Alton, MD, served as the Principal Investigator for the study. Investigators are listed in **Appendix 9.3**.

The Sponsor (Alydia Health) was responsible for study administration, monitoring, and investigational device management. Monitors were qualified by training and experience and were employed by, or consultants to, Alydia Health. No contract research organization was employed. The curriculum vitae of the monitors are on file at Alydia Health.

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Alydia Health.

8.2. List of Investigators and Affiliations

A list of investigators and affiliate sites are included as **Appendix 9.3.**

8.3. Names and Addresses of Third Parties

A list of names and addresses of third parties are included as **Appendix 9.4.**

8.4. Name and Address of Sponsor

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Alydia Health, Inc.
3495 Edison Way
Menlo Park, CA 94025

9. APPENDICES TO THE REPORT

9.1 CIP (version 2.6)

Attached is the most recent version of the protocol that was used for the study (version 2.6), dated February 25, 2019.

9.2 Instructions for Use (version 3.2)

Attached is the most recent version of the IFU that was used in the study (version 3.2).

9.3 List of Investigators and Affiliated Sites

9.4 List of Third Parties

9.5 List of Monitors

9.6 List of IRBs/ECs

9.7 List of Failures

9.8 Raw Data Listings

SECTION 10: PRIOR SUBMISSIONS

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(b)(4) Proprietary Information

(b)(4) Proprietary Information

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Sponsor:
(b)(4)
Alydia Health, Inc.
3495 Edison Wy
Menlo Park, CA 94025

Rabbit Pyrogen Test (Material Mediated) – ISO (GLP)

Test Article:
Purchase Order:
Study Number:
Study Received Date:
Testing Facility:
Deviations:

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28 Feb 2020
Date

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(b)(4) TEST PROTOCOL
FDA GLP REGULATIONS
FILE COPY/CONFIDENTIAL PROPERTY OF TOXIKON

RABBIT PYROGEN TEST (MATERIAL MEDIATED) – ISO

(b)(4)

21 CFR Part 58 Compliance
Good Laboratory Practice for Nonclinical Laboratory Studies

MANAGEMENT OF THE STUDY

(b)(4)

Sponsor

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CE 0088

Bakri Postpartum Balloon
Instructions for Use

Tampónovací balónek Bakri
Návod k použití

Bakri postpartum-ballon
Brugsanvisning

Bakri Postpartum-Ballon
Gebrauchsanweisung

Επιλόχειο μπαλόνι Bakri
Οδηγίες χρήσης

Balón de postparto de Bakri
Instrucciones de uso

Ballonnet post-partum de Bakri
Mode d'emploi

Bakri post partum ballon
Használati utasítás

Palloncino post-parto Bakri
Istruzioni per l'uso

Bakri-postpartumballon
Gebruiksaanwijzing

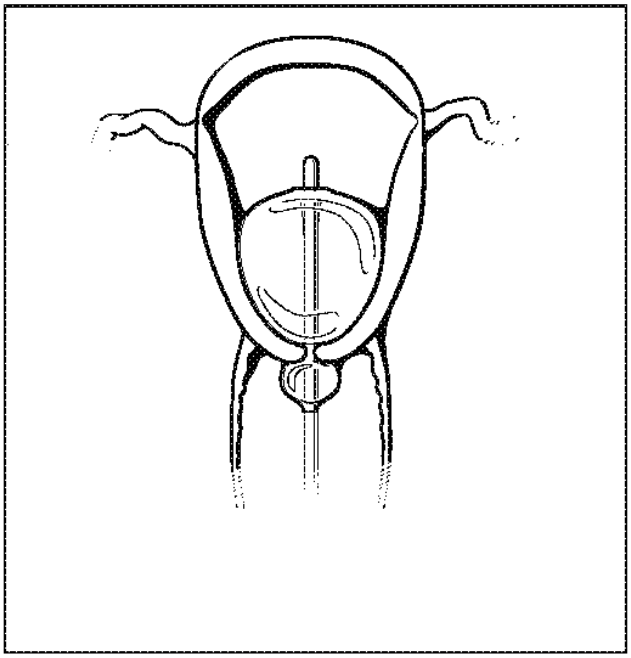
Bakri-postpartumballong
Bruksanvisning

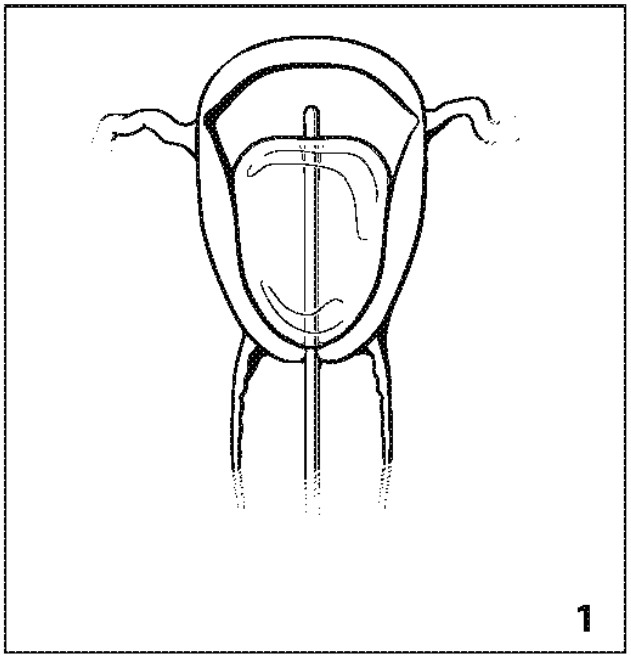
Balon poporodowy Bakriego
Instrukcja użycia

Balão pós-parto Bakri
Instruções de utilização

Bakri postpartumballong
Bruksanvisning

T_J-SOSR_REV2





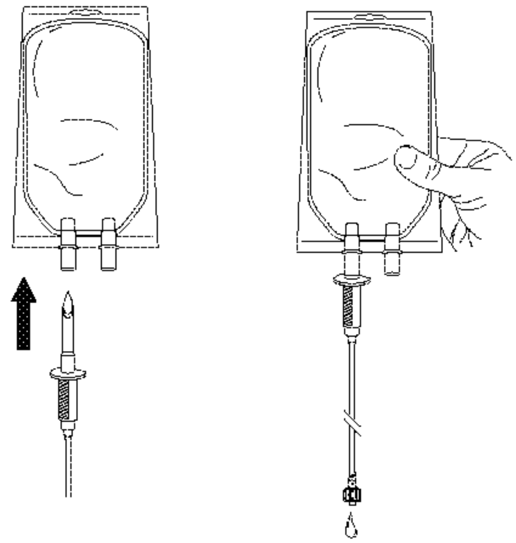
1

Improper Placement

Nesprávné umístění
Ukorrekt anlæggelse
Falsche Platzierung
Εσφαλμένη τοποθέτηση
Colocación incorrecta
Mise en place incorrecte
Nem megfelelő behelyezés
Posizionamento errato
Verkeerd geplaatst
Feil plassering
Umieszczenie nieprawidłowe
Colocação incorreta
Felaktig placering

Proper Placement

Správné umístění
Korrekt anlæggelse
Richtige Platzierung
Σωστή τοποθέτηση
Colocación correcta
Mise en place correcte
Megfelelő behelyezés
Posizionamento corretto
Correct geplaatst
Riktig plassering
Umieszczenie prawidłowe
Colocação correta
Korrekt placering



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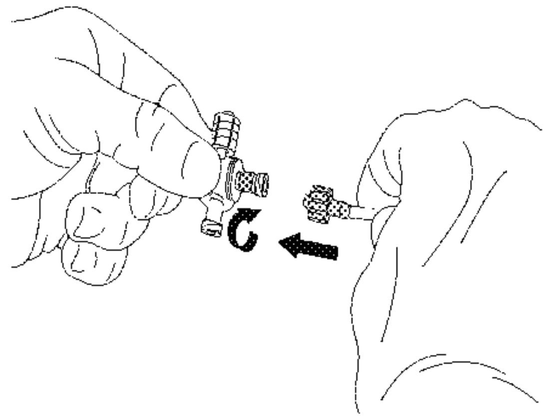

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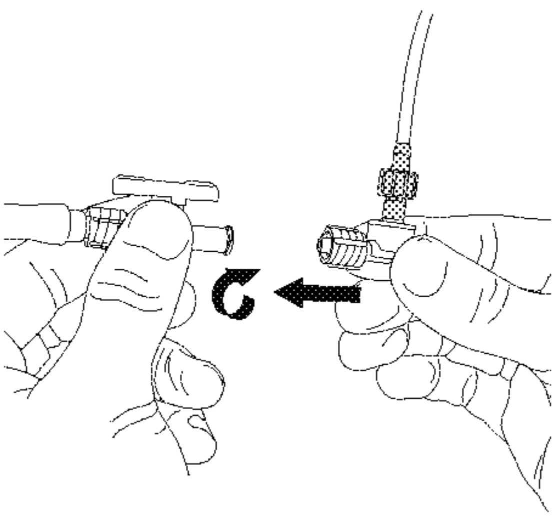

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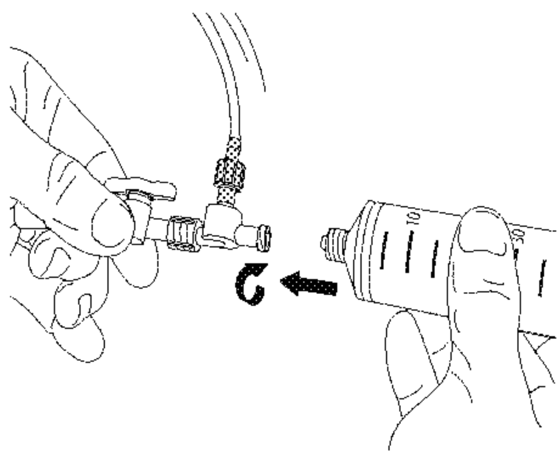

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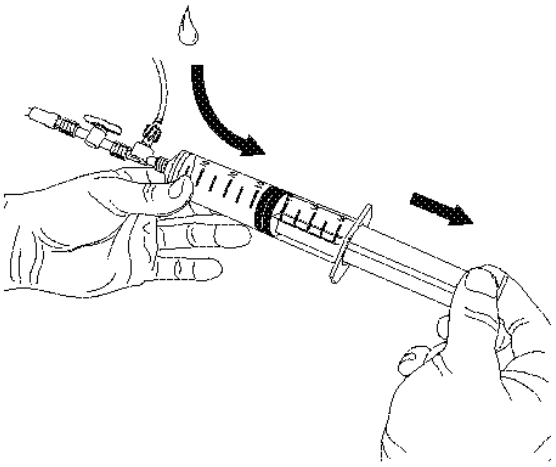

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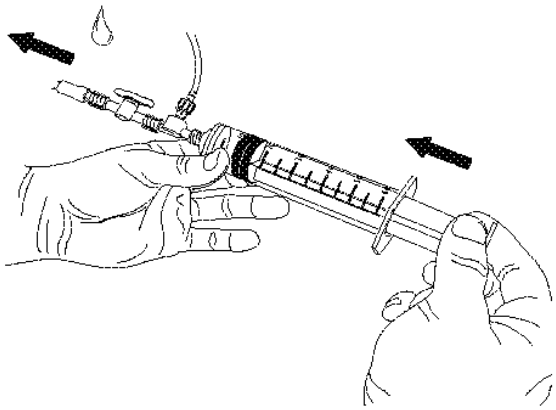

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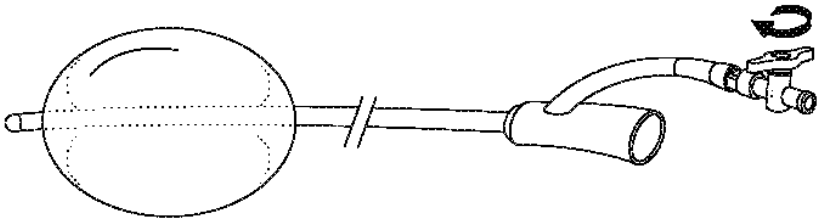

8

BAKRI POSTPARTUM BALLOON

CAUTION: U.S. federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

DEVICE DESCRIPTION

The Bakri Postpartum Balloon is a silicone balloon catheter with a maximum inflation volume of 500 mL. The Rapid Instillation Components include polymer tubing with an IV bag spike and three-way valve.

INTENDED USE

This device is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.

CONTRAINDICATIONS

- Arterial bleeding requiring surgical exploration or angiographic embolization
- Cases indicating hysterectomy
- Pregnancy
- Cervical cancer
- Purulent infections in the vagina, cervix, or uterus
- Untreated uterine anomaly
- Disseminated intravascular coagulation
- A surgical site that would prohibit the device from effectively controlling bleeding

WARNINGS

- This device is intended as a temporary means of establishing hemostasis in cases indicating conservative management of postpartum uterine bleeding.
- The Bakri Postpartum Balloon is indicated for use in the event of primary postpartum hemorrhage within 24 hours of delivery.
- The device should not be left indwelling for more than 24 hours.
- The balloon should be inflated with a sterile liquid such as sterile water, sterile saline, or lactated ringers solution. The balloon should never be inflated with air, carbon dioxide or any other gas.
- The maximum inflation is 500 mL. Do not overinflate the balloon. Overinflation of the balloon may result in the balloon being displaced into the vagina.
- Patients in whom this device is being used should be closely monitored for signs of worsening bleeding and/or disseminated intravascular coagulation (DIC). In such cases, emergency intervention per hospital protocol should be followed.
- There are no clinical data to support use of this device in the setting of DIC.
- Patient monitoring is an integral part of managing postpartum hemorrhage. Signs of deteriorating or non-improving condition should lead to a more aggressive treatment and management of patient uterine bleeding.
- Patient urine output should be monitored while the Bakri Postpartum Balloon is in use.

PRECAUTIONS

- This product is intended for use by physicians trained and experienced in obstetrics and gynecological techniques.
- Avoid excessive force when inserting the balloon into the uterus.

INSTRUCTIONS FOR USE

IMPORTANT: Prior to transvaginal or transabdominal placement of the Bakri Postpartum Balloon, the uterus should be free of all placental fragments, and the patient should be evaluated to ensure that there are no lacerations or trauma to the genital tract and that the source of the bleeding is not arterial.

Transvaginal Placement

1. Determine uterine volume by direct examination or ultrasound examination.
2. Insert the balloon portion of the catheter into the uterus, making certain that the entire balloon is inserted past the cervical canal and internal ostium.
3. Place an indwelling urinary bladder Foley catheter at this time, if not already in place, to collect and monitor urine output.

Transabdominal Placement, Post-Cesarean Section

1. Determine uterine volume by direct examination.
2. From above, via access of the cesarean incision, pass the tamponade balloon, inflation port first, through the uterus and cervix.

NOTE: Remove the stopcock to aid in placement and reattach prior to filling balloon.

3. Have an assistant pull the shaft of the balloon through the vaginal canal until the deflated balloon base comes into contact with the internal cervical ostium.
4. Close the incision per normal procedure, taking care to avoid puncturing the balloon while suturing.

NOTE: Ensure that all product components are intact and the hysterotomy is securely sutured prior to inflating the balloon. If clinically relevant, the abdomen may remain open upon inflation of the balloon to closely monitor uterine distention and confirm the hysterotomy closure.

NOTE: If clinically relevant, a B-Lynch compression suture may be used in conjunction with the Bakri Postpartum Balloon.

Balloon Inflation

With Syringe

WARNING: Always inflate the balloon with sterile liquid. Never inflate with air, carbon dioxide or any other gas.

WARNING: The maximum inflation is 500 mL. Do not overinflate the balloon. Overinflation of the balloon may result in the balloon being displaced into the vagina.

NOTE: To ensure that the balloon is filled to the desired volume, it is recommended that the predetermined volume of fluid be placed in a separate container, rather than relying on a syringe count to verify the amount of fluid that has been instilled into the balloon.

1. Place an indwelling urinary bladder Foley catheter at this time, if not already in place, to collect and monitor urine output.
2. Using the enclosed syringe, begin filling the balloon to the predetermined volume through the stopcock.
3. Once the balloon has been inflated to the predetermined volume, confirm placement via ultrasound. **NOTE: See Fig. 1 for proper placement.**
4. If desired, traction can be applied to the balloon shaft. In order to maintain tension, secure the balloon shaft to the patient's leg or attach to a weight, not to exceed 500 grams.

NOTE: To prevent displacement of the balloon into the vagina, counterpressure can be applied by packing the vaginal canal with iodine- or antibiotic-soaked vaginal gauze.

5. Connect the drainage port to a fluid collection bag to monitor hemostasis.

NOTE: To adequately monitor hemostasis, the balloon drainage port and tubing may be flushed clear of clots with sterile isotonic saline.

6. Monitor the patient continuously for signs of increased bleeding and uterine cramping.

Balloon Inflation

With Rapid Instillation Components

See **Figs. 2-8**, at the front of this booklet.

NOTE: Ultrasound should be used to confirm proper placement of the balloon once the balloon is inflated to the predetermined volume.

Balloon Removal

NOTE: The timing of balloon removal should be determined by the attending clinician upon evaluation of the patient once bleeding has been controlled and the patient has been stabilized. The balloon may be removed sooner upon the clinician's determination of hemostasis. The maximum indwell time is 24 hours.

1. Remove tension from the balloon shaft.
2. Remove any vaginal packing.
3. Using an appropriate syringe, aspirate the contents of the balloon until fully deflated. The fluid may be removed incrementally to allow periodic observation of the patient.

NOTE: In an emergent situation, the catheter shaft may be cut to facilitate more rapid deflation.

4. Gently retract the balloon from the uterus and vaginal canal and discard.
5. Monitor patient for signs of bleeding.

HOW SUPPLIED

Supplied sterilized by ethylene oxide gas in peel-open packages. Intended for one-time use. Sterile if package is unopened and undamaged. Do not use the product if there is doubt as to whether the product is sterile. Store in a dark, dry, cool place. Avoid extended exposure to light. Upon removal from the package, inspect the product to ensure no damage has occurred.

REFERENCE

These instructions for use are based on experience from physicians and (or) their published literature. Refer to your local Cook sales representative for information on available literature.

ČESKY

TAMPÓNOVACÍ BALÓNEK BAKRI

POZOR: Federální zákony USA dovolují prodej tohoto prostředku pouze lékařům nebo na předpis lékaře (nebo kvalifikovaného zdravotníka s licencí).

POPIS PROSTŘEDKU

Tampónovací balónek Bakri je silikonový balónkový katetr s maximálním plnicím objemem 500 mL. Komponenty pro rychlé vstřikování zahrnují polymerovou hadičku s bodcem na IV vak a trojcestný ventil.

URČENÉ POUŽITÍ

Tento prostředek je určen k dočasnému zvládnutí nebo ke snížení postpartálního krvácení z dělohy, pokud jsou důvody ke konzervativní léčbě.

KONTRAINDIKACE

- Tepenné krvácení vyžadující chirurgickou revizi nebo angiografickou embolizaci
- Případy, kdy je indikována hysterektomie
- Těhotenství
- Rakovina děložního hrdla
- Hnisavé infekce pochvy, děložního hrdla nebo dělohy
- Neléčený abnormální stav dělohy

- Diseminovaná intravaskulární koagulopatie
- Místo chirurgického zákroku, kde prostředek nemůže účinně fungovat při zástavě krvácení

VAROVÁNÍ

- Tento prostředek je určen k dočasnému navození hemostáze v případech, kde je indikována konzervativní léčba postpartálního děložního krvácení.
- Tampónovací balónek Bakri je indikován k použití v případě primárního postpartálního krvácení v období 24 hodin po porodu.
- Prostředek se nesmí ponechat zavedený v těle déle než 24 hodin.
- Balónek se plní sterilní kapalinou, např. sterilní vodou, sterilním fyziologickým roztokem nebo složeným roztokem mléčnanu sodného (Ringer-laktátový roztok). Balónek nikdy nenaplňujte vzduchem, oxidem uhličitým ani jiným plynem.
- Maximální objem náplně je 500 mL. Balónek nepřeplňte. Přeplnění balónků může vést k jeho dislokaci do vagíny.
- Pacientky, u kterých se tento prostředek použije, musí být pečlivě sledovány, zda nejeví známky zhoršeného krvácení nebo diseminované intravaskulární koagulopatie. V takových případech se musí provést nouzová intervence podle nemocničního protokolu.
- Neexistují žádné klinické údaje na podporu použití tohoto prostředku v případech diseminované intravaskulární koagulopatie.
- Monitorování pacientky je nedílnou součástí léčby postpartálního krvácení. Známky nezlepšujícího se nebo zhoršeného stavu musí vést k agresivnějším způsobům léčby pacientky s děložním krvácením.
- Při použití tampónovacího balónku Bakri se musí u pacientky monitorovat výdej moči.

UPOZORNĚNÍ

- Tento výrobek je určen k použití lékaři, kteří jsou vyškoleni v porodnických a gynekologických výkonech a mají s nimi zkušenosti.
- Při zavádění balónku do dělohy nepoužívejte nadměrnou sílu.

NÁVOD K POUŽITÍ

DŮLEŽITÉ: Před transvaginálním (pochvou) nebo transabdominálním (břichem) umístěním tampónovacího balónku Bakri nesmí být v děloze zbytky placenty a pacientka musí být vyhodnocena, zda nemá tržné rány nebo jiná poranění genitálií, a zda se nejedná o tepenné krvácení.

Zavedení pochvou

1. Zjistěte objem dělohy přímým nebo ultrazvukovým vyšetřením.
2. Zaveďte balónkovou část katetru do dělohy a zkontrolujte, že je celý balkónek zaveden za kanál děložního hrdla a vnitřního ústí.
3. V této fázi zaveďte trvalou cévku Foley do močového měchýře, pokud již není zavedena, pro sledování odtoku moči a její sběr.

Zavedení břichem, po císařském řezu

1. Zjistěte objem dělohy přímým vyšetřením.
2. Přístupem skrz incizi císařského řezu shora zaveďte tampónovací balónek skrz dělohu a děložní hrdlo, plnicím portem napřed.

POZNÁMKA: Na pomoc při zavedení sejměte uzavírací kohout a před plněním balónku jej znovu připevněte.

3. Požádejte asistenta, aby zatáhl za tubus balónku skrz poševní kanál, až se základna vyprázdněného balónku dotkne vnitřního ústí děložního hrdla.
4. Normální technikou uzavřete incizi a dávejte pozor, aby při šití nedošlo k propíchnutí balónku.

POZNÁMKA: Před naplněním balónku se přesvědčte, že všechny součásti výrobku jsou intaktní a že

hysterotomie je bezpečně uzavřená suturou. Pokud je to klinicky relevantní, břicho může po naplnění balónku zůstat otevřené pro sledování distenze dělohy a potvrzení uzavření hysterotomie.

POZNÁMKA: Pokud je to klinicky relevantní, může se společně s tampónovacím balónkem Bakri použít kompresní steh B-Lynch.

Plnění balónku

Se stříkačkou

VAROVÁNÍ: Balónek naplňujte vždy sterilní tekutinou. Nikdy je nenaplňujte vzduchem, oxidem uhličitým ani jiným plynem.

VAROVÁNÍ: Maximální objem náplně je 500 mL. Balónek nepřeplňte. Přeplnění balónků může vést k jeho dislokaci do vagíny.

POZNÁMKA: Je nutno zajistit, aby balónek byl naplněn na požadovaný objem. Doporučujeme připravit předem určený objem kapaliny do samostatné nádobky. Pro ověření objemu, který byl vstříknut do balónku, nespoléhejte na dávkování stříkačkou.

1. V této fázi zaveďte trvalou cévku Foley do močového měchýře, pokud již není zavedena, pro sledování odtoku moči a její sběr.
2. Přiloženou stříkačkou začněte plnit balónek skrz uzavírací kohout na předem určený objem.
3. Jakmile je balónek naplněn na předem určený objem, potvrďte umístění ultrazvukem.
   POZNÁMKA: Správné umístění ilustruje obr. 1.
4. Pokud je to žádoucí, je možné aplikovat tah na tubus balónku. Pro udržení tahu připevněte tubus balónku k noze pacientky nebo na něj připevněte závaží o maximální hmotnosti 500 g.

POZNÁMKA: Abyste předešli nesprávnému umístění balónku v pochvě, lze aplikovat protitlak vyložením poševního kanálu gázovými tampony namočenými v jódovém nebo antibiotikovém přípravku.

5. Připojte drenážní port k vaku určenému pro sběr tekutin a monitorujte hemostázu.

POZNÁMKA: Pro adekvátní monitorování hemostázy se drenážní port balónku a hadičky mohou propláchnout sterilním izotonickým fyziologickým roztokem, aby v nich nebyly krevní sraženiny.

6. Nepřetržitě sledujte, zda se u pacientky neobjevují známky zvýšeného krvácení a děložních křečí.

Plnění balónku

S komponentami pro rychlé vstřikování

Viz **obr. 2-8** na začátku této brožurky.

POZNÁMKA: Jakmile je balónek naplněn na předem určený objem, musí se ultrazvukem potvrdit správná poloha balónku.

Vyjmutí balónku

POZNÁMKA: Dobu odstranění balónku určí ošetřující lékař po vyhodnocení pacientky, jakmile se krvácení dostane pod kontrolu a pacientka je stabilizována. Balónek lze vyjmout dříve, podle lékařova hodnocení hemostázy. Maximální doba zavedení je 24 hodin.

1. Odstraňte tah aplikovaný na tubus balónku.
2. Vyjměte všechny tampónovací materiály z pochvy.
3. Vhodnou stříkačkou odsajte obsah balónku a zcela jej vyprázdněte. Kapalina se může odstraňovat po částech, aby bylo možné pravidelné sledování pacientky.

POZNÁMKA: V naléhavé situaci se může tubus katetru odstřihnout, aby se urychlilo vyprazdňování.

4. Jemně vytáhněte balónek z dělohy a poševního kanálu a zlikvidujte jej.
5. Sledujte, zda u pacientky nedochází ke krvácení.

STAV PŘI DODÁNÍ

Výrobek je dodáván v odtrhovacím obalu a je sterilizován plynným ethylenoxidem. Určeno pro jednorázové použití. Sterilní, pokud obal není otevřen nebo poškozen. Nepoužívejte výrobek, pokud existují pochybnosti o jeho sterilitě. Skladujte na tmavém, suchém a chladném místě. Zamezte dlouhodobému vystavení světlu. Po odstranění obalu výrobek prohlédněte a zkontrolujte, zda není poškozený.

LITERATURA

Tento návod k použití je založen na zkušenostech lékařů a (nebo) na jejich publikované odborné literatuře. S otázkami na dostupnou literaturu se obraťte na svého nejbližšího obchodního zástupce společnosti Cook.

DANSK

BAKRI POSTPARTUM-BALLON

FORSIGTIG: I henhold til amerikansk lovgivning må dette produkt kun sælges af en læge eller efter en læges ordination (eller en autoriseret behandler).

BESKRIVELSE AF PRODUKTET

Bakri postpartum-ballonen er et silikoneballonkateter med et maksimalt inflationsvolumen på 500 mL. De hurtige instillationskomponenter omfatter polymerslange med en kanyle og trevejs ventil til I.V.-pose.

TILSIGTET ANVENDELSE

Denne anordning er beregnet til at give midlertidig kontrol eller reduktion af postpartum blødning i uterus, hvor konservativ behandling er berettiget.

KONTRAINDIKATIONER

- Arterieblødning, der kræver en kirurgisk undersøgelse eller angiografisk embolisering
- Tilfælde, hvor hysterektomi er indiceret
- Graviditet
- Livmoderhalskræft
- Pusdannende infektioner i vagina, cervix eller uterus
- Ubehandlet anomali i uterus
- Dissemineret intravaskulær koagulation
- Et operationssted, der ville forhindre anordningen i at kontrollere blødning effektivt

ADVARSLER

- Anordningen er beregnet som et midlertidigt middel til etablering af hæmostase i tilfælde, hvor konservativ behandling af postpartum blødning i uterus er indiceret.
- Bakri postpartum-ballonen er indiceret til brug i tilfælde af primær postpartum blødning inden 24 timer efter fødslen.
- Anordningen må ikke forblive indlagt længere end 24 timer.
- Ballonen skal inflateres med en steril væske såsom sterilt vand, sterilt saltvand eller Ringers laktat. Ballonen må aldrig inflateres med luft, kuldioxid eller nogen anden luftart.
- Maksimal fyldning er 500 mL. Ballonen må ikke overudspiles. Overudspiling af ballonen kan resultere i, at ballonen forskubbes i vagina.
- Patienter, hos hvem anordningen anlægges, skal overvåges nøje for tegn på forværret blødning og/eller dissemineret intravaskulær koagulation (DIC). I disse tilfælde skal akut intervention finde sted, i henhold til hospitalsprotokollen.
- Der findes ingen kliniske data til understøttelse af brugen af anordningen ved DIC.
- Patientovervågning er en integreret del af behandlingen af postpartum blødning. Tegn på en tilstand i forværring og som ikke viser tegn på bedring, bør følges af mere aggressiv behandling og styring af patientens blødning i uterus.
- Patientens urinproduktion skal overvåges, så længe Bakri postpartum-ballonen er i brug.

FORHOLDSREGLER

- Dette produkt er beregnet til brug for læger med uddannelse og erfaring i obstetrik og gynækologiske teknikker.

- Undgå for stor kraft ved indsætning af ballonen i uterus.

BRUGSANVISNING

VIGTIGT: Inden transvaginal eller transabdominal anlæggelse af Bakri postpartum-ballonen skal uterus være fri for alle placentarester, og patienten skal evalueres for at sikre, at der ikke er rifter eller traume i genitaltrakten, og at årsagen til blødningen ikke er arteriel.

Transvaginal anlæggelse

1. Bestem volumen af uterus ved direkte undersøgelse eller med ultralyd.
2. Indsæt ballondelen af kateteret i uterus, og sørg for, at hele ballonen føres forbi cervikalkanalen og interne ostium.
3. Anlæg et indlagt Foley-kateter i urinblæren på dette tidspunkt, hvis dette ikke allerede er gjort, for at opsamle og overvåge urinproduktionen.

Transabdominal anlæggelse, efter kejsersnit

1. Bestem volumen af uterus ved direkte undersøgelse.
2. Fra oven føres tamponadeballonen via kejsersnitåbningen, og med inflationsporten først, igennem uterus og cervix.

BEMÆRK: Fjern stophanen for at lette anlæggelse og sæt den på igen, inden ballonen fyldes.

3. Få en assistent til at trække ballonens skaft igennem vaginalkanalen, indtil det nederste af den tømte ballon kommer i kontakt med interne cervicale ostium.
4. Luk incisionen på normal vis. Udvis forsigtighed for at undgå at stikke hul i ballonen ved sutureringen.

BEMÆRK: Sørg for at alle produktkomponenter er intakte, og at hysterotomien er sutureret korrekt, inden ballonen inflateres. Hvis det er klinisk relevant, kan abdomen forblive åbent efter fyldning af ballonen, så udspilingen af uterus kan overvåges, og lukning af hysterotomien bekræftes.

BEMÆRK: Hvis det er klinisk relevant, kan der anvendes en B-Lynch-sutur sammen med Bakri postpartum-ballonen.

Balloninflation

Med sprøjte

ADVARSEL: Ballonen skal altid inflateres med steril væske. Ballonen må aldrig inflateres med luft, kuldioxid eller nogen anden luftart.

ADVARSEL: Maksimal fyldning er 500 mL. Ballonen må ikke overudspiles. Overudspiling af ballonen kan resultere i, at ballonen forskubbes i vagina.

BEMÆRK: For at sikre, at ballonen fyldes til det ønskede volumen, anbefales det, at det forudfastlagte væskevolumen hældes i en særskilt beholder frem for at stole på en måling med sprøjten til at bekræfte den mængde væske, der er instilleret i ballonen.

1. Anlæg et indlagt Foley-kateter i urinblæren på dette tidspunkt, hvis dette ikke allerede er gjort, for at opsamle og overvåge urinproduktionen.
2. Brug den vedlagte sprøjte, og start påfyldningen af ballonen til det forudfastlagte volumen via stophanen.
3. Når ballonen er fyldt til det forudfastlagte volumen, skal anlæggelsen bekræftes med ultralyd.
   BEMÆRK: Se fig. 1 vedrørende korrekt anlæggelse.
4. Hvis ønsket, kan der påføres træk på ballonskaftet. For at opretholde spændingen fastgøres ballonskaftet til patientens ben eller til en vægt, der ikke må overstige 500 gram.

BEMÆRK: For at forhindre at ballonen forskubbes i vagina, kan der påføres modtryk ved at udfylde vaginalkanalen med vaginalgazetamponer gennemvædet med jod eller antibiotika.

5. Tilslut drænageporten til en væskeopsamlingspose for at overvåge hæmostase.

BEMÆRK: For at overvåge hæmostase på korrekt vis, kan ballonens drænageport og slange skylles fri for koagler med sterilt isotonisk saltvand.

6. Overvåg patienten konstant for tegn på øget blødning og uteruskramper.

Balloninflation

Med komponenter til hurtig instillation

Se **fig. 2-8** forrest i denne brochure.

BEMÆRK: Der skal bruges ultralyd til at bekræfte den korrekte placering af ballonen, efter at ballonen er fyldt til det forudfastlagte volumen.

Fjernelse af ballonen

BEMÆRK: Tidspunktet for fjernelse af ballonen skal bestemmes af den tilsynsførende læge efter evaluering af patienten, når blødningen er under kontrol og patienten er stabiliseret. Ballonen kan fjernes tidligere afhængigt af lægens bedømmelse af hæmostase. Den maksimale indlæggelsestid er 24 timer.

1. Udløs spændingen på ballonens skaft.
2. Fjern eventuelle gazetamponer fra vagina.
3. Brug en passende sprøjte, og aspirér indholdet af ballonen, indtil den er helt tom. Væsken kan fjernes gradvist, så patienten kan observeres regelmæssigt.

BEMÆRK: I en nødsituation kan kateterskaftet skæres, så tømningen sker hurtigere.

4. Træk ballonen forsigtigt ud af uterus og vaginalkanalen, og kassér den.
5. Overvåg patienten for tegn på blødning.

LEVERING

Leveres steriliseret med ethylenoxid i peel-open pakninger. Beregnet til engangsbrug. Steril, hvis pakningen er uåbnet eller ubeskadiget. Produktet må ikke bruges, hvis der er tvivl om produktets sterilitet. Opbevares mørkt, tørt og køligt. Undgå længere eksponering for lys. Inspicér produktet efter udtagning fra pakningen for at sikre, at det ikke er beskadiget.

LITTERATUR

Denne brugsanvisning er baseret på lægers erfaring og (eller) lægers publicerede litteratur. Kontakt den lokale salgsrepræsentant for Cook for at få information om tilgængelig litteratur.

DEUTSCH

BAKRI POSTPARTUM-BALLON

VORSICHT: Laut US-Gesetzgebung darf dieses Instrument nur von einem Arzt oder im Auftrag eines Arztes gekauft werden.

BESCHREIBUNG DES INSTRUMENTS

Der Bakri Postpartum-Ballon ist ein Ballonkatheter aus Silikon mit einem maximalen Inflationsvolumen von 500 mL. Die Schnell-Instillationskomponenten umfassen einen Polymerschlauch mit IV-Beuteldorn und Drei-Wege-Ventil.

VERWENDUNGSZWECK

Dieses Produkt dient zur vorübergehenden Kontrolle bzw. Reduzierung postpartaler Uterusblutungen, wenn eine konservative Behandlung gerechtfertigt ist.

KONTRAINDIKATIONEN

- Arterielle Blutungen, die eine chirurgische Sondierung oder angiographische Embolisation erfordern
- Bestehende Indikation für eine Hysterektomie
- Schwangerschaft
- Zervixkarzinom
- Eitrige Infektionen in Vagina, Zervix oder Uterus
- Unbehandelte Uterusanomalien

- Disseminierte intravasale Koagulopathie
- Operationsstelle, die eine wirksame Blutungskontrolle durch das Produkt verhindern würde

WARNHINWEISE

- Dieses Produkt ist zur vorübergehenden Anwendung bei der Stillung von postpartalen Uterusblutungen bestimmt, wenn eine konservative Behandlung gerechtfertigt ist.
- Der Bakri Postpartum-Ballon ist zur Anwendung im Falle von primären postpartalen Blutungen innerhalb von 24 Stunden nach der Geburt bestimmt.
- Das Produkt darf nicht länger als 24 Stunden im Körper verweilen.
- Der Ballon ist mit einer sterilen Flüssigkeit wie sterilem Wasser, steriler Kochsalzlösung oder Ringer-Laktat-Lösung zu inflatieren. Der Ballon darf niemals mit Luft, Kohlendioxid oder sonstigem Gas inflatiert werden.
- Das maximale Inflationsvolumen beträgt 500 mL. Den Ballon nicht überinflatieren. Wird der Ballon überinflatiert, kann es dazu kommen, dass der Ballon in die Vagina verschoben wird.
- Patientinnen mit diesem Produkt müssen sorgfältig auf Anzeichen einer verschlimmerten Blutung und/oder disseminierten intravasalen Koagulopathie (DIC) überwacht werden. In solchen Fällen ist eine Notintervention nach dem Protokoll des jeweiligen Krankenhauses einzuleiten.
- Zum Einsatz dieses Produkts bei DIC liegen keine klinischen Daten vor.
- Die Überwachung der Patientin ist ein integraler Bestandteil der Beherrschung postpartaler Blutungen. Bei Anzeichen einer Verschlimmerung oder ausbleibenden Besserung der Symptome ist eine aggressivere Behandlung der Uterusblutung einzuleiten.
- Während der Anwendung des Bakri Postpartum-Ballons ist die ausgeschiedene Urinmenge der Patientin zu überwachen.

VORSICHTSMASSNAHMEN

- Dieses Produkt ist zur Verwendung durch Ärzte bestimmt, die in obstetrischen und gynäkologischen Techniken geschult und erfahren sind.
- Beim Einführen des Ballons in den Uterus keine übermäßige Kraft aufwenden.

GEBRAUCHSANWEISUNG

WICHTIG: Vor der transvaginalen bzw. transabdominalen Einführung des Bakri Postpartum-Ballons sollte der Uterus frei von Plazentaresten sein und es sollte eine Beurteilung der Patientin stattfinden, um sicherzustellen, dass im Genitaltrakt weder Lazerationen noch Traumata vorliegen und dass der Ursprung der Blutung nicht arteriell ist.

Transvaginale Einführung

1. Uterusvolumen durch direkte Untersuchung oder Ultraschall ermitteln.
2. Den Ballonanteil des Katheters in den Uterus einführen und darauf achten, dass der gesamte Ballon den Zervixkanal und den inneren Muttermund passiert.
3. Zum Auffangen von Urin und zur Kontrolle des Urinvolumens einen Foley-Verweilkatheter in die Harnblase legen, falls nicht bereits geschehen.

Transabdominale Einführung nach einer Kaiserschnittentbindung

1. Uterusvolumen durch direkte Untersuchung ermitteln.
2. Den Tamponadeballon von oben her und mit dem Inflationszugang voran über die Kaiserschnittinzision durch Uterus und Zervix führen.

HINWEIS: Zur leichteren Einführung Absperrhahn entfernen und vor der Füllung des Ballons wieder anbringen.

3. Die Assistenz bitten, den Ballonschaft durch den Vaginalkanal zu ziehen, bis die Basis des deflatierten Ballons den inneren Muttermund berührt.
4. Die Inzision wie üblich verschließen und dabei darauf achten, dass der Ballon beim Anlegen der Naht nicht punktiert wird.

HINWEIS: Vor der Inflation des Ballons sicherstellen, dass alle Produktkomponenten intakt sind und die Hysterotomie gut vernäht ist. Falls klinisch relevant, kann das Abdomen bei der Inflation des Ballons geöffnet bleiben, um die Uterusdistension engmaschig zu überwachen und den Verschluss der Hysterotomie zu bestätigen.

HINWEIS: Falls klinisch relevant, kann in Verbindung mit dem Bakri Postpartum-Ballon eine B-Lynch-Kompressionsnaht angebracht werden.

Balloninflation

mittels Spritze

WARNHINWEIS: Den Ballon grundsätzlich mit einer sterilen Flüssigkeit inflatieren. Zur Inflation niemals Luft, Kohlendioxid oder ein anderes Gas verwenden.

WARNHINWEIS: Das maximale Inflationsvolumen beträgt 500 mL. Den Ballon nicht überinflatieren. Wird der Ballon überinflatiert, kann es dazu kommen, dass der Ballon in die Vagina verschoben wird.

HINWEIS: Um sicherzustellen, dass der Ballon auf das vorgesehene Volumen gefüllt wird, wird empfohlen, das zuvor ermittelte Flüssigkeitsvolumen in einen separaten Behälter zu füllen. Dies erleichtert die Kontrolle über die in den Ballon instillierte Flüssigkeitsmenge im Vergleich zum Zählen der Spritzen.

1. Zum Auffangen von Urin und zur Kontrolle des Urinvolumens einen Foley-Verweilkatheter in die Harnblase legen, falls nicht bereits geschehen.
2. Mithilfe der beiliegenden Spritze den Ballon durch den Absperrhahn bis zum zuvor bestimmten Volumen füllen.
3. Sobald der Ballon bis zum zuvor bestimmten Volumen gefüllt wurde, die Platzierung mittels Ultraschall bestätigen.

   HINWEIS: Die richtige Platzierung ist aus Abb. 1 ersichtlich.
4. Bei Bedarf kann Zug auf den Ballonschaft ausgeübt werden. Um den Zug aufrecht zu erhalten, den Ballonschaft am Bein der Patientin befestigen oder ein Gewicht (maximal 500 g) anbringen.

HINWEIS: Um ein Abrutschen des Ballons in die Vagina zu vermeiden, kann ein Gegendruck aufgebaut werden, indem der Vaginalkanal mit in Iodtinktur oder Antibiotika getränktem Vaginalmull ausgefüllt wird.

5. Den Drainageanschluss zur Kontrolle der Hämostase an einen Auffangbeutel für Flüssigkeiten anschließen.

HINWEIS: Um die Hämostase adäquat zu überwachen, können Gerinnsel mit steriler isotonischer Kochsalzlösung aus dem Drainageanschluss des Ballons und dem Schlauch gespült werden.

6. Die Patientin muss kontinuierlich auf Anzeichen für eine verstärkte Blutung oder Uteruskrämpfe überwacht werden.

Balloninflation

mit Schnell-Instillationskomponenten

Siehe **Abb. 2-8** vorne in diesem Handbuch.

HINWEIS: Sobald der Ballon bis zum zuvor bestimmten Volumen gefüllt wurde, sollte seine richtige Platzierung mittels Ultraschall bestätigt werden.

Entfernung des Ballons

HINWEIS: Der Zeitpunkt zur Entfernung des Ballons sollte vom behandelnden Arzt nach erfolgter Auswertung der Patientin, sobald die Blutung kontrolliert und die Patientin stabilisiert wurde, festgelegt werden. Der Ballon kann nach Einschätzung der Hämostase durch den Arzt früher entfernt werden. Die maximale Verweildauer beträgt 24 Stunden.

1. Den Zug am Ballonschaft lösen.
2. Mullfüllung (falls verwendet) aus der Vagina entfernen.
3. Den Inhalt des Ballons mit einer geeigneten Spritze aspirieren, bis dieser vollständig deflatiert ist. Die Flüssigkeit kann schrittweise entfernt werden, um eine periodische Überwachung der Patientin zu ermöglichen.

HINWEIS: In einer Notfallsituation kann der Katheterschaft zur rascheren Deflation eingeschnitten werden.

4. Den Ballon vorsichtig aus dem Uterus und dem Vaginalkanal ziehen und entsorgen.
5. Die Patientin auf Anzeichen für eine Blutung überwachen.

LIEFERFORM

Produkt mit Ethylenoxid gassterilisiert; in Aufreißverpackungen. Nur für den einmaligen Gebrauch. Bei ungeöffneter und unbeschädigter Verpackung steril. Produkt nicht verwenden, falls Zweifel an der Sterilität bestehen. An einem dunklen, trockenen, kühlen Ort lagern. Längere Lichteinwirkung vermeiden. Nachdem das Produkt der Verpackung entnommen wurde, auf Beschädigungen überprüfen.

LITERATUR

Diese Gebrauchsanweisung basiert auf der Erfahrung von Ärzten und/oder auf Fachliteratur. Informationen über verfügbare Literatur erhalten Sie bei Ihrem Cook Außendienstmitarbeiter.

ΕΛΛΗΝΙΚΑ

ΕΠΙΛΟΧΕΙΟ ΜΠΑΛΟΝΙ BAKRI

ΠΡΟΣΟΧΗ: Η ομοσπονδιακή νομοθεσία των Η.Π.Α. επιτρέπει την πώληση της συσκευής αυτής μόνον από ιατρό ή κατόπιν εντολής ιατρού (ή επαγγελματία υγείας ο οποίος έχει λάβει την κατάλληλη άδεια).

ΠΕΡΙΓΡΑΦΗ ΤΗΣ ΣΥΣΚΕΥΗΣ

Το επιλόχειο μπαλόνι Bakri είναι ένας καθετήρας με μπαλόνι σιλικόνης με μέγιστο όγκο πλήρωσης 500 mL. Τα εξαρτήματα ταχείας ενστάλλαξης περιλαμβάνουν σωλήνωση από πολυμερές με ακίδα ασκού ενδοφλέβιας έγχυσης και τρίοδη βαλβίδα.

ΧΡΗΣΗ ΓΙΑ ΤΗΝ ΟΠΟΙΑ ΠΡΟΟΡΙΖΕΤΑΙ

Αυτή η συσκευή προορίζεται για την παροχή προσωρινού ελέγχου ή μείωσης της επιλόχειας αιμορραγίας της μήτρας, όταν είναι επιβεβλημένη η συντηρητική αντιμετώπιση.

ΑΝΤΕΝΔΕΙΞΕΙΣ

- Αρτηριακή αιμορραγία που απαιτεί χειρουργική διερεύνηση ή αγγειογραφικό εμβολισμό
- Περιπτώσεις στις οποίες ενδείκνυται υστερεκτομή
- Κύηση
- Καρκίνος του τραχήλου της μήτρας
- Πυώδεις λοιμώξεις στον κόλπο, στον τράχηλο ή στη μήτρα
- Μη αντιμετωπισθείσα ανωμαλία της μήτρας
- Διάχυτη ενδαγγειακή πήξη
- Θέση χειρουργικής επέμβασης, η οποία δεν θα επέτρεπε τον αποτελεσματικό έλεγχο της αιμορραγίας από τη συσκευή

ΠΡΟΕΙΔΟΠΟΙΗΣΕΙΣ

- Αυτή η συσκευή προορίζεται για χρήση ως προσωρινό μέτρο εξασφάλισης αιμόστασης σε περιπτώσεις στις οποίες ενδείκνυται η συντηρητική αντιμετώπιση της επιλόχειας αιμορραγίας της μήτρας.
- Το επιλόχειο μπαλόνι Bakri ενδείκνυται για χρήση σε περίπτωση πρωτοπαθούς επιλόχειας αιμορραγίας, εντός 24 ωρών από τον τοκετό.
- Η συσκευή δεν θα πρέπει να παραμένει εντός του σώματος για περισσότερες από 24 ώρες.
- Το μπαλόνι θα πρέπει να πληρώνεται με στείρο υγρό, όπως στείρο νερό, στείρος φυσιολογικός ορός ή διάλυμα Ringer's lactate. Η πλήρωση του μπαλονιού δεν θα πρέπει να γίνεται ποτέ με αέρα, διοξείδιο του άνθρακα ή οποιοδήποτε άλλο αέριο.

- Ο μέγιστος όγκος πλήρωσης είναι 500 mL. Μην πληρώσετε υπερβολικά το μπαλόνι. Η υπερβολική πλήρωση του μπαλονιού ενδέχεται να προκαλέσει παρεκτόπιση του μπαλονιού μέσα στον κόλπο.
- Οι ασθενείς στις οποίες χρησιμοποιείται αυτή η συσκευή θα πρέπει να παρακολουθούνται στενά για σημεία επιδείνωσης της αιμορραγίας ή/και διάχυτης ενδαγγειακής πήξης (ΔΕΠ). Σε τέτοιες περιπτώσεις, θα πρέπει να ακολουθείται επείγουσα παρέμβαση σύμφωνα με το πρωτόκολλο του νοσοκομείου.
- Δεν υπάρχουν κλινικά δεδομένα που να υποστηρίζουν τη χρήση αυτής της συσκευής σε περίπτωση ΔΕΠ.
- Η παρακολούθηση της ασθενούς αποτελεί αναπόσπαστο μέρος της αντιμετώπισης της επιλόχειας αιμορραγίας. Σημεία επιδείνωσης ή μη βελτίωσης της κατάστασης θα πρέπει να οδηγήσουν σε πιο επιθετική θεραπεία και αντιμετώπιση της αιμορραγίας της μήτρας της ασθενούς.
- Θα πρέπει να παρακολουθείται η παραγωγή ούρων της ασθενούς για όσο διάστημα χρησιμοποιείται το επιλόχειο μπαλόνι Bakri.

ΠΡΟΦΥΛΑΞΕΙΣ

- Αυτό το προϊόν προορίζεται για χρήση από ιατρούς εκπαιδευμένους και πεπειραμένους σε μαιευτικές και γυναικολογικές τεχνικές.
- Αποφύγετε την άσκηση υπερβολικής δύναμης κατά την εισαγωγή του μπαλονιού στη μήτρα.

ΟΔΗΓΙΕΣ ΧΡΗΣΗΣ

ΣΗΜΑΝΤΙΚΟ: Πριν από τη διακοπλική ή τη διακοιλιακή τοποθέτηση του επιλόχειου μπαλονιού Bakri, θα πρέπει να έχουν αφαιρεθεί από τη μήτρα όλα τα τμήματα του πλακούντα και η ασθενής θα πρέπει να αξιολογείται για να διασφαλιστεί ότι δεν φέρει ρήξεις ή τραύματα στο ουρογεννητικό σύστημα και ότι η πηγή της αιμορραγίας δεν είναι αρτηριακή.

Διακολπική τοποθέτηση

1. Προσδιορίστε τον όγκο της μήτρας με άμεση εξέταση ή με υπερηχογραφική εξέταση.
2. Εισαγάγετε το τμήμα του μπαλονιού του καθετήρα στη μήτρα, επιβεβαιώνοντας ότι ολόκληρο το μπαλόνι έχει εισαχθεί πέρα από τον αυλό του τραχήλου και το έσω στόμιο.
3. Τοποθετήστε έναν μόνιμο καθετήρα Foley ουροδόχου κύστης, εάν δεν έχει ήδη τοποθετηθεί, για συλλογή και παρακολούθηση της παραγωγής ούρων.

Διακοιλιακή τοποθέτηση, μετά από καισαρική τομή

1. Προσδιορίστε τον όγκο της μήτρας με άμεση εξέταση.
2. Από επάνω, διαμέσου της καισαρικής τομής, περάστε το μπαλόνι επιπωματισμού, εισάγοντας πρώτη τη θύρα πλήρωσης, διαμέσου της μήτρας και του τραχήλου της μήτρας.

ΣΗΜΕΙΩΣΗ: Αφαιρέστε τη στρόφιγγα ώστε να διευκολυνθεί η τοποθέτηση και η εκ νέου προσάρτηση πριν από την πλήρωση του μπαλονιού.

3. Ζητήστε από έναν βοηθό να τραβήξει το στέλεχος του μπαλονιού διαμέσου του αυλού του κόλπου μέχρι η βάση του συμπτυγμένου μπαλονιού να έρθει σε επαφή με το έσω τραχηλικό στόμιο.
4. Συγκλείστε την τομή σύμφωνα με την τυπική διαδικασία, προσέχοντας να αποφύγετε την τρώση του μπαλονιού κατά τη συρραφή.

ΣΗΜΕΙΩΣΗ: Βεβαιωθείτε ότι όλα τα εξαρτήματα του προϊόντος είναι άθικτα και ότι η υστεροτομή έχει συρραφεί καλά πριν από την πλήρωση του μπαλονιού. Εάν ενδείκνυται κλινικά, η κοιλιά μπορεί να παραμείνει ανοικτή μετά την πλήρωση του μπαλονιού για τη στενή παρακολούθηση της διάτασης της μήτρας και για την επιβεβαίωση της σύγκλεισης της υστεροτομής.

ΣΗΜΕΙΩΣΗ: Εάν ενδείκνυται κλινικά, μπορεί να χρησιμοποιηθεί ράμμα συμπίεσης B-Lynch σε συνδυασμό με το επιλόχειο μπαλόνι Bakri.

Πλήρωση του μπαλονιού

Με σύριγγα

ΠΡΟΕΙΔΟΠΟΙΗΣΗ: Η πλήρωση του μπαλονιού πρέπει να γίνεται πάντα με στείρο υγρό. Η πλήρωση δεν πρέπει να γίνεται ποτέ με αέρα, διοξείδιο του άνθρακα ή οποιοδήποτε άλλο αέριο.

ΠΡΟΕΙΔΟΠΟΙΗΣΗ: Ο μέγιστος όγκος πλήρωσης είναι 500 mL. Μην πληρώσετε υπερβολικά το μπαλόνι. Η υπερβολική πλήρωση του μπαλονιού ενδέχεται να προκαλέσει παρεκτόπιση του μπαλονιού μέσα στον κόλπο.

ΣΗΜΕΙΩΣΗ: Για να διασφαλίσετε ότι το μπαλόνι θα πληρωθεί έως τον επιθυμητό όγκο, συνιστάται η τοποθέτηση του προκαθορισμένου όγκου του υγρού σε ξεχωριστό περιέκτη, αντί να βασίζεστε στην ποσότητα που μετράται με τη σύριγγα για την επιβεβαίωση της ποσότητας του υγρού που ενσταλάζεται στο μπαλόνι.

1. Τοποθετήστε έναν μόνιμο καθετήρα Foley ουροδόχου κύστης, εάν δεν έχει ήδη τοποθετηθεί, για συλλογή και παρακολούθηση της παραγωγής ούρων.
2. Χρησιμοποιώντας την εσωκλειόμενη σύριγγα, ξεκινήστε την πλήρωση του μπαλονιού έως τον προκαθορισμένο όγκο διαμέσου της στρόφιγγας.
3. Μετά από την πλήρωση του μπαλονιού έως τον προκαθορισμένο όγκο, επιβεβαιώστε την τοποθέτηση με υπέρηχο. **ΣΗΜΕΙΩΣΗ: Για τη σωστή τοποθέτηση, δείτε την Εικ. 1.**
4. Εάν επιθυμείτε, μπορείτε να εφαρμόσετε ήπια έλξη στο στέλεχος του μπαλονιού. Για να διατηρήσετε την τάση, σταθεροποιήστε το στέλεχος του μπαλονιού στην κνήμη της ασθενούς ή προσαρτήστε το σε βάρος που δεν υπερβαίνει τα 500 g.

ΣΗΜΕΙΩΣΗ: Για να αποτραπεί η παρεκτόπιση του μπαλονιού εντός του κόλπου, μπορείτε να εφαρμόσετε αντίθετη πίεση επιπωματίζοντας το κολπικό κανάλι με κολπική γάζα εμποτισμένη με ιώδιο ή αντιβιοτικό.

5. Συνδέστε τη θύρα παροχέτευσης σε ασκό συλλογής υγρών για να παρακολουθείτε την αιμόσταση.

ΣΗΜΕΙΩΣΗ: Για επαρκή παρακολούθηση της αιμόστασης, η θύρα παροχέτευσης του μπαλονιού και η σωλήνωση είναι δυνατόν να εκπλυθούν με στείρο ισότονο φυσιολογικό ορό για να απομακρυνθούν οι θρόμβοι.

6. Παρακολουθείτε συνεχώς την ασθενή για σημεία αυξημένης αιμορραγίας και σπασμών της μήτρας.

Πλήρωση του μπαλονιού

Με εξαρτήματα ταχείας ενστάλαξης

Δείτε τις **Εικ. 2-8**, στο πρόσθιο τμήμα αυτού του φυλλαδίου.

ΣΗΜΕΙΩΣΗ: Θα πρέπει να χρησιμοποιείται υπέρηχος για την επιβεβαίωση της σωστής τοποθέτησης του μπαλονιού μετά από την πλήρωση του μπαλονιού έως τον προκαθορισμένο όγκο.

Αφαίρεση μπαλονιού

ΣΗΜΕΙΩΣΗ: Ο χρόνος αφαίρεσης του μπαλονιού θα πρέπει να προσδιορίζεται από τον θεράποντα κλινικό ιατρό, μετά από αξιολόγηση της ασθενούς, αφού τεθεί υπό έλεγχο η αιμορραγία και σταθεροποιηθεί η κατάσταση της ασθενούς. Είναι δυνατή η αφαίρεση του μπαλονιού νωρίτερα, αφού προσδιοριστεί η επίτευξη αιμόστασης από τον κλινικό ιατρό. Ο μέγιστος χρόνος παραμονής εντός του σώματος είναι 24 ώρες.

1. Άρετε την τάση από το στέλεχος του μπαλονιού.
2. Αφαιρέστε τυχόν επιπωματισμό του κόλπου.
3. Χρησιμοποιώντας κατάλληλη σύριγγα, αναρροφήστε το περιεχόμενο του μπαλονιού μέχρι να συμπτυχθεί πλήρως. Η αφαίρεση του υγρού μπορεί να γίνει σταδιακά για να είναι δυνατή η περιοδική παρακολούθηση της ασθενούς.

ΣΗΜΕΙΩΣΗ: Σε κατάσταση έκτακτης ανάγκης, μπορεί να αποκοπεί το στέλεχος του καθετήρα για να διευκολυνθεί η ταχύτερη σύμπτυξη.

4. Αποσύρετε με ήπιες κινήσεις το μπαλόνι από τη μήτρα και τον αυλό του κόλπου και απορρίψτε το.
5. Παρακολουθείτε την ασθενή για σημεία αιμορραγίας.

ΤΡΟΠΟΣ ΔΙΑΘΕΣΗΣ

Παρέχεται αποστειρωμένο με αέριο οξείδιο του αιθυλενίου σε αποκολλούμενες συσκευασίες. Προορίζεται για μία χρήση μόνο. Στείρο, εφόσον η συσκευασία δεν έχει ανοιχτεί ή δεν έχει υποστεί ζημιά. Μη χρησιμοποιείτε το προϊόν εάν υπάρχει αμφιβολία για τη στειρότητά του. Φυλάσσετε σε σκοτεινό, στεγνό και δροσερό χώρο. Αποφεύγετε την παρατεταμένη έκθεση στο φως. Κατά την αφαίρεση από τη συσκευασία, επιθεωρήστε το προϊόν για να βεβαιωθείτε ότι δεν έχει υποστεί ζημιά.

ΒΙΒΛΙΟΓΡΑΦΙΚΕΣ ΑΝΑΦΟΡΕΣ

Αυτές οι οδηγίες χρήσης βασίζονται στην εμπειρία από ιατρούς ή/και τη δημοσιευμένη βιβλιογραφία τους. Απευθυνθείτε στον τοπικό σας σντιπρόσωπο πωλήσεων της Cook για πληροφορίες σχετικά με τη διαθέσιμη βιβλιογραφία.

ESPAÑOL

BALÓN DE POSTPARTO DE BAKRI

AVISO: Las leyes federales estadounidenses restringen la venta de este dispositivo a médicos o por prescripción facultativa (o a profesionales con la debida autorización).

DESCRIPCIÓN DEL DISPOSITIVO

El balón de postparto de Bakri es un catéter balón de silicona con un volumen máximo de hinchado de 500 mL. Los componentes para instilación rápida incluyen un tubo de polímero con una púa para bolsa intravenosa y una válvula de tres vías.

INDICACIONES DE USO

Este dispositivo está indicado para detener o reducir temporalmente hemorragias uterinas postparto cuando sea adecuado emplear un tratamiento conservador.

CONTRAINDICACIONES

- Hemorragia arterial que requiera exploración quirúrgica o embolización angiográfica
- Casos en los que esté indicada una histerectomía
- Embarazo
- Cáncer de cuello uterino
- Infecciones purulentas de la vagina, el cuello uterino o el útero
- Anomalía uterina sin tratar
- Coagulación intravascular diseminada
- Una zona quirúrgica que impida que el dispositivo controle de manera eficaz la hemorragia

ADVERTENCIAS

- Este dispositivo está indicado como medio temporal para el establecimiento de la hemostasia en casos en que esté indicado el tratamiento conservador de la hemorragia uterina postparto.
- El balón de postparto de Bakri está indicado para utilizarse en casos de hemorragia postparto primaria en las 24 horas posteriores al parto.
- El dispositivo no debe permanecer implantado más de 24 horas.
- El balón debe hincharse con un líquido estéril, como agua estéril, solución salina estéril o solución láctica de Ringer. El balón nunca debe hincharse con aire, dióxido de carbono ni ningún otro gas.
- El hinchado máximo es de 500 mL. No hinche demasiado el balón. Si se hincha demasiado, el balón puede desplazarse en el interior de la vagina.
- Se debe vigilar estrechamente a las pacientes en las que se esté utilizando este dispositivo para detectar cualquier signo de aumento de la hemorragia o de coagulación intravascular diseminada (CID). En esos casos, se debe realizar una intervención de urgencia siguiendo el protocolo del hospital.
- No hay datos clínicos que apoyen el uso de este dispositivo en caso de CID.
- La vigilancia de la paciente forma parte integral del tratamiento de la hemorragia postparto. Si hay signos de deterioro o el proceso no mejora, se debe aplicar un tratamiento y un control más intensivos de la hemorragia uterine de la paciente.
- Cuando se esté utilizando el balón de postparto de Bakri, deberá vigilarse la emisión de orina de la paciente.

PRECAUCIONES

- Este producto está concebido para que lo utilicen médicos con formación y experiencia en obstetricia y técnicas ginecologicas.
- Evite utilizar una fuerza excesiva al introducir el balón en el útero.

INSTRUCCIONES DE USO

IMPORTANTE: Antes de la colocación transvaginal o transabdominal del balón de postparto de Bakri, el útero debe estar libre de todos los fragmentos de la placenta, y la paciente debe evaluarse para comprobar que no haya laceraciones o traumatismos en el aparato genital, y que el origen de la hemorragia no sea arterial.

Colocación transvaginal

1. Determine el volumen uterino mediante examen directo o ecográfico.
2. Introduzca en el útero la parte del catéter en la que está el balón y asegúrese de introducir todo el balón hasta que haya sobrepasado el canal cervical y el ostium interno.
3. Introduzca un catéter Foley permanente en la vejiga urinaria, si no hay uno ya colocado, para recoger y vigilar la emisión de orina.

Colocación transabdominal tras cesárea

1. Determine el volumen uterino por visualización directa.
2. Desde arriba, y empleando como acceso la incisión de la cesárea, haga pasar el balón de taponamiento, con el orificio de hinchado primero, a través del útero y del cuello uterino.

NOTA: Retire la llave de paso para facilitar la colocación y vuelva a colocarla antes de llenar el balón.

3. Haga que un ayudante tire del cuerpo del balón para hacerlo pasar a través del canal vaginal hasta que la base del balón deshinchado entre en contacto con el ostium cervical interno.
4. Cierre la incisión mediante el procedimiento normal, con cuidado para no pinchar el balón al suturar.

NOTA: Asegúrese de que todos los componentes del producto estén intactos y de que la histerotomía esté bien suturada antes de hinchar el balón. Si es conveniente por motivos clínicos, el abdomen puede permanecer abierto tras el hinchado del balón, para vigilar estrechamente la distensión uterina y confirmar el cierre de la histerotomía.

NOTA: Si es conveniente por motivos clínicos, puede utilizarse una sutura compresiva de B-Lynch junto con el balón de postparto de Bakri.

Hinchado del balón

con jeringa

ADVERTENCIA: Hinche siempre el balón con un líquido estéril. No lo hinche nunca con aire, dióxido de carbono ni ningún otro gas.

ADVERTENCIA: El hinchado máximo es de 500 mL. No hinche demasiado el balón. Si se hincha demasiado, el balón puede desplazarse en el interior de la vagina.

NOTA: Para asegurarse de llenar el balón con el volumen deseado, se recomienda colocar el volumen de líquido predeterminado en un recipiente aparte, en vez de ir calculando con la jeringa la cantidad de líquido que se ha introducido en el balón.

1. Introduzca un catéter Foley permanente en la vejiga urinaria, si no hay uno ya colocado, para recoger y vigilar la emisión de orina.
2. Con la jeringa suministrada, empiece a llenar el balón hasta el volumen predeterminado a través de la llave de paso.
3. Una vez que el balón se haya hinchado al volumen predeterminado, confirme su colocación mediante ecografía. **NOTA: Vea la colocación correcta en la figura 1.**
4. Si lo desea, puede aplicar tracción al cuerpo del balón. Para mantener la tensión, fije el cuerpo del balón a la pierna de la paciente o póngale encima un peso de no más de 500 g.

NOTA: Para evitar el desplazamiento del balón hacia el interior de la vagina, puede aplicarse contrapresión rellenando el canal vaginal con gasa vaginal empapada en yodo o antibiótico.

5. Conecte el orificio de drenaje a una bolsa de recogida de líquido para vigilar la hemostasia.

NOTA: El orificio de drenaje del balón y el tubo pueden lavarse con solución salina isotónica estéril para eliminar los coágulos y poder así vigilar correctamente la hemostasia.

6. Vigile continuamente a la paciente para comprobar si presenta signos de aumento de la hemorragia o de calambres uterinos.

Hinchado del balón

con componentes para instilación rápida

Vea las **figuras 2-8**, incluidas al principio de este folleto.

NOTA: Una vez hinchado el balón al volumen predeterminado, debe utilizarse ecografía para confirmar la colocación correcta del balón.

Extracción del balón

NOTA: El momento de la extracción del balón debe ser determinado por el médico a cargo tras la evaluación de la paciente una vez que se haya detenido la hemorragia y estabilizado a la paciente. El balón puede extraerse antes si el médico determina que se ha conseguido la hemostasia. El tiempo de permanencia máximo es de 24 horas.

1. Libere la tensión del cuerpo del balón.
2. Retire el material que se haya empleado para el relleno vaginal.
3. Con una jeringa adecuada, aspire el contenido del balón hasta que se deshinche por completo. El líquido puede extraerse poco a poco para permitir la observación periódica de la paciente.

NOTA: En situaciones de urgencia, el cuerpo del catéter puede cortarse para facilitar un deshinchado más rápido.

4. Retire suavemente el balón del útero y del canal vaginal, y deséchelo.
5. Vigile a la paciente por si hubiera signos de hemorragia.

PRESENTACIÓN

El producto se suministra esterilizado con óxido de etileno en envases de apertura pelable. Producto indicado para un solo uso. El producto se mantendrá estéril si el envase no está abierto y no ha sufrido ningún daño. No utilice el producto si no está seguro de que esté estéril. Almacénelo en un lugar fresco, seco y oscuro. Evite la exposición prolongada a la luz. Tras extraerlo del envase, inspeccione el producto para asegurarse de que no haya sufrido ningún daño.

REFERENCIA

Estas instrucciones de uso se basan en la experiencia de médicos y (o) en la bibliografía publicada por ellos. Si desea más información sobre la bibliografía disponible, consulte a su representante comercial local de Cook.

FRANÇAIS

BALLONNET POST-PARTUM DE BAKRI

MISE EN GARDE : En vertu de la législation fédérale des États-Unis, ce dispositif ne peut être vendu que par un médecin (ou un praticien autorisé) ou sur ordonnance médicale.

DESCRIPTION DU DISPOSITIF

Le ballonnet post-partum de Bakri est un cathéter à ballonnet en silicone avec un volume d'inflation maximum de 500 mL. Les composants d'instillation rapide incluent une tubulure en polymère avec un perforateur de poche IV et une valve à trois voies.

UTILISATION

Ce dispositif est prévu pour assurer le contrôle temporaire ou la réduction de l'hémorragie utérine post-partum lorsqu'une prise en charge conservatrice est justifiée.

CONTRE-INDICATIONS

- Toute hémorragie artérielle nécessitant une exploration chirurgicale ou une embolisation angiographique
- Cas nécessitant une hystérectomie
- Grossesse
- Cancer du col de l'utérus
- Infections purulentes du vagin, du col de l'utérus ou de l'utérus
- Anomalie utérine non traitée
- Coagulation intravasculaire disséminée
- Site chirurgical empêchant le contrôle efficace de l'hémorragie par le dispositif

AVERTISSEMENTS

- Ce dispositif est destiné à être utilisé comme un moyen provisoire pour obtenir l'hémostase dans des cas où une prise en charge conservatrice d'un saignement utérin post-partum est préconisée.
- Le ballonnet post-partum de Bakri est indiqué pour une utilisation en cas d'hémorragie primaire du post-partum dans les 24 heures après l'accouchement.
- La durée à demeure du dispositif ne doit pas dépasser 24 heures.
- Le ballonnet doit être gonflé à l'aide d'un liquide stérile tel que de l'eau stérile, du sérum physiologique stérile ou un soluté lactate de Ringer. Le ballonnet ne doit jamais être gonflé avec de l'air, du dioxyde de carbone ou tout autre gaz.
- Le volume d'inflation maximal est de 500 mL. Ne pas inflater excessivement le ballonnet. L'inflation excessive du ballonnet peut entraîner le déplacement du ballonnet dans le vagin.
- Les patientes chez lesquelles ce dispositif est utilisé doivent faire l'objet d'une surveillance étroite pour déceler tout signe de saignement aggravé et/ou de coagulation intravasculaire disséminée (CIVD). Dans de tels cas, procéder à une intervention d'urgence conformément au protocole hospitalier.
- Il n'existe aucune donnée clinique soutenant l'utilisation de ce dispositif dans le cadre d'une CIVD.
- La surveillance de la patiente est un composant essentiel de la prise en charge des hémorragies du post-partum. Si l'état de la patiente montre des signes de détérioration ou ne s'améliore pas, envisager un traitement et une prise en charge plus agressifs du saignement utérin de la patiente.
- L'écoulement d'urine de la patiente doit être surveillé pendant l'utilisation du ballonnet post-partum de Bakri.

MISES EN GARDE

- Ce produit est destiné à être utilisé par des médecins ayant acquis la formation et l'expérience nécessaires aux techniques obstétriques et gynécologiques.
- Éviter d'utiliser une force excessive lors de l'introduction du ballonnet dans l'utérus.

MODE D'EMPLOI

IMPORTANT : Avant la mise en place transvaginale ou transabdominale du ballonnet post-partum de Bakri, l'utérus doit être exempt de tout fragment de placenta et la patiente doit être examinée pour s'assurer que les voies génitales ne présentent aucune lacération ni traumatisme et que la source de l'hémorragie n'est pas artérielle.

Mise en place transvaginale

1. Déterminer le volume utérin par examen direct ou examen échographique.
2. Introduire la section à ballonnet du cathéter dans l'utérus, en s'assurant que la totalité du ballonnet est introduite au-delà du canal cervical et de l'orifice interne.

3. À ce stade, mettre en place dans la vessie urinaire une sonde de Foley à demeure, si ce n'est pas déjà fait, pour recueillir et surveiller l'écoulement d'urine.

Mise en place transabdominale, après une césarienne

1. Déterminer le volume utérin par examen direct.
2. Par le haut, introduire le ballonnet de tamponnement avec l'orifice d'inflation en premier, à travers l'incision de la césarienne, puis l'utérus et le col de l'utérus.

REMARQUE : Retirer le robinet afin de faciliter la mise en place, puis réinstaller avant de remplir le ballonnet.

3. Demander à un assistant de tirer l'âme du ballonnet à travers le canal vaginal jusqu'à ce que le bas du ballonnet déflaté vienne au contact de l'orifice interne du col.
4. Fermer l'incision selon la procédure habituelle, en prenant garde de ne pas transpercer le ballonnet durant la suture.

REMARQUE : S'assurer que tous les composants du produit sont intacts et l'hystérotomie est suturée de manière correcte avant d'inflater le ballonnet. Si cela est cliniquement pertinent, l'abdomen peut rester ouvert lors de l'inflation du ballonnet pour permettre au chirurgien de surveiller étroitement la distension de l'utérus et confirmer la fermeture de l'hystérotomie.

REMARQUE : Si cela est cliniquement pertinent, une suture de compression de type B-Lynch peut être utilisée avec le ballonnet post-partum de Bakri.

Inflation du ballonnet

Avec une seringue

AVERTISSEMENT : Toujours inflater le ballonnet avec un liquide stérile. Ne jamais inflater avec de l'air, du dioxyde de carbone ou un autre gaz.

AVERTISSEMENT : Le volume d'inflation maximum est de 500 mL. Ne pas inflater excessivement le ballonnet. L'inflation excessive du ballonnet peut entraîner le déplacement du ballonnet dans le vagin.

REMARQUE : Pour s'assurer que le ballonnet est rempli au volume souhaité, il est recommandé de placer le volume prédéterminé de liquide dans un récipient à part plutôt que de se fier au volume mesuré avec la seringue pour confirmer la quantité de liquide injectée dans le ballonnet.

1. À ce stade, mettre en place dans la vessie urinaire une sonde de Foley à demeure, si ce n'est pas déjà fait, pour recueillir et surveiller l'écoulement d'urine.
2. À l'aide de la seringue fournie, commencer à remplir le ballonnet avec le volume prédéterminé de liquide à travers le robinet.
3. Une fois le ballonnet inflaté au volume prédéterminé, vérifier sa mise en place par échographie.
   REMARQUE : Voir la Fig. 1 pour la mise en place correcte.
4. Si cela est souhaité, une traction peut être exercée sur l'âme du ballonnet. Pour maintenir la tension, fixer l'âme du ballonnet sur la jambe de la patiente ou y fixer un poids ne dépassant pas 500 grammes.

REMARQUE : Pour empêcher le déplacement du ballonnet dans le vagin, une contre-pression peut être appliquée en remplissant le canal vaginal avec des compresses vaginales imprégnées d'iode ou d'antibiotique.

5. Raccorder l'orifice de drainage à une poche de recueil de liquide pour surveiller l'hémostase.

REMARQUE : Afin de surveiller correctement l'hémostase, l'orifice de drainage du ballonnet et la tubulure peuvent être rincés avec du sérum physiologique isotonique stérile pour éliminer d'éventuels caillots.

6. Surveiller la patiente continuellement pour détecter tout signe d'augmentation du saignement ou de crampes utérines.

Inflation du ballonnet

Avec les composants d'instillation rapide

Voir les **Fig. 2 à 8**, au début de cette brochure.

REMARQUE : La mise en place correcte du ballonnet doit être confirmée par échographie une fois que celui-ci a été inflaté au volume prédéterminé.

Retrait du ballonnet

REMARQUE : Le moment du retrait du ballonnet doit être déterminé par le clinicien traitant après examen de la patiente une fois que l'hémorragie a été maîtrisée et que l'état de la patiente a été stabilisé. Le ballonnet peut être retiré plus tôt si le médecin juge qu'une hémostase adéquate a été obtenue. La durée à demeure maximum du dispositif est de 24 heures.

1. Relâcher la tension exercée sur l'âme du ballonnet.
2. Retirer tout pansement vaginal.
3. À l'aide d'une seringue appropriée, aspirer le contenu du ballonnet jusqu'à ce que celui-ci soit entièrement déflaté. Le liquide peut être retiré progressivement pour permettre une observation périodique de la patiente.

REMARQUE : Dans une situation d'urgence, l'âme du cathéter peut être coupée pour faciliter une déflation plus rapide.

4. Retirer doucement le ballonnet de l'utérus et du canal vaginal et le jeter.
5. Surveiller la patiente pour détecter tout signe de saignement.

PRÉSENTATION

Produit(s) fourni(s) stérilisé(s) à l'oxyde d'éthylène, sous emballage déchirable. Produit(s) destiné(s) à un usage unique. Contenu stérile lorsque l'emballage est scellé d'origine et intact. En cas de doute quant à la stérilité du produit, ne pas l'utiliser. Conserver à l'obscurité, au sec et au frais. Éviter une exposition prolongée à la lumière. Examiner le produit après son déballage pour s'assurer de son bon état.

BIBLIOGRAPHIE

Le présent mode d'emploi a été rédigé en fonction de l'expérience de médecins et/ou de leurs publications médicales. Pour obtenir des renseignements sur la documentation existante, s'adresser au représentant Cook local.

MAGYAR

BAKRI POST PARTUM BALLON

FIGYELEM: Az USA szövetségi törvényeinek értelmében ez az eszköz kizárólag orvos (vagy megfelelő engedéllyel rendelkező egészségügyi szakember) által vagy rendeletére forgalmazható.

AZ ESZKÖZ LEÍRÁSA

A Bakri post partum ballon 500 mL maximális feltöltési térfogatú szilikon ballonkatéter. A gyors feltöltő komponensek között polimer csővezeték is található infúziós zsákhoz való kiszúró tüskével és háromutas szeleppel.

RENDELTETÉS

Ez az eszköz a post partum méhvérzés ideiglenes kontrollálására vagy csökkentésére szolgál olyan esetekben, amikor konzervatív kezelés indokolt.

ELLENJAVALLATOK

- Sebészeti feltárást vagy angiográfiás embolizációt igénylő artériás vérzés
- Olyan esetek, amikor hysterectomia alkalmazása javallott
- Terhesség
- Méhnyakrák
- Gennyes fertőzés a hüvelyben, a méhnyakban vagy a méhben
- Méh nem kezelt anomáliája

- Disszeminált intravaszkuláris koaguláció
- Olyan műtéti hely, amely akadályozná az eszközt a vérzés hatékony kontrollálásában

„VIGYÁZAT" SZINTŰ FIGYELMEZTETÉSEK

- Az eszköz a vérzéscsillapítás ideiglenes biztosítására szolgál olyan esetekben, amikor a post partum méhvérzés konzervatív kezelése javallott.
- A Bakri post partum ballon használata a szüléstől számított 24 órán belül jelentkező primer post partum vérzés esetén javallott.
- Az eszköz nem maradhat a testben 24 óránál hosszabb ideig.
- A ballont steril folyadékkal, például steril vízzel, steril fiziológiás sóoldattal vagy Ringer-laktát oldattal kell feltölteni. A ballont soha nem szabad levegővel, szén-dioxiddal vagy bármilyen más gázzal feltölteni.
- A maximális feltöltési térfogat 500 mL. Ne töltse túl a ballont. A ballon túltöltésének eredményeképp a ballon átkerülhet a hüvelybe.
- Szorosan nyomon kell követni azokat a betegeket, akikben ez az eszköz használatos, és figyelni kell a vérzés rosszabbodására és/vagy a disszeminált intravaszkuláris koagulációra (DIC) utaló jeleket. Ilyen esetekben a sürgősségi beavatkozást a kórház protokolljának megfelelően kell végrehajtani.
- Az eszköz használatát DIC-ben szenvedő betegek esetében nem támasztják alá klinikai adatok.
- A betegek monitorozása a post partum vérzés kezelésének részét képezi. Az állapot romlását vagy javulásának elmaradását mutató jelek esetén a beteg méhvérzésének terápiájához és kezeléséhez agresszívebb módszert kell választani.
- A betegből távozó vizeletet monitorozni kell a Bakri post partum ballon használata folyamán.

ÓVINTÉZKEDÉSEK

- Ez a termék a szülészeti és nőgyógyászati technikákra kiképzett és azokban járatos orvosok általi használatra készült.
- A ballon méhbe történő behelyezése során ne alkalmazzon túl nagy erőt.

HASZNÁLATI UTASÍTÁS

FONTOS: A Bakri post partum ballon hüvelyen vagy hason keresztüli behelyezése előtt a méhnek minden méhlepénydarabtól mentesnek kell lennie, és a beteg állapotát értékelni kell, hogy meggyőződjön arról: a nemi szerveket nem érte szakadás vagy sérülés, és a vérzés nem arteriális eredetű.

Hüvelyen keresztüli behelyezés

1. Közvetlen vizsgálattal vagy ultrahangos vizsgálattal állapítsa meg a méh térfogatát.
2. Helyezze a katéter ballonrészét a méhbe, ügyelve arra, hogy a ballon egésze túljusson a méhcsatornán és a belső méhszájon.
3. Ha még nem lett behelyezve, akkor helyezzen be egy testben maradó Foley-típusú húgyhólyagkatétert, hogy összegyűjtse és monitorozza a távozó vizeletet.

Hason keresztüli behelyezés, császármetszés után

1. Közvetlen vizsgálattal állapítsa meg a méh térfogatát.
2. Felülről, a császármetszésen keresztül hozzáférve vezesse át a tamponáló ballont a méhen és a méhnyakon, feltöltőnyílásával előre.

MEGJEGYZÉS: A behelyezés elősegítése érdekében távolítsa el az elzárócsapot, majd a ballon feltöltése előtt helyezze vissza.

3. Utasítsa asszisztensét, hogy húzza a ballon szárát a hüvelycsatornán keresztül, egészen addig, amíg a leeresztett ballon alapja hozzá nem ér a belső méhszájhoz.
4. A szokásos eljárással zárja le a bemetszést, ügyelve arra, hogy ne szúrja meg a ballont az öltések során.

MEGJEGYZÉS: A ballon feltöltése előtt győződjön meg arról, hogy a termék valamennyi komponense sértetlen, és hogy a méhen ejtett vágás biztonságosan össze van varrva. Ha ez klinikailag fontos, a ballon

feltöltése után a has nyitva hagyható a méh kitágításának szoros megfigyelése és a méhen ejtett vágás záródásának igazolása céljából.

MEGJEGYZÉS: Ha ez klinikailag fontos, a Bakri post partum ballonnal együtt B-Lynch öltés is alkalmazható.

A ballon feltöltése

Fecskendővel

FIGYELMEZTETÉS: Mindig steril folyadékkal töltse fel a ballont. A ballon feltöltésére tilos levegőt, szén-dioxidot, vagy bármilyen egyéb gázt használni!

FIGYELMEZTETÉS: A maximális feltöltési térfogat 500 mL. Ne töltse túl a ballont. A ballon túltöltésének eredményeképp a ballon átkerülhet a hüvelybe.

MEGJEGYZÉS: A ballon kellő térfogatra történő feltöltésének biztosításához ajánlott az előre meghatározott térfogatú folyadékot egy külön edénybe helyezni, nem pedig a fecskendő feltöltéseinek megszámolására hagyatkozni a ballonba töltött folyadék mennyiségének vonatkozásában.

1. Ha még nem lett behelyezve, akkor helyezzen be egy testben maradó Foley-típusú húgyhólyagkatétert, hogy összegyűjtse és monitorozza a távozó vizeletet.
2. A mellékelt fecskendővel kezdje meg a ballon feltöltését az előre meghatározott térfogatra az elzárócsapon keresztül.
3. Miután megtörtént a ballon feltöltése az előre meghatározott térfogatra, ultrahanggal ellenőrizze a behelyezését. **MEGJEGYZÉS: A megfelelő behelyezést az 1. ábra mutatja.**
4. Ha szükséges, alkalmazzon húzást a ballon szárára. A feszesség fenntartásához rögzítse a ballon szárát a beteg lábához, vagy kapcsoljon hozzá 500 g-nál nem nehezebb súlyt.

MEGJEGYZÉS: Annak megelőzésére, hogy a ballon áthelyeződjék a hüvelybe, ellennyomást lehet alkalmazni a hüvelycsatorna jódba vagy antibiotikumba áztatott hüvelygézzel való kitömésével.

5. Csatlakoztassa a lecsapolónyílást egy folyadékgyűjtő tasakhoz a vérzéscsillapítás monitorozása céljából.

MEGJEGYZÉS: A vérzéscsillapítás megfelelő monitorozásához a ballon lecsapolónyílását és csövezetét steril izotóniás sóoldattal tisztára lehet mosni a véralvadéktól.

6. Folyamatosan monitorozza a beteget, és figyelje, hogy vannak-e a vérzés fokozódására vagy a méh görcsére utaló jelek.

A ballon feltöltése

Gyorsfeltöltő komponensekkel

Lásd a **2-8. ábrákat**, e könyvecske elején.

MEGJEGYZÉS: A ballon előre meghatározott térfogatra történő feltöltése után ultrahanggal kell ellenőrizni a ballon megfelelő behelyezését.

A ballon eltávolítása

MEGJEGYZÉS: A ballon eltávolításának időzítését a beteget ellátó orvosnak kell meghatároznia a beteg állapotának értékelését követően, amint a vérzést elállították és a beteg állapota stabilizálódott. Miután az orvos megállapította a vérzéscsillapítást, a ballon hamarabb eltávolítható. A ballon legfeljebb 24 óráig maradhat a testben.

1. Szüntesse meg a ballon szárának feszességét.
2. Távolítsa el a hüvelyből az összes kitöltőanyagot.
3. Megfelelő fecskendővel aspirálja a ballon tartalmát, amíg a ballon teljesen le nem ereszt. A folyadék lépésenként is eltávolítható a beteg időszakos megfigyelése érdekében.

MEGJEGYZÉS: Vészhelyzetben a katéter szárát el lehet vágni a gyorsabb leeresztés megkönnyítése érdekében.

4. Finoman húzza vissza a ballont a méhből és a hüvelycsatornából, majd helyezze a hulladékba.
5. Monitorozza, hogy fellépnek-e vérzésre utaló jelek a betegben.

KISZERELÉS

Kiszerelés: etilén-oxiddal sterilizálva, széthúzható csomagolásban. Egyszeri használatra. Felbontatlan vagy sértetlen csomagolásban steril. Ha a termék sterilitása kétséges, ne használja. Száraz, sötét, hűvös helyen tárolandó. Tartós megvilágítása kerülendő. A csomagolásból való eltávolítás után vizsgálja meg a terméket annak ellenőrzésére, hogy az nem sérült-e meg.

REFERENCIA

Ez a használati utasítás orvosok tapasztalatán és/vagy az általuk közölt szakirodalmon alapul. A rendelkezésre álló szakirodalomról a Cook helyi értékesítési képviselője tud felvilágosítással szolgálni.

ITALIANO

PALLONCINO POST-PARTO BAKRI

ATTENZIONE - Le leggi federali degli Stati Uniti d'America limitano la vendita del presente dispositivo a medici, a personale autorizzato o a operatori sanitari abilitati.

DESCRIZIONE DEL DISPOSITIVO

Il palloncino post-parto Bakri è un catetere a palloncino in silicone con un volume massimo di gonfiaggio di 500 mL. I componenti per l'instillazione rapida includono un tubo in polimero con un puntale di foratura della sacca endovenosa e una valvola a tre vie.

USO PREVISTO

Questo dispositivo è previsto per il controllo o la riduzione temporanei del sanguinamento uterino post-parto nei casi in cui sia indicata una gestione terapeutica conservativa.

CONTROINDICAZIONI

- Sanguinamento arterioso che richieda esplorazione chirurgica o embolizzazione angiografica
- Casi in cui è indicata un'isterectomia
- Gravidanza
- Cancro della cervice
- Infezioni purulente della vagina, della cervice o dell'utero
- Anomalia uterina non trattata
- Coagulazione intravascolare disseminata
- Un sito chirurgico che impedirebbe al dispositivo di controllare efficacemente il sanguinamento

AVVERTENZE

- Questo dispositivo è previsto come mezzo temporaneo di emostasi nei casi in cui sia indicata la gestione conservativa del sanguinamento uterino post-parto.
- Il palloncino post-parto Bakri è indicato per l'uso nei casi di emorragia primaria post-parto entro 24 ore dal parto.
- Il periodo di permanenza del dispositivo non deve superare le 24 ore.
- Il palloncino deve essere gonfiato con un liquido sterile come acqua sterile, soluzione fisiologica sterile o soluzione di Ringer lattato. Non gonfiarlo mai con aria, anidride carbonica o altri gas.
- Il volume massimo di gonfiaggio è di 500 mL. Non gonfiare eccessivamente il palloncino. Il gonfiaggio eccessivo del palloncino può causarne lo sposizionamento nella vagina.
- Le pazienti sulle quali viene usato il presente dispositivo devono essere sottoposte ad attento monitoraggio per evidenziare la presenza di eventuali segni di aggravamento del sanguinamento e/o coagulazione intravascolare disseminata (CID). In tali casi, seguire le procedure interventistiche di emergenza secondo quanto previsto dal protocollo ospedaliero.

- Non vi sono dati clinici a supporto dell'uso di questo dispositivo nei casi di CID.
- Il monitoraggio della paziente costituisce parte integrante della gestione dell'emorragia post-parto. Segni di deterioramento oppure il mancato miglioramento della condizione richiedono un trattamento e una gestione del sanguinamento uterino più aggressivi.
- Durante l'uso del palloncino post-parto Bakri è necessario monitorare la produzione di urina della paziente.

PRECAUZIONI

- Questo prodotto è previsto per essere usato da medici debitamente addestrati ed esperti nelle tecniche ostetriche e ginecologiche.
- Evitare di forzare eccessivamente nell'introdurre il palloncino nell'utero.

ISTRUZIONI PER L'USO

IMPORTANTE - Prima del posizionamento transvaginale o transaddominale del palloncino post-parto Bakri, eliminare dall'utero tutti i frammenti di placenta ed esaminare la paziente per escludere la presenza di lacerazioni o traumi al tratto genitale e accertarsi che il sanguinamento non sia di origine arteriosa.

Posizionamento transvaginale

1. Determinare il volume uterino mediante esame diretto o esame ecografico.
2. Inserire nell'utero la sezione a palloncino del catetere, assicurandosi che il palloncino sia interamente posizionato oltre il canale cervicale e l'ostio interno.
3. A questo punto inserire un catetere a permanenza Foley per vescica urinaria (nel caso non fosse già inserito), per raccogliere e monitorare la produzione di urina.

Posizionamento transaddominale in seguito a taglio cesareo

1. Determinare il volume uterino mediante esame diretto.
2. Accedendo dal taglio cesareo e procedendo dall'alto, fare passare il palloncino per tamponamento attraverso l'utero e la cervice, inserendo per primo il raccordo per il gonfiaggio.

NOTA - Togliere il rubinetto per agevolare il posizionamento e riapplicarlo prima di riempire il palloncino.

3. Avvalersi di un assistente che eserciti trazione sullo stelo del palloncino attraverso il canale vaginale, fino a portare la base del palloncino sgonfio a contatto con l'ostio cervicale interno.
4. Chiudere l'incisione con la prassi consueta, facendo attenzione a evitare di pungere il palloncino durante le operazioni di sutura.

NOTA - Prima di gonfiare il palloncino, assicurarsi che tutti i componenti del prodotto siano integri e che l'isterotomia sia stata adeguatamente suturata. Se clinicamente rilevante, l'addome può rimanere aperto al momento del gonfiaggio del palloncino, al fine di monitorare attentamente la distensione uterina e confermare la chiusura dell'isterotomia.

NOTA - Se clinicamente rilevante, insieme al palloncino post-parto Bakri si può usare una sutura compressiva di B-Lynch.

Gonfiaggio del palloncino

Mediante siringa

AVVERTENZA - Gonfiare sempre il palloncino con un liquido sterile. Non gonfiarlo mai con aria, anidride carbonica o alcun altro gas.

AVVERTENZA - Il volume massimo di gonfiaggio è di 500 mL. Non gonfiare eccessivamente il palloncino. Il gonfiaggio eccessivo del palloncino può causarne lo sposizionamento nella vagina.

NOTA - Per essere certi che il palloncino sia riempito fino al volume desiderato, si consiglia di collocare in un contenitore separato il volume predeterminato di fluido, invece di affidarsi al conteggio delle siringhe per verificare la quantità di fluido instillato nel palloncino.

1. A questo punto inserire un catetere a permanenza Foley per vescica urinaria (nel caso non fosse già inserito), per raccogliere e monitorare la produzione di urina.

2. Utilizzando la siringa acclusa, iniziare a gonfiare il palloncino attraverso il rubinetto fino a raggiungere il volume predeterminato.
3. Dopo avere gonfiato il palloncino con il volume predeterminato, confermare il posizionamento per via ecografica. **NOTA - La Fig. 1 illustra il posizionamento corretto.**
4. Se lo si desidera, è possibile applicare trazione allo stelo del palloncino. Per mantenere la tensione, fissare lo stelo del palloncino alla gamba della paziente oppure collegarlo a un peso che non superi i 500 grammi.

NOTA - Per impedire lo sposizionamento del palloncino nella vagina, è possibile applicare una contropressione inserendo nel canale vaginale compresse di garza imbevute di iodio o antibiotico.

5. Collegare il raccordo di drenaggio a una sacca di raccolta dei fluidi per monitorare l'emostasi.

NOTA - Per un adeguato monitoraggio dell'emostasi, il raccordo di drenaggio del palloncino e il tubicino possono essere liberati dai coaguli mediante lavaggio con soluzione fisiologica isotonica sterile.

6. Mantenere la paziente sotto monitoraggio continuo per rilevare segni di aumentato sanguinamento e crampi uterini.

Gonfiaggio del palloncino

Mediante componenti a instillazione rapida

Vedere le **Figg. 2-8**, all'inizio di questo opuscolo.

NOTA - Confermare per via ecografica il corretto posizionamento del palloncino, dopo averlo gonfiato con il volume predeterminato.

Rimozione del palloncino

NOTA - Sta al medico curante decidere quando è giunto il momento di rimuovere il palloncino dopo aver valutato la paziente, una volta tenuto sotto controllo il sanguinamento e stabilizzata la paziente. Il palloncino può essere rimosso in anticipo dopo che il medico ha determinato l'ottenimento dell'emostasi. Il tempo massimo di permanenza è di 24 ore.

1. Eliminare la tensione dallo stelo del palloncino.
2. Rimuovere l'eventuale impaccatura vaginale.
3. Utilizzando una siringa adeguata, aspirare il contenuto del palloncino fino a sgonfiarlo completamente. Il liquido può essere rimosso a poco a poco per consentire l'osservazione periodica della paziente.

NOTA - In una situazione di emergenza si può tagliare il corpo del catetere per sgonfiare più rapidamente il palloncino.

4. Estrarre delicatamente il palloncino dall'utero e dal canale vaginale e gettarlo.
5. Monitorare la paziente per individuare eventuali segni di sanguinamento.

CONFEZIONAMENTO

Il prodotto è sterilizzato mediante ossido di etilene ed è fornito in confezione con apertura a strappo. Esclusivamente monouso. Il prodotto è sterile se la sua confezione è chiusa e non danneggiata. Non utilizzare il prodotto in caso di dubbi sulla sua sterilità. Conservarlo in luogo fresco e asciutto, al riparo dalla luce. Evitarne l'esposizione prolungata alla luce. Dopo l'estrazione dalla confezione, esaminare il prodotto per accertarsi che non abbia subito danni.

BIBLIOGRAFIA

Le presenti istruzioni per l'uso sono basate sull'esperienza dei medici e/o sulle loro pubblicazioni specialistiche. Per ottenere informazioni sulla letteratura specializzata disponibile, rivolgersi al rappresentante Cook di zona.

BAKRI-POSTPARTUMBALLON

LET OP: Krachtens de federale wetgeving van de Verenigde Staten mag dit hulpmiddel uitsluitend worden verkocht door, of op voorschrift van, een arts (of een naar behoren gediplomeerde zorgverlener).

BESCHRIJVING VAN HET HULPMIDDEL

De Bakri-post-partumballon is een van silicone vervaardigde ballonkatheter met een vulvolume maximaal van 500 mL. De snel indruppelbare componenten bevatten polymeren slangen met een infuuszakspike en een driewegklep.

BEOOGD GEBRUIK

Dit hulpmiddel is bedoeld om postpartumbloedingen uit de baarmoeder tijdelijk te beheersen of te verminderen wanneer conservatieve behandeling verantwoord is.

CONTRA-INDICATIES

- Arteriële bloeding waarvoor chirurgische exploratie of angiografische embolisatie is vereist
- Gevallen die hysterectomie indiceren
- Zwangerschap
- Baarmoederhalskanker
- Purulente infecties in de vagina, baarmoederhals of baarmoeder
- Onbehandelde baarmoederafwijking
- Diffuse intravasale stolling
- Een operatieplaats waar het hulpmiddel de bloeding niet effectief kan beheersen

WAARSCHUWINGEN

- Dit hulpmiddel is bedoeld als tijdelijk middel om hemostase te verkrijgen in gevallen waarbij conservatieve behandeling van postpartumbloedingen uit de baarmoeder is geïndiceerd.
- De Bakri-postpartumballon is geïndiceerd voor gebruik in geval van een primaire postpartumhemorragie binnen 24 uur na de bevalling.
- Het hulpmiddel mag niet meer dan 24 uur in het lichaam verblijven.
- De ballon moet worden gevuld met een steriele vloeistof zoals steriel water, steriel fysiologisch zout of ringerlactaat. De ballon mag nooit worden gevuld met lucht, kooldioxide of welk ander gas dan ook.
- Het maximale vulvolume is 500 mL. Zorg dat de ballon niet overvuld wordt. Overvullen van de ballon kan ertoe leiden dat de ballon tot in de vagina verschuift.
- Patiëntes bij wie dit hulpmiddel wordt gebruikt, moeten nauwgezet worden gemonitord op tekenen van verhoogd bloedverlies en/of diffuse intravasale stolling (DIS). In dergelijke gevallen moet urgente interventie volgens het ziekenhuisprotocol worden geboden.
- Er zijn geen klinische gegevens beschikbaar ter ondersteuning van het gebruik van dit hulpmiddel bij DIS.
- Het monitoren van de patiënte is een integraal onderdeel van de behandeling van postpartumbloedingen. Tekenen van verslechtering of niet-verbetering van de toestand moeten leiden tot agressiever behandeling van de baarmoederbloeding bij de patiënte.
- De urineproductie van de patiënte moet worden gemonitord terwijl de Bakri-postpartumballon in gebruik is.

VOORZORGSMAATREGELEN

- Dit product is bestemd voor gebruik door artsen met een opleiding in en ervaring met verloskundige en gynaecologische technieken.
- Vermijd overmatige kracht bij het inbrengen van de ballon in de baarmoeder.

GEBRUIKSAANWIJZING

BELANGRIJK: Vóór de transvaginale of transabdominale plaatsing van de Bakri-postpartumballon moet de baarmoeder vrij zijn van alle placentafragmenten en moet de patiënte worden geëvalueerd om er zeker van te zijn dat de geslachtsorganen geen rijtwonden of trauma vertonen en dat de oorsprong van de bloeding niet arterieel is.

Transvaginale plaatsing

1. Bepaal het volume van de baarmoeder door direct onderzoek of echografisch onderzoek.
2. Breng het ballongedeelte van de katheter in de baarmoeder in en zorg daarbij dat de gehele ballon voorbij het baarmoederhalskanaal en het ostium internum is ingebracht.
3. Plaats nu een Foley-verblijfsblaaskatheter, indien deze nog niet is geplaatst, om de urineproductie op te vangen en te monitoren.

Transabdominale plaatsing, na keizersnede

1. Bepaal het volume van de baarmoeder door direct onderzoek.
2. Breng van bovenaf, door de keizersnede, de tamponnadeballon in de baarmoeder en de baarmoederhals in, met de vulpoort het eerst.

NB: Verwijder de afsluitkraan om het plaatsen van de ballon te vergemakkelijken en bevestig opnieuw voordat de ballon wordt gevuld.

3. Laat een assistent de schacht van de ballon door het vaginale kanaal trekken totdat de basis van de geleegde ballon in contact komt met het ostium internum.
4. Sluit de incisie volgens de normale procedure en let er daarbij goed op dat u de ballon tijdens het hechten niet aanprikt.

NB: Controleer of alle componenten van het product intact zijn en de hysterotomie stevig gehecht is alvorens de ballon te vullen. Indien klinisch relevant kan het abdomen na het vullen van de ballon openblijven om de uitzetting van de baarmoeder nauwgezet te bewaken en de sluiting van de hysterotomie te bevestigen.

NB: Indien klinisch relevant kan een B-Lynch-compressiehechting worden gebruikt in combinatie met de Bakri-postpartumballon.

De ballon vullen

Met spuit

WAARSCHUWING: Vul de ballon altijd met een steriele vloeistof. Vul de ballon nooit met lucht, kooldioxide of welk ander gas dan ook.

WAARSCHUWING: Het maximale vulvolume is 500 mL. Zorg dat de ballon niet overvuld wordt. Overvullen van de ballon kan ertoe leiden dat de ballon tot in de vagina verschuift.

NB: Om de ballon tot het gewenste volume te vullen, verdient het aanbeveling het vooraf bepaalde vloeistofvolume in een aparte houder te gieten, in plaats van de hoeveelheid in de ballon ingespoten vloeistof te verifiëren aan de hand van de schaalverdeling van de spuit.

1. Plaats nu een Foley-verblijfsblaaskatheter, indien deze nog niet is geplaatst, om de urineproductie op te vangen en te monitoren.
2. Gebruik de meegeleverde spuit om de ballon via de afsluitkraan tot het vooraf bepaalde volume te vullen.
3. Nadat de ballon is gevuld tot het vooraf bepaalde volume, controleert u via echografisch onderzoek of de ballon correct is geplaatst. **NB: Zie Afb. 1 voor correcte plaatsing.**
4. Indien gewenst kan trekkracht op de ballonschacht worden uitgeoefend. Om de spanning te handhaven, maakt u de ballonschacht aan het been van de patiënte vast of bevestigt u de schacht aan een gewicht van maximaal 500 g.

NB: Om verschuiving van de ballon in de vagina te voorkomen, kan tegendruk worden uitgeoefend door het vaginale kanaal op te vullen met vaginaal gaas dat met jodium of antibiotica is doordrenkt.

5. Sluit de drainagepoort aan op een vloeistofopvangzak om de hemostase te monitoren.

NB: Om de hemostase afdoende te monitoren, kunnen de drainagepoort en de slang met steriel isotoon fysiologisch zout worden doorgespoeld zodat ze vrij van stolsels zijn.

6. Monitor de patiënte continu op tekenen van verhoogd bloedverlies en baarmoederkrampen.

De ballon vullen

Met componenten voor snelle instillatie

Zie **Afb. 2-8** aan het begin van dit boekje.

NB: Nadat de ballon met het vooraf bepaalde volume is gevuld, moet via echografisch onderzoek worden gecontroleerd of hij correct is geplaatst.

De ballon verwijderen

NB: Het tijdstip waarop de ballon wordt verwijderd, moet worden bepaald door de behandelend arts na evaluatie van de patiënte wanneer de bloeding beheerst is en de patiënte is gestabiliseerd. De ballon mag eerder worden verwijderd bij vaststelling van hemostase door de arts. De maximale verblijfsduur is 24 uur.

1. Verlicht de spanning op de ballonschacht.
2. Verwijder eventueel vaginaal opvulgaas.
3. Gebruik een geschikte spuit om de inhoud van de ballon te aspireren totdat de ballon helemaal leeg is. De vloeistof kan stapsgewijs worden verwijderd zodat de patiënte periodiek kan worden geobserveerd.

NB: In urgente gevallen kan de katheterschacht worden doorgeknipt om het legen van de ballon te versnellen.

4. Trek de ballon zachtjes uit de baarmoeder en het vaginale kanaal terug en voer de ballon af.
5. Monitor de patiënte op tekenen van bloedverlies.

WIJZE VAN LEVERING

Wordt steriel (gesteriliseerd met ethyleenoxide) in gemakkelijk open te trekken verpakkingen geleverd. Bestemd voor eenmalig gebruik. Steriel indien de verpakking ongeopend en onbeschadigd is. Gebruik het product niet indien er twijfel bestaat over de steriliteit van het product. Koel, donker en droog bewaren. Vermijd langdurige blootstelling aan licht. Inspecteer het product wanneer u het uit de verpakking haalt om te controleren of het niet beschadigd is.

LITERATUUR

Deze gebruiksaanwijzing is gebaseerd op de ervaringen van artsen en/of hun publicaties. Neem contact op met de plaatselijke verkoopvertegenwoordiger van Cook voor informatie over beschikbare literatuur.

NORSK

BAKRI-POSTPARTUMBALLONG

FORSIKTIG: I henhold til amerikansk lovgivning skal dette instrumentet bare selges av eller forskrives av en lege (eller en autorisert behandler).

BESKRIVELSE AV ANORDNINGEN

Bakri-postpartumballongen er et ballongkateter i silikon med et maksimalt fyllevolum på 500 mL. Komponentene for hurtig instillasjon inkluderer polymerslanger med IV-posefeste og treveisventil.

TILTENKT BRUK

Dette instrumentet er beregnet for å gi midlertidig kontroll, eller reduksjon, av blødning i livmoren etter fødsel når konservativ behandling er garantert.

KONTRAINDIKASJONER

- Arteriell blødning som krever kirurgisk inngripen eller angiografisk embolisering

- Tilfeller som indikerer hysterektomi
- Graviditet
- Livmorhalskreft
- Purulente infeksjoner i skjede, livmorhals eller livmor
- Ubehandlet uterusanomali
- Disseminert intravaskulær koagulasjon
- Et kirurgisk område som vil hindre instrumentet i å kontrollere blødningen på en effektiv måte

ADVARSLER

- Dette instrumentet er ment å være en midlertidig metode for å oppnå hemostase i tilfeller som krever konservativ behandling av blødning i livmoren etter fødsel.
- Bakri-postpartumballong er beregnet for bruk ved primær blødning etter fødsel innen 24 timer etter forløsning.
- Instrumentet skal ikke være lagt inn i mer enn 24 timer.
- Ballongen skal fylles med en steril væske, for eksempel sterilt vann, steril saltoppløsning eller Ringers løsning. Ballongen må aldri fylles med luft, karbondioksid eller noen annen gass.
- Maksimal fylling er 500 mL. Fyll ikke ballongen for mye. Hvis ballongen fylles for mye, kan ballongen bli forskjøvet inn i skjeden.
- Pasienter som bruker dette instrumentet, skal overvåkes nøye for tegn på økt blødning og/eller disseminert intravaskulær koagulasjon (DIC). I slike tilfeller bør sykehusets nødprosedyrer følges.
- Det finnes ingen kliniske data som støtter bruken av dette instrumentet ved tilfeller av DIC.
- Pasientovervåking er en viktig del av behandlingen av blødning etter fødsel. Tegn på forverret eller ikke forbedret tilstand bør føre til en mer aggressiv behandling og håndtering av den uterine blødningen hos pasienten.
- Pasienturinvolum skal overvåkes mens Bakri-postpartumballong er i bruk.

FORHOLDSREGLER

- Dette produktet er tiltenkt for bruk av leger som er opplært i og har erfaring med obstetrikk og gynekologiske teknikker.
- Unngå bruk av for mye makt når du setter inn ballongen i livmoren.

BRUKSANVISNING

VIKTIG: Før transvaginal eller transabdominal plassering av Bakri-postpartumballongen, må livmoren være fri for alle placenta-fragmenter og pasienten må evalueres for å sikre at det ikke er noen laserasjoner eller traumer i genitaltraktus og at blødningskilden ikke er arteriell.

Transvaginal plassering

1. Fastsett livmorvolum ved manuell undersøkelse eller ultralyd.
2. Sett ballongdelen av kateteret inn i livmoren og sørg for at hele ballongen settes inn forbi livmorshalskanalen og den interne åpningen.
3. Hvis det ikke allerede er lagt inn et Foley-kateter i urinblæren for oppsamling og overvåking av urinstrømmen, bør dette gjøres nå.

Transabdominal plassering, etter keisersnitt

1. Fastsett livmorvolum ved direkte undersøkelse.
2. Før tamponeringsballongen, ovenfra via keisersnittet, med fylleporten først gjennom livmor og cervix.

MERKNAD: Fjern stoppekranen for å lette plassering, og sett den på igjen før ballongen fylles.

3. La en assistent trekke skaftet til ballongen gjennom skjeden helt til enden av den tomme ballongen kommer i kontakt med den interne livmorshalsåpningen.
4. Lukk snittet i henhold til normal prosedyre, og påse at det ikke stikkes hull på ballongen under sutureringen.

MERKNAD: Kontroller at alle produktkomponentene er intakte og at hysterotomien er sikkert suturert før ballongen fylles. Hvis det er klinisk relevant, kan abdomen være åpen når ballongen fylles, for å overvåke distensjonen av livmoren nøye og bekrefte hysterotomilukkingen.

MERKNAD: Hvis det er klinisk relevant, kan en B-Lynch-kompresjonssutur brukes sammen med Bakri-postpartumballongen.

Ballonginflasjon

Med sprøyte

ADVARSEL: Fyll alltid ballongen med en steril væske. Ballongen skal aldri fylles med luft, karbondioksid eller andre gasser.

ADVARSEL: Maksimal fylling er 500 mL. Fyll ikke ballongen for mye. Hvis ballongen fylles for mye, kan ballongen bli forskjøvet inn i skjeden.

MERKNAD: Sørg for at ballongen er fylt til ønsket volum. Når du skal verifisere mengden væske som skal fylles i ballongen, anbefales det å plassere det forhåndsbestemte volumet med væske i en egen beholder i stedet for å bruke flere fylte sprøyter.

1. Hvis det ikke allerede er lagt inn et Foley-kateter i urinblæren for oppsamling og overvåking av urinstrømmen, bør dette gjøres nå.
2. Bruk vedlagt sprøyte, og fyll ballongen til det forhåndsbestemte volumet gjennom stoppekranen.
3. Når ballongen er fylt til det forhåndsbestemte volumet, bekreft plassering ved hjelp av ultralyd.
   MERKNAD: Se fig. 1 for riktig plassering.
4. Hvis ønskelig, kan det brukes traksjon på ballongskaftet. Opprettholdstrammingen ved å feste ballongskaftet til pasientens ben eller til en vekt som ikke overstiger 500 gram.

MERKNAD: For å unngå at ballongen forflyttes til skjeden kan det brukes mottrykk ved å pakke skjeden med vaginal gas fuktet med jod eller antibiotika.

5. Koble tømmeporten til en væskeoppsamlingspose for å overvåke hemostasen.

MERKNAD: For å overvåke hemostasen tilstrekkelig kan ballongens tømmeport og slanger skylles fri for klumper med steril isotonisk saltoppløsning.

6. Overvåk pasienten kontinuerlig for tegn på økt blødning og krampetrekninger i livmoren.

Ballonginflasjon

Med komponenter for hurtig instillasjon

Se **fig. 2–8** foran i dette heftet.

MERKNAD: Ultralyd skal brukes til å bekrefte riktig plassering av ballongen når ballongen er fylt til det forhåndsbestemte volumet.

Fjerning av ballongen

MERKNAD: Tidspunktet for fjerning av ballongen skal bestemmes av behandlende lege etter evaluering av pasienten når blødningen har blitt kontrollert og pasienten har blitt stabilisert. Ballongen kan fjernes tidligere, etter legens bestemmelse av hemostasen. Maksimal tid for innlegging er 24 timer.

1. Fjern strammingen fra ballongskaftet.
2. Fjern eventuelle tamponader fra skjeden.
3. Bruk en egnet sprøyte og aspirer innholdet i ballongen til den er helt tømt. Væsken kan fjernes trinnvis, slik at pasienten kan observeres periodemessig.

MERKNAD: I en nødsituasjon kan kateterskaftet kuttes for å muliggjøre hurtigere tømming.

4. Trekk ballongen forsiktig ut av livmoren og skjeden, og kast den.
5. Overvåk pasienten for tegn på blødning.

LEVERINGSFORM

Leveres sterilisert med etylenoksidgass i peel-open-innpakninger. Kun til engangsbruk. Steril hvis pakningen ikke er åpnet eller skadet. Bruk ikke produktet hvis du er i tvil om det er sterilt. Oppbevares på et mørkt, tørt og kjølig sted. Må ikke utsettes for lys i lengre perioder. Etter utpakking må du kontrollere at det ikke har oppstått skader på produktet.

REFERANSE

Denne bruksanvisningen er basert på legers erfaring og (eller) deres publiserte litteratur. Henvend deg til Cooks salgsrepresentant hvis du vil ha informasjon om tilgjengelig litteratur.

POLSKI

BALON POPORODOWY BAKRIEGO

PRZESTROGA: Zgodnie z prawem federalnym Stanów Zjednoczonych sprzedaż opisywanego urządzenia może być prowadzona wyłącznie przez lekarza lub na zlecenie lekarza (bądź uprawnionej osoby posiadającej odpowiednie zezwolenie).

OPIS URZĄDZENIA

Balon poporodowy Bakriego jest silikonowym cewnikiem balonowym o maksymalnej objętości napełniania 500 mL. Elementy do szybkiego zakroplenia obejmują polimerowy wężyk, kolec do worka infuzyjnego i zawór trójdrożny.

PRZEZNACZENIE URZĄDZENIA

Urządzenie to jest przeznaczone do zapewnienia czasowej kontroli lub zredukowania poporodowego krwotoku macicznego w przypadkach uzasadnionego postępowania zachowawczego.

PRZECIWWSKAZANIA

- Krwotok tętniczy wymagający postępowania chirurgicznego lub embolizacji angiograficznej
- Przypadki, w których wskazana jest histerektomia
- Ciąża
- Rak szyjki macicy
- Ropne zakażenia pochwy, szyjki macicy lub macicy
- Nieleczona anomalia macicy
- Rozsiane wykrzepianie wewnątrznaczyniowe
- Lokalizacja chirurgiczna uniemożliwiająca skuteczną kontrolę krwawienia za pomocą tego urządzenia

OSTRZEŻENIA

- Niniejsze urządzenie jest zaprojektowane jako tymczasowy środek do zapewnienia hemostazy w przypadkach poporodowego krwotoku macicznego, gdzie wskazane jest postępowanie zachowawcze.
- Balon poporodowy Bakriego jest przeznaczony do użycia w przypadku pierwotnego krwotoku poporodowego w ciągu 24 godzin od porodu.
- Urządzenia nie należy pozostawiać w miejscu na dłużej niż 24 godziny.
- Balon należy napełniać sterylnym płynem, takim jak woda jałowa, jałowa sól fizjologiczna lub roztwór Ringera z dodatkiem mleczanu. Nigdy nie wolno napełniać balonu powietrzem, dwutlenkiem węgla ani żadnym innym gazem.
- Maksymalna objętość napełnienia wynosi 500 mL. Nie należy nadmiernie wypełniać balonu. Nadmierne napełnienie balonu może spowodować jego przemieszczenie do pochwy.
- Pacjentki, u których zastosowano urządzenie, powinny być ściśle monitorowane pod kątem objawów nasilania się krwotoku i/lub rozsianego wykrzepiania wewnątrznaczyniowego (DIC). W takich przypadkach należy wdrożyć procedurę ratunkową zgodnie z protokołem szpitalnym.
- Brak danych klinicznych uzasadniających zastosowanie tego urządzenia w przypadku DIC.
- Monitorowanie pacjentek jest integralną częścią postępowania w przypadkach krwotoków poporodowych. Objawy pogorszania się lub braku poprawy powinny prowadzić do zastosowania bardziej agresywnego leczenia i postępowania u pacjentek z krwawieniem macicznym.
- Podczas stosowania balonu poporodowego Bakriego u pacjentek należy prowadzić monitorowanie diurezy.

ŚRODKI OSTROŻNOŚCI

- Produkt ten jest przeznaczony do użytku przez lekarzy przeszkolonych i doświadczonych w stosowaniu technik położniczych i ginekologicznych.
- Unikać nadmiernej siły przy wprowadzaniu balonu do jamy macicy.

INSTRUKCJA UŻYCIA

WAŻNE: Przed umieszczeniem przezpochwowym lub przezbrzusznym balonu poporodowego Bakriego macica powinna być oczyszczona ze wszystkich fragmentów łożyska; należy również przeprowadzić kontrolę pacjentki, aby upewnić się, że nie nastąpiło rozerwanie lub uraz dróg rodnych, i że źródłem krwawienia nie jest tętnica.

Umieszczanie przezpochwowe

1. Określić objętość macicy w badaniu bezpośrednim lub badaniem ultrasonograficznym.
2. Wprowadzić balonową część cewnika do jamy macicy upewniając się, że cały balon przeszedł przez kanał szyjki i ujście wewnętrzne.
3. Teraz założyć cewnik pęcherzowy Foleya, o ile nie został wcześniej założony, w celu zbierania moczu i monitorowania diurezy.

Umieszczanie przezbrzuszne, po cięciu cesarskim

1. Określić objętość macicy w badaniu bezpośrednim.
2. Od góry, z dostępu przez nacięcie do cięcia cesarskiego, wsunąć balon do tamponady, portem do napełniania wprzód, przez macicę i szyjkę.

UWAGA: Kranik można odłączyć dla ułatwienia umieszczania i ponownie przyłączyć przed napełnieniem balonu.

3. Poprosić asystenta o przeciągnięcie trzonu balonu przez kanał pochwy, aż do zetknięcia podstawy pustego balonu z ujściem wewnętrznym szyjki.
4. Zamknąć nacięcie zgodnie z normalną procedurą uważając, aby nie przebić balonu przy zakładaniu szwów.

UWAGA: Przed napełnieniem balonu sprawdzić, czy wszystkie elementy wyrobu są nienaruszone oraz czy nacięcie macicy zostało należycie zszyte. Jeżeli jest to klinicznie uzasadnione, brzuch może pozostać otwarty po napełnieniu balonu, aby ściśle monitorować rozszerzenie macicy i potwierdzić zamknięcie nacięcia macicy.

UWAGA: Jeżeli jest to klinicznie uzasadnione, można zastosować szew uciskowy B-Lyncha w połączeniu z balonem poporodowym Bakriego.

Wypełnianie balonu

Przy pomocy strzykawki

OSTRZEŻENIE: Balon napełniać zawsze sterylnym płynem. Nie wolno napełniać balonu powietrzem, dwutlenkiem węgla ani żadnym innym gazem.

OSTRZEŻENIE: Maksymalna objętość napełnienia wynosi 500 mL. Nie należy nadmiernie wypełniać balonu. Nadmierne napełnienie balonu może spowodować jego przemieszczenie do pochwy.

UWAGA: Dla zapewnienia napełnienia balonu do żądanej objętości zaleca się, aby określona wcześniej objętość płynu została wlana do osobnego naczynia, nie zaleca się ustalania ilości płynu podanego do balonu tylko na podstawie napełnienia według liczby strzykawek.

1. Teraz założyć cewnik pęcherzowy Foleya, o ile nie został wcześniej założony, w celu zbierania moczu i monitorowania diurezy.
2. Za pomocą dołączonej strzykawki rozpocząć napełnianie balonu do określonej wcześniej objętości przez kranik.
3. Po napełnieniu balonu do określonej wcześniej objętości potwierdzić jego umieszczenie za pomocą ultrasonografii. **UWAGA: Poprawne umieszczenie przedstawiono na rys. 1.**
4. Jeśli wymagane można zastosować naprężenie trzonu balonu. Aby utrzymać naprężenie, zamocować trzon balonu do nogi pacjentki lub przymocować ciężarek nieprzekraczający 500 g.

UWAGA: Aby zapobiec przemieszczeniu balonu w pochwie, można zastosować przeciwciśnienie poprzez uszczelnienie kanału pochwy za pomocą tamponu dopochwowego z gazy, nasączonego jodyną lub antybiotykiem.

5. Podłączyć port drenujący do worka na zbiórkę płynu w celu monitorowania hemostazy.

UWAGA: W celu odpowiedniego monitorowania hemostazy, port drenujący balonu i przewody można przepłukać jałową, izotoniczną solą fizjologiczną, aby wyczyścić je z zakrzepów.

6. Monitorować pacjentkę w sposób ciągły pod kątem wystąpienia objawów nasilenia krwotoku i skurczów macicy.

Wypełnianie balonu

Przy pomocy komponentów do szybkiego napełniania

Patrz **rys. 2-8**, na początku tej broszury.

UWAGA: Po napełnieniu balonu do określonej wcześniej objętości, potwierdzić jego poprawne umieszczenie za pomocą ultrasonografii.

Usuwanie balonu

UWAGA: Czas usunięcia balonu powinien ustalić lekarz prowadzający na podstawie oceny pacjentki, po opanowaniu krwawienia i ustabilizowaniu pacjentki. Balon można usunąć wcześniej, jeżeli lekarz ustali, że nastąpiła hemostaza. Maksymalny czas pozostawienia balonu w miejscu wynosi 24 godziny.

1. Usunąć naprężenie z trzonu balonu.
2. Usunąć wszelkie tampony dopochwowe.
3. Za pomocą odpowiedniej strzykawki zaaspirować zawartość balonu do momentu jego całkowitego opróżnienia. Płyn można usuwać stopniowo, co pozwoli na okresową obserwację pacjentki.

UWAGA: W przypadku nagłej potrzeby można odciąć trzon cewnika, aby ułatwić szybsze opróżnianie balonu.

4. Delikatnie wycofać balon z jamy macicy i kanału pochwy, i wyrzucić.
5. Monitorować pacjentkę pod kątem objawów krwawienia.

SPOSÓB DOSTARCZENIA

Produkt wyjałowiony tlenkiem etylenu; dostarczany w rozrywalnych opakowaniach. Urządzenie jest przeznaczone do jednorazowego użytku. Urządzenie zachowuje jałowość, jeśli opakowanie nie jest otwarte ani uszkodzone. Jeśli jałowość budzi wątpliwości, nie należy używać produktu. Przechowywać w ciemnym, suchym i chłodnym miejscu. Unikać przedłużonej ekspozycji na światło. Po wyjęciu z opakowania sprawdzić produkt, aby upewnić się, że nie doszło do uszkodzenia.

PIŚMIENNICTWO

Niniejszą instrukcję użycia opracowano na podstawie doświadczeń lekarzy i (lub) ich publikacji. W celu uzyskania informacji na temat dostępnego piśmiennictwa należy się zwrócić do lokalnego przedstawiciela handlowego firmy Cook.

PORTUGUÊS

BALÃO PÓS-PARTO BAKRI

ATENÇÃO: A lei federal dos EUA restringe a venda deste dispositivo a um médico ou um profissional de saúde licenciado ou mediante prescrição de um destes profissionais.

DESCRIÇÃO DO DISPOSITIVO

O Balão Pós-Parto Bakri é um cateter de balão de silicone com um volume de máximo de enchimento de 500 mL. Os componentes de instilação rápida incluem tubagem de polímero com um espigão de saco IV e uma válvula de três vias.

UTILIZAÇÃO PREVISTA

Este dispositivo destina-se a proporcionar controlo temporário ou redução da hemorragia uterina pós-parto quando se necessita de tratamento conservador.

CONTRA-INDICAÇÕES

- Hemorragia arterial que requer exploração cirúrgica ou embolização angiográfica
- Casos indicadores de histerectomia
- Gravidez
- Cancro do colo do útero
- Infeções purulentas da vagina, colo do útero ou útero
- Anomalia uterina não tratada
- Coagulação intravascular disseminada
- Um local cirúrgico que impediria que o dispositivo controlasse eficazmente a hemorragia

ADVERTÊNCIAS

- Este dispositivo destina-se a funcionar como um meio temporário de estabelecimento da hemóstase em casos indicadores de tratamento conservador da hemorragia uterina pós-parto.
- O balão pós-parto Bakri está indicado para utilização em caso de hemorragia pós-parto primária no período de 24 horas após o parto.
- O dispositivo não deve ser deixado no interior do organismo por mais de 24 horas.
- O balão deve ser enchido com um líquido estéril como, por exemplo, água estéril, soro fisiológico estéril ou solução de Ringer com lactato. O balão nunca deve ser enchido com ar, dióxido de carbono ou qualquer outro gás.
- O enchimento máximo corresponde a 500 mL. Não encha excessivamente o balão. O enchimento excessivo do balão pode provocar a deslocação do balão para a vagina.
- As doentes nas quais este dispositivo está a ser utilizado devem ser monitorizadas de perto para deteção de sinais de agravamento da hemorragia e/ou de coagulação intravascular disseminada (CID). Nesses casos, é necessário seguir a intervenção de emergência de acordo com o protocolo hospitalar.
- Não existem dados clínicos que fundamentem a utilização deste dispositivo no contexto da CID.
- A monitorização da doente constitui uma parte integral do controlo da hemorragia no pós-parto. Os sinais de deterioração ou ausência de melhoria do estado devem conduzir a um tratamento e controlo mais agressivos da hemorragia uterina da doente.
- O débito urinário da doente deve ser monitorizado durante a utilização do balão pós-parto Bakri.

PRECAUÇÕES

- Este produto destina-se a utilização por médicos com formação e experiência em técnicas obstétricas e ginecológicas.
- Evite exercer força excessiva ao inserir o balão no útero.

INSTRUÇÕES DE UTILIZAÇÃO

IMPORTANTE: Antes da colocação transvaginal ou transabdominal do balão pós-parto Bakri, o útero não deve apresentar quaisquer fragmentos de placenta, a doente deve ser avaliada por forma a garantir que não há lacerações ou traumatismo no trato genital e que a origem da hemorragia não é arterial.

Colocação transvaginal

1. Determine o volume uterino por exame direto ou exame ecográfico.
2. Insira a parte do balão do cateter no útero e certifique-se de que o balão fica completamente inserido para lá do canal cervical e do óstio interno.
3. Caso ainda não se encontre inserido, coloque nesta altura um cateter Foley permanente na bexiga para colher e monitorizar o débito urinário.

Colocação transabdominal, pós-cesariana

1. Determine o volume uterino por exame direto.
2. A partir de cima, através do acesso da incisão da cesariana, faça passar o balão de tamponamento, com o orifício de enchimento primeiro, através do útero e do colo do útero.

NOTA: Remova a torneira de passagem para auxiliar na colocação e fixação antes de encher o balão.

3. Peça a um assistente para puxar a haste do balão através do canal vaginal até a base do balão esvaziado ficar em contacto com o óstio cervical interno.
4. Feche a incisão de acordo com o procedimento normal, tomando o devido cuidado para evitar perfurar o balão durante a sutura.

NOTA: Antes de encher o balão, certifique-se de que todos os componentes do produto estão intactos e de que a histerotomia está suturada em segurança. Se for clinicamente relevante, o abdómen pode permanecer aberto aquando do enchimento do balão para assim se monitorizar atentamente a distensão uterina e confirmar o fecho da histerotomia.

NOTA: Se for clinicamente relevante, pode utilizar-se uma sutura de compressão B-Lynch em conjunto com o balão pós-parto Bakri.

Enchimento do balão

Com seringa

ADVERTÊNCIA: Encha sempre o balão com líquido estéril. Nunca encha o balão com ar, dióxido de carbono ou qualquer outro gás.

ADVERTÊNCIA: O enchimento máximo corresponde a 500 mL. Não encha excessivamente o balão. O enchimento excessivo do balão pode provocar a deslocação do balão para a vagina.

NOTA: Para garantir que o balão é enchido até ao volume pretendido, recomenda-se a colocação do volume predeterminado do líquido num recipiente separado, em vez de se basear numa contagem da seringa para verificar a quantidade de líquido que foi instilada no balão.

1. Caso ainda não se encontre inserido, coloque nesta altura um cateter Foley permanente na bexiga para colher e monitorizar o débito urinário.
2. Utilizando a seringa fornecida, comece a encher o balão até ao volume predeterminado através da torneira de passagem.
3. Depois de o balão ter sido enchido até ao volume predeterminado, confirme a colocação por meios ecográficos. **NOTA: Consulte a colocação correta na Fig. 1.**
4. Se desejar, pode aplicar tração na haste do balão. Para manter a tensão, fixe a haste do balão à perna da doente ou prenda-a a um peso que não exceda 500 g.

NOTA: Para evitar a deslocação do balão para a vagina, pode aplicar uma contrapressão enchendo o canal vaginal com gaze vaginal embebida em iodo ou antibiótico.

5. Ligue a porta de drenagem a um saco de recolha de líquido para monitorizar a hemóstase.

NOTA: Para monitorizar adequadamente a hemostase, pode irrigar o orifício e a tubagem de drenagem do balão com soro fisiológico isotónico para eliminar coágulos.

6. Monitorize continuamente a doente em relação a sinais de aumento da hemorragia e cólicas uterinas.

Enchimento do balão

Com componentes de instilação rápida

Consulte as **Figs. 2-8**, na parte da frente deste folheto.

NOTA: Deve realizar-se uma ecografia para confirmar a colocação correta do balão depois de este ser enchido até ao volume predeterminado.

Remoção do balão

NOTA: O momento da remoção do balão deve ser determinado pelo médico assistente aquando da avaliação da doente depois de a hemorragia estar controlada e a doente estabilizada. O balão pode ser removido antes, assim que o médico determinar a hemostase. O tempo de permanência máximo é de 24 horas.

1. Elimine a tensão da haste do balão.
2. Retire qualquer gaze vaginal.
3. Com uma seringa adequada, aspire o conteúdo do balão até ficar totalmente esvaziado. O líquido pode ser removido incrementalmente de modo a permitir observar a doente com regularidade.

NOTA: Em caso de emergência, a haste do cateter pode ser cortada para facilitar um esvaziamento mais rápido.

4. Retire cuidadosamente o balão do útero e do canal vaginal e elimine-o.
5. Monitorize a doente para a deteção de sinais de hemorragia.

APRESENTAÇÃO

Fornecido esterilizado pelo gás óxido de etileno em embalagens de abertura fácil. Destina-se a uma única utilização. Estéril desde que a embalagem não esteja aberta nem danificada. Se tiver alguma dúvida quanto à esterilidade do produto, não o utilize. Guarde num local protegido da luz, seco e fresco. Evite a exposição prolongada à luz. Depois de retirar o produto da embalagem, inspecione-o para se certificar de que não ocorreram danos.

REFERÊNCIA

Estas instruções de utilização baseiam-se na experiência de médicos e/ou na literatura publicada por médicos. Consulte o representante local de vendas da Cook para obter informações sobre a literatura disponível.

SVENSKA

BAKRI POSTPARTUMBALLONG

VAR FÖRSIKTIG: Enligt federal lagstiftning i USA får denna produkt endast säljas av eller på ordination från en läkare (eller korrekt legitimerad praktiker).

PRODUKTBESKRIVNING

Bakri postpartumballong är en ballongkateter av silikon med en högsta fyllnadsvolym på 500 mL. Komponenterna för snabb instillation inkluderar en polymerslang med en spetsanslutning för infusionspåse och en trevägsventil.

AVSEDD ANVÄNDNING

Denna anordning är avsedd att ge tillfällig kontroll över eller reduktion av uterusblödning postpartum när konservativ hantering är motiverad.

KONTRAINDIKATIONER

- Arteriell blödning som kräver kirurgisk undersökning eller angiografisk embolisering
- Fall som indikerar hysterektomi
- Graviditet
- Livmoderhalscancer
- Infektioner med varbildningar i vagina, cervix eller uterus
- Obehandlad uterusanomali
- Spridd intravaskulär koagulation
- Ett operationsställe som skulle hindra anordningen från att hålla blödningen under kontroll på ett effektivt sätt

VARNINGAR

- Denna anordning är avsedd som ett sätt att tillfälligt upprätta hemostas i fall som indikerar konservativ hantering av uterusblödning postpartum.

- Bakri postpartumballong är indicerad för användning vid primär postpartumblödning inom 24 timmar efter förlossningen.
- Anordningen får inte lämnas kvar i mer än 24 timmar.
- Ballongen ska fyllas med en steril vätska, t.ex. sterilt vatten, steril koksaltlösning eller lakterad Ringerlösning. Ballongen får aldrig fyllas med luft, koldioxid eller någon annan gas.
- Högsta fyllningsvolym är 500 mL. Ballongen får inte överfyllas. Överfyllning av ballongen kan leda till att ballongen rubbas in i vaginan.
- Patienter som denna anordning används på ska övervakas noga för tecken på förvärrad blödning och/eller spridd intravaskulär koagulation (DIC). I sådana fall ska akut intervention enligt sjukhusets rutiner utföras.
- Det finns inga kliniska data som stödjer användning av denna anordning vid DIC.
- Patientövervakning är en ingående del i hanteringen av postpartumblödningar. Tecken på att tillståndet förvärras eller inte förbättras ska leda till en mer aggressiv behandling och hantering av patientens uterusblödning.
- Patientens urinavgång ska övervakas medan Bakri postpartumballong används.

FÖRSIKTIGHETSÅTGÄRDER

- Denna produkt är avsedd att användas av läkare med utbildning i och erfarenhet av obstetrik och gynekologiska tekniker.
- Undvik alltför stor kraft när ballongen förs in i livmodern.

BRUKSANVISNING

VIKTIGT: Före transvaginal eller transabdominal placering av Bakri postpartumballong ska uterus vara helt fri från placentafragment och patienten ska undersökas för att säkerställa att det inte förekommer några lacerationer eller trauman i genitalvägarna och att källan till blödningen inte är arteriell.

Transvaginal placering

1. Fastställ uterus volym genom direkt undersökning eller ultraljudsundersökning.
2. För in ballongdelen av katetern i uterus och se till att hela ballongen förs in förbi cervixkanalen och den inre livmodermunnen.
3. Placera nu en inneliggande Foley-kateter i urinblåsan om det inte redan finns en på plats för att samla upp och övervaka urinavgången.

Transabdominell placering efter kejsarsnitt

1. Fastställ uterus volym genom direkt undersökning.
2. För in tamponadballongen med fyllningsporten först uppifrån genom kejsarsnittet och genom uterus och cervix.

OBS! Avlägsna infusionskranen för att underlätta placeringen och sätt tillbaka innan ballongen fylls.

3. Låt en assistent dra ballongskaftet genom den vaginala kanalen tills den tömda ballongbasen kommer i kontakt med den inre livmodermunnen.
4. Förslut snittet på normalt sätt, och var försiktig så att ballongen inte punkteras när du syr.

OBS! Säkerställ att alla produktkomponenter är oskadade och att hysterotomin har suturerats på ett säkert sätt före fyllning av ballongen. Om det är kliniskt relevant kan buken lämnas öppen vid fyllningen av ballongen för att nära övervaka utspänningen av uterus och bekräfta förslutningen av hysterotomin.

OBS! Om det är kliniskt relevant kan en kompressionssutur av typen B-Lynch användas i kombination med Bakri postpartumballong.

Ballongfyllning

Med spruta

VARNING: Fyll alltid ballongen med steril vätska. Den får aldrig fyllas med luft, koldioxid eller någon annan gas.

VARNING: Högsta fyllningsvolym är 500 mL. Ballongen får inte överfyllas. Överfyllning av ballongen kan leda till att ballongen rubbas in i vaginan.

OBS! För att säkerställa att ballongen fylls till önskad volym rekommenderas att den i förväg fastställda vätskevolymen placeras i en separat behållare, istället för att förlita sig på markeringarna på sprutan för att verifiera vilken vätskemängd som har fyllts i ballongen.

1. Placera nu en inneliggande Foley-kateter i urinblåsan om det inte redan finns en på plats för att samla upp och övervaka urinavgången.
2. Använd medföljande spruta och börja fylla ballongen med den i förväg fastställda volymen genom injektionskranen.
3. Så snart ballongen har fyllts till den i förväg fastställda volymen ska dess placering kontrolleras med ultraljud. **OBS! Se figur 1 för korrekt placering.**
4. Om så önskas kan traktion tillämpas på ballongskaftet. För att bibehålla denna spänning ska ballongskaftet fästas vid patientens ben eller vid en vikt på högst 500 g.

OBS! För att förhindra att ballongen placeras fel i vaginan kan ett mottryck appliceras genom att packa den vaginala kanalen med vaginal gasväv som blötlagts i jod eller antibiotika.

5. Anslut dräneringsporten till en vätskeuppsamlingspåse för att övervaka hemostasen.

OBS! För fullgod övervakning av hemostas kan koagel spolas ut ur ballongdränageporten och slangarna med steril isotonisk koksaltlösning.

6. Övervaka patienten kontinuerligt för tecken på ökad blödning och uteruskramper.

Ballongfyllning

Med komponenter för snabb instillation

Se **figurerna 2-8**, i broschyrens främre del.

OBS! Ultraljud ska användas för att bekräfta korrekt placering av ballongen så snart ballongen har fyllts till den i förväg fastställda volymen.

Avlägsnande av ballongen

OBS! Tidpunkten för avlägsnande av ballongen ska fastställas av den behandlande klinikern vid bedömning av patienten efter att blödningen har kunnat kontrolleras och patienten har stabiliserats. Ballongen kan avlägsnas tidigare, i samband med att klinikern fastställer hemostas. Längsta kvarliggningstid är 24 timmar.

1. Avlägsna spänningen från ballongskaftet.
2. Avlägsna eventuell fyllning från vaginan.
3. Använd lämplig spruta och aspirera innehållet i ballongen tills denna har tömts helt. Vätskan kan avlägsnas stegvis för att möjliggöra regelbunden observation av patienten.

OBS! I en nödsituation kan kateterskaftet kapas för att underlätta snabbare tömning.

4. Dra försiktigt ut ballongen ur livmodern och den vaginala kanalen och kassera den.
5. Övervaka patienten för tecken på blödning.

LEVERANSFORM

Levereras i etylenoxidgassteriliserade "peel-open"-förpackningar. Avsedd för engångsbruk. Steril såvida förpackningen är oöppnad och oskadad. Använd inte produkten om det är tveksamt att produkten är steril. Förvaras mörkt, torrt och svalt. Undvik långvarig exponering för ljus. Undersök produkten vid uppackningen för att säkerställa att den inte är skadad.

REFERENS

Denna bruksanvisning är baserad på erfarenheter från läkare och (eller) deras publicerade litteratur. Kontakta din lokala Cook-återförsäljare för information om tillgänglig litteratur.

If symbol appears on product label, X = quantity per box
Pokud je symbol uveden na označení výrobku, X = množství v krabici
Hvis symbolet vises på produktetiketten, er X = antal pr. æske
Sofern das Symbol auf dem Verpackungsetikett erscheint: X = Anzahl pro Karton
Εάν εμφανίζεται κάποιο σύμβολο στην ετικέτα του προϊόντος, X = ποσότητα ανά κουτί
Si el símbolo aparece en la etiqueta del producto, X = cantidad por caja
Si le symbole est visible sur l'étiquette du produit, X = quantité par boîte
Ha ez a szimbólum szerepel a termék címkéjén, akkor X a dobozonkénti mennyiség
Se questo simbolo compare sull'etichetta del prodotto, X = quantità per scatola
Als dit symbool op het productetiket staat: X = hoeveelheid per doos
Hvis symbolet vises på produktetiketten, X = antall per eske
Jeżeli symbol występuje na etykiecie produktu, X oznacza ilość sztuk w kartonie
Se o símbolo aparecer no rótulo do produto, X = quantidade por caixa
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2016-10
T_J-SOSR_REV2

K201199
Alydia Health
Trade/Device Name: Jada System
Contact Name: Cindy Domecus

This document is being communicated via e-mail as an attachment. The date on which FDA sent this e-mail is the official date of this correspondence.

We have reviewed your submission K201199 and have determined that additional information is required. Your file is being placed on hold pending a complete response to the attached deficiencies.

Please submit your response, referencing the submission number K201199 to:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Please refer to the eCopy guidance at https://www.fda.gov/media/83522/download for current information on eCopy requirements.

Your response is due within 180 days from the date of this request, which is the hold date plus 180 days. If a complete response is not received in CDRH's Document Control Center by this date, we will consider this submission to be withdrawn, and we will delete it from our review system.

You may not market this device until you have received a letter from FDA allowing you to do so. If you market the device without FDA clearance, you will be in violation of the Federal Food, Drug, and Cosmetic Act.

If you would like a meeting or teleconference with the review team and management to discuss your planned approach for responding to the attached deficiencies, please submit your request for feedback as a Submission Issue Q-Submission (Q-Sub). Please note that a Submission Issue Q-Sub does not take the place of a formal response to this email notification. As noted above, FDA will consider this submission to be withdrawn if FDA does not receive, in a submission to the Document Control Center, a complete response to all of the attached deficiencies within 180 calendar days of the date of this request.

This request for additional information has undergone supervisory review to ensure that the deficiencies cited are least burdensome and relevant to the marketing decision. Please see the revised guidance "Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions" issued

on September 29, 2017 (https://www.fda.gov/media/71735/download) for clarification regarding major and minor deficiencies.

MAJOR DEFICIENCY LIST

(b)(4) Deficiencies

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FDA is offering a teleconference within 10 calendar days from the date on this letter to address any clarification questions you may have pertaining to the deficiencies. If you are interested in a teleconference, please provide (1) proposed dates and (2) a list of your clarification questions via email at least 48 hours before the teleconference to the contact information listed below. We would like to emphasize that the purpose of the meeting is to address specific clarification questions. The teleconference is not intended for review of new information, test methods or data; these types of questions could be better addressed via a Submission Issue Q-Submission (Q-Sub). For additional information regarding Q-Subs, please refer to the Guidance for Industry and FDA Staff on Medical Devices: Requests for Feedback and Meetings for Medical Device Submissions at https://www.fda.gov/media/114034/download.

Least Burdensome (LB) Flag

The LB flag is an approach to allow 510(k) submitters the opportunity for the informal review by or on behalf of Division management of an issue raised in an FDA request for additional information (i.e., a deficiency letter). The goal of the LB flag is to quickly address FDA requests that submitters do not believe

are least burdensome or when submitters believe they are being held to a different standard than their legally marketed predicate device. The LB flag is not intended to clarify deficiencies, is not an appeal under 21 CFR 10.75, and is not intended to provide a review of a proposed response to deficiencies.

If you would like to throw the LB flag, FDA has several criteria that should be met before you submit your request:

- You should have tried to address your concern by discussing it with Division management before attempting to throw the LB flag. This discussion with Division management may take place as part of a teleconference (such as the voluntary teleconference held within 10 days following transmission of an Additional Information letter to clarify deficiencies), email, or a Q-Submission Submission Issue Request.
- Your flag should generally be limited to two topic areas. Topic areas are common premarket review deficiency categories that apply to many device types across multiple reviewing Divisions. Examples of topic areas include biocompatibility, sterility, reprocessing, software, electromagnetic compatibility, wireless, electrical safety, clinical, and non-clinical performance testing.
- If you would like to discuss issues pertaining to more than two topic areas, you should contact 510K_Program@fda.hhs.gov for more information.
- You should throw the LB flag within 60 calendar days of the date that FDA sent the deficiency letter.

Upon meeting the criteria, you should send a short email (e.g., 1-2 page) that includes: 1) a summary of the deficiencies under disagreement, 2) a summary of relevant communications with Division management, and 3) a proposed path forward. The LB flag should be sent to the lead reviewer and their Assistant Director. You should also copy 510K_Program@fda.hhs.gov on your LB flag email request. Within two business days of your email, your request will be acknowledged by the reviewing Division. If you do not meet the criteria for the LB flag, you will be notified in this acknowledgement email.

Your LB flag should contain sufficient information to determine whether the deficiency letter was not least burdensome, or you are being held to a different standard than your predicate device. FDA may request a phone call with you to discuss your concern further and intends to communicate feedback from Division management on LB flags through email no later than 21 calendar days of their receipt. Please note that the LB flag does not change the deadline for your response to the Document Control Center. If you have any questions, please contact 510K_Program@fda.hhs.gov.

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SECTION 6: 510(k) SUMMARY (21 CFR § 807.92(a))

The 510(k) Summary is provided in this section. The 510(k) Summary complies with 807.92(a) and has been prepared in accordance with the formatting in Appendix C of FDA's July 28, 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

510(k) Summary

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On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? **If possible, please provide a response by noon on Tuesday, August 25, 2020.**

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

Hello Cindy,

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

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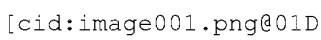
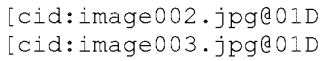
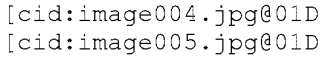
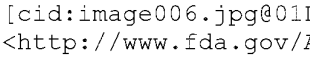
Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>









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From: Cindy Domecus <DomecusConsulting@comcast.net>

Sent: Thursday, August 27, 2020 10:41 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>

Cc: K201199@docs.fda.gov

Subject: Re: **(b)(4) Deficiencies** (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 27, 2020, at 4:47 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

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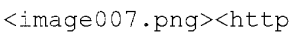
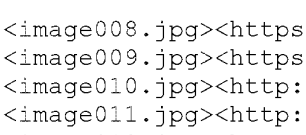
White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>





From: Cindy Domecus
<DomecusConsulting@comcast.net<mailto:DomecusConsulting@comcast.net>>

Sent: Thursday, August 27, 2020 12:50 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

(b)(4) Deficiencies

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Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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Clinical Investigation Report

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510(k) Summary – K201199

I. SUBMITTER

510(k) Owner
Colby Holtshouse
Alydia Health
3495 Edison Way
Menlo Park, CA 94025
Phone: 650-275-3772
Fax: 415-354-3473
Email: colby@alydiahealth.com

Submission Correspondent
Cindy Domecus, R.A.C. (US & EU)
Domecus Consulting Services LLC
Phone: (650) 343-4813
Fax: (650) 343-7822
Email: DomecusConsulting@comcast.net

Date Prepared
August 28, 2020

II. DEVICE

Name of Device:	Jada® System
Common or Usual Name:	Vacuum-induced Hemorrhage Control
Regulation Name:	Obstetric-Gynecologic Specialized Manual Instrument
Regulation Number:	21 CFR § 884.4530
Regulatory Class:	II
Product Code:	OQY (Intrauterine Tamponade Balloon)

III. PREDICATE DEVICE

The predicate device is the Bakri® Postpartum Balloon, Bakri® Postpartum Balloon with Rapid Instillation Components, K170622. The predicate device has not been subject to a design-related recall.

IV. DEVICE DESCRIPTION

The Jada® System is a 41 cm long intrauterine device primarily made of silicone. The vacuum connector and seal valve are made of polyvinylchloride and acrylonitrile-butadiene-styrene. The device consists of an intrauterine loop on the distal end of a translucent tube. The proximal end of the tube has a vacuum connector for connection to a vacuum tube. Proximal to the connection of the Intrauterine Loop is

a donut-shaped cervical seal. The cervical seal is filled with and emptied of 60-120 mL of sterile fluid by attaching a syringe to the seal valve. The intrauterine loop has 20 vacuum pores oriented toward its inside diameter. The outer surface of the intrauterine loop is a silicone shield which overhangs the vacuum pores to protect tissue from vacuum and to prevent the vacuum pores from plugging with tissue and blood clots.

Before placing the Jada® System device inside the uterus, the intrauterine loop is compressed. The compressed loop is inserted into the uterus transvaginally. The cervical seal is placed within the vagina, at the external cervical os, and inflated. Vacuum is then applied to a maximum value of 90 mmHg until bleeding is controlled. The device should be fixed to the thigh along the tube.

V. INDICATIONS FOR USE

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

VI. COMPARISON OF INTENDED USE AND TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Attribute	**K201199 Subject Device: Jada® System**	**K170622 Predicate Device: Bakri® Postpartum Balloon** **Bakri® Postpartum Balloon with Rapid Instillation Components**	**Comparison**
Manufacturer	Alydia Health	Cook Incorporated	N/A
Product Code	OQY	OQY	Same
Indications for Use	The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.	Bakri® Postpartum Balloon is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted. Bakri® Postpartum Balloon with Rapid	Different

		Instillation Components is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.	
Principle of Action	Inserted into the uterus and establishes a vacuum to cause the uterine walls to press against one another, producing a tamponade of the bleeding vessels	Inserted into the uterus and is inflated to press outward on the uterine walls, producing tamponade of the bleeding vessels	Different
Design	Inflatable cervical seal and intrauterine loop with vacuum pore	Inflatable uterine balloon and a single drainage side port	Different
Rx/OTC	Rx	Rx	Same
Materials	Silicone, Polyvinylchloride (PVC), Acrylonitrile-Butadiene-Styrene (ABS)	Silicone	Different
Sterile	SAL 10^{-6}	SAL 10^{-6}	Same
Single-use	Yes	Yes	Same

The Indications for Use statement for the Jada® System is not identical to the predicate device; however, the differences do not alter the intended use of the device. Both the subject and predicate devices have the same intended use for the treatment of abnormal uterine bleeding when conservative management is warranted.

The following technological differences exist between the subject and predicate devices:

- Principle of Operation: The subject device utilizes vacuum to affect tamponade on uterine walls, whereas the predicate device utilizes the fluidic pressure of an expanding balloon to affect tamponade
- Design: The subject device's intrauterine loop has a looped (drain) tube with a series of Vacuum Pores on the inside surface. The intrauterine loop features an elliptical pattern that lays flat on the uterine tissue bed, whereas the

predicate device has a single opening drain tube protruding out of the middle of the inflated balloon
- Materials: The patient contacting portions of both devices are made of silicone. However, the subject device includes a seal valve and vacuum connector made of ABS and PVC, respectively. All patient contacting devices are made of silicone for the subject and predicate device.

These differences in technological characteristics do not raise different questions of safety and effectiveness. Non-clinical and clinical data provided by Alydia Health were used to address the differences related to design and principle of operation to demonstrate substantial equivalence to the predicate device.

VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Mechanical Testing

The following mechanical tests were performed:

- Cervical Seal and Tube Dimensions: Verification of tube and seal dimensions
- Intrauterine Loop Portion Dimensional Test – Verification of intrauterine loop dimensions
- Removal of Intrauterine Portion Test – Verification that intrauterine loop and shield remain intact during removal
- Vacuum Pore Diameter – Verification of vacuum pore size
- No Sharp Edges – Verification of smooth edges and surfaces of device
- Attaining Pressure Drop – Verification that cervical seal withstands pressure differential of 180 mmHg vacuum
- Static Load Test – Verification that the cervical seal withstands a static load of 1 lb. applied axially along the tube without failure
- Overfill Capacity – Verification that cervical seal does not fail when filled with 180 mL water.
- Cervical Seal Inflation – Verification that cervical seal can be filled with 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Impact Load Test – Verification that the cervical seal withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Connection Tube Junction Impact Load Test - Verification that the intrauterine loop withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Flow Rate – Verification that the device with vacuum is able to evacuate 400 mL of simulated blood in 1 minute or less
- Device Integrity Leak Test – Verification that the joints of the device do not leak when 180 mmHg of vacuum is applied

- Integration to Hospital Vacuum Line – Verification that the device connects to a vacuum tube
- Inflation Tube Geometry – Verification that the cervical seal inflation lumen is functional
- Syringe Accommodation – Verification that a luer tapered syringe can be attached to the seal valve
- Cervical Seal Deflation – Verification that cervical seal can be emptied of 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Cervical Seal Diameter and Bond Stability – Verification that the seal maintains a diameter of 70 mm and maintains integrity after 48 hours
- Clotted Blood Test – Verification that the device can evacuate simulated blood in the presence of clotted blood without occluding
- Vacuum Connector Bond Test – Verification that the vacuum connector withstands a tensile load of 8.8 lbf
- Seal Valve Bond Test – Verification that the seal valve withstands a tensile load of 3.7 lbf

Biocompatibility Testing

The Jada® System is a surface device in contact with a breached surface, with limited duration (≤ 24 hours).

The biocompatibility evaluation for the Jada® System was conducted in accordance with the FDA June 2016 guidance *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process", Guidance for Industry and Food and Drug Administration Staff*. The battery of testing included the following tests:

- Cytotoxicity (ISO 10993-5:2009)
- Maximization Sensitization (ISO 10993-10:2010)
- Vaginal Irritation (ISO 10993-10:2010)
- Systemic toxicity (ISO 10993-11:2017)
- Material Mediated Pyrogenicity (ISO 10993-11:2017)

Sterilization and Shelf-Life Testing

The Jada® System is sterilized using gamma radiation to a SAL = 10^{-6}, according to ISO 11137-2: 2013. A shelf-life of 4 years has been established based on real-time aging.

Clinical Studies

Clinical testing of the Jada® System included an initial pilot study of 10 women in Indonesia, an initial phase of the pivotal study of 13 women in Uganda, and an IDE pivotal study of 107 women in the U.S. Substantial equivalence was based in part on the pivotal study, as described below.

Pivotal Study

The pivotal study was a prospective, multicenter, single-arm, open label, literature-controlled study at 12 sites in the U.S. A total of 107 subjects were enrolled into the study, of which 106 subjects were evaluable. Study entrance criteria included the following estimated blood loss (EBL) ranges:

Vaginal delivery: 500 – 1500 mL EBL or
C-section delivery: 1000 – 1500 mL EBL

Primary Effectiveness Endpoint

The primary effectiveness endpoint was as follows:
Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line or surgical intervention to control uterine hemorrhage after the use of the Jada® System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada® System use is standard of care and does not constitute failure of the primary effectiveness endpoint.

Primary Safety Endpoint

The primary safety endpoint was the incidence, severity and seriousness of device-related adverse events.

Effectiveness Results

The analysis of effectiveness was based on the 106 subjects in the ITT Cohort. Results from the 104 subjects in the mITT and 97 subjects in the PP Cohort are also presented. The treatment success rate in the ITT Cohort was 94.3% (100/106, $p<0.001$), with a lower bound 95% confidence limit of 88.1%. The success rate performance goal was 82.0% (95% CI: 73.4% to 89.2%), based on a meta-analysis of data from literature assessing the performance of the Bakri Postpartum Balloon. The treatment success rate in the mITT Cohort was 96.2% (100/104; 95% CI: 90.4%, 98.9%). The treatment success rate in the PP Cohort was 99% (96/97; 95% CI: 94.4% to 100%).

Safety Results

There were no adverse events judged definitely related to the device or the procedure and there was a low rate of possibly related adverse events, all of which were anticipated in this patient population and with introduction of an intrauterine device. Five possibly device-related adverse events were rated as “mild” and three were rated as “moderate” without any event in this group rated “severe”. The three moderate events were cases of endometritis, which is a known risk of long labor, vaginal exam, and postpartum hemorrhage.

Summary

In summary, the pivotal trial of the Jada® System demonstrates the device's safety and effectiveness in the treatment of abnormal postpartum uterine bleeding and hemorrhage.

VIII. CONCLUSIONS

The nonclinical and clinical performance data described above demonstrate that the Jada® System is as safe and effective as the predicate device and supports a determination of substantial equivalence.

Hello Cindy,

I did receive the email you sent on Saturday. Thank you for following up.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

cid:image001.png@01D1C57E.DFA022A0

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Monday, August 24, 2020 12:50 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Fwd: Request for information for Jada System (K201199/S001)

Hello Reginald,

Would you mind confirming receipt of my below email sent on Saturday? I have received a temporary delivery failure notice for the K number email address, but not yours. Nevertheless, I wanted to make sure you received it. Since the beginning of COVID, I have noticed that emails to FDA don't always get through on first attempt. I imagine that your servers are overloaded with pandemic-related communications.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

Begin forwarded message:

From: Cindy Domecus <domecusconsulting@comcast.net>
Subject: Re: Request for information for Jada System (K201199/S001)
Date: August 22, 2020 at 7:06:42 PM PDT
To: "Avery, Reginald" <Reginald.Avery@fda.hhs.gov>
Cc: "K201199@docs.fda.gov" <K201199@docs.fda.gov>

Hello Reginald,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thank you for your continued reivew of our file.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? **If possible, please provide a response by noon on Tuesday, August 25, 2020.**

(b)(4) Deficiencies

Do not hesitate to contact me if you have any questions or concerns.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

August 28, 2020</br></br> We have completed our review. Please refer to the attached letter for details.

If you have any questions, please contact the lead reviewer assigned to your submission, Reginald Avery.

 *** This is a system-generated email notification ***

U.S. FOOD & DRUG ADMINISTRATION

Food and Drug Administration
CDRH/OPEQ/OHT3/DHT3B
WO66 RM2646
10903 New Hampshire Ave
Silver Spring, MD 20993-0002
301-796-7048

Premarket Notification 510(k) Review

Date: June 29, 2020

Reviewer: Poulomi Nandy

Subject: Traditional 510(k)# K201199

Applicant: Alydia Health	**Device Trade Name:** Jada System
Contact Name: Cindy Domecus	**Contact Title:** Principal
Correspondent Firm: Domecus Consulting Services LLC	**Phone:** (650) 343-4813 **Email:** domecusconsulting@comcast.net
Received Date: May 4, 2020	**Due Date:** August 2, 2020
Pro Code(s): OQY **Class:** II **Reg #:** 884.4530	**Reg Name:** Obstetric-Gynecologic Specialized Manual Instrument

Predicate Devices:

Submission #	Pro Code	Device Trade Name	Applicant
K170622	OQY	Bakri Postpartum Balloon, Bakri Postpartum Balloon with Rapid Instillation Component	Cook Incorporated

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Thanks Reginald. FYI, I have a Pre-Sub call for another client from 3:00 to 4:00 ET today, so will be "out of pocket" for that hour.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) 5 (cell)

On Aug 27, 2020, at 4:37 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Thank you. We will let you know if we have any additional requests as soon as possible.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

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Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:
>
> Hello,
>

(b)(4) Deficiencies

>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
> OPEQ: Office of Product Evaluation and Quality
> CDRH | Food and Drug Administration
>
> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
> Ph: 240-402-6152
> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>
> <image001.png> <http://www.fda.gov/>
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> <image002.jpg> <https://www.facebook.com/FDA> <image003.jpg>
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<http://www.flickr.com/photos/fdaphotos/> <image006.jpg>
<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>

>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E
<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

>

> From: Cindy Domecus <domecusconsulting@comcast.net
<mailto:domecusconsulting@comcast.net>>

> Sent: Thursday, August 27, 2020 6:36 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re (b)(4) Deficiencies (K201199/S001)

>

> Hello Reginald,

>

(b)(4) Deficiencies

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>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

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> Reginald Avery, Ph.D.

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>

> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

> Ph: 240-402-6152

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> Sent: Thursday, August 27, 2020 10:41 AM

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510(k) Summary – K201199

I. SUBMITTER

510(k) Owner
Colby Holtshouse
Alydia Health
3495 Edison Way
Menlo Park, CA 94025
Phone: 650-275-3772
Fax: 415-354-3473
Email: colby@alydiahealth.com

Submission Correspondent
Cindy Domecus, R.A.C. (US & EU)
Domecus Consulting Services LLC
Phone: (650) 343-4813
Fax: (650) 343-7822
Email: DomecusConsulting@comcast.net

Date Prepared
August 28, 2020

II. DEVICE

Name of Device:	Jada® System
Common or Usual Name:	Vacuum-induced Hemorrhage Control
Regulation Name:	Obstetric-Gynecologic Specialized Manual Instrument
Regulation Number:	21 CFR § 884.4530
Regulatory Class:	II
Product Code:	OQY (Intrauterine Tamponade Balloon)

III. PREDICATE DEVICE

The predicate device is the Bakri® Postpartum Balloon, Bakri® Postpartum Balloon with Rapid Instillation Components, K170622. The predicate device has not been subject to a design-related recall.

IV. DEVICE DESCRIPTION

The Jada® System is a 41 cm long intrauterine device primarily made of silicone. The vacuum connector and seal valve are made of polyvinylchloride and acrylonitrile-butadiene-styrene. The device consists of an intrauterine loop on the distal end of a translucent tube. The proximal end of the tube has a vacuum connector for connection to a vacuum tube. Proximal to the connection of the Intrauterine Loop is

a donut-shaped cervical seal. The cervical seal is filled with and emptied of 60-120 mL of sterile fluid by attaching a syringe to the seal valve. The intrauterine loop has 20 vacuum pores oriented toward its inside diameter. The outer surface of the intrauterine loop is a silicone shield which overhangs the vacuum pores to protect tissue from vacuum and to prevent the vacuum pores from plugging with tissue and blood clots.

Before placing the Jada® System device inside the uterus, the intrauterine loop is compressed. The compressed loop is inserted into the uterus transvaginally. The cervical seal is placed within the vagina, at the external cervical os, and inflated. Vacuum is then applied to a maximum value of 90 mmHg until bleeding is controlled. The device should be fixed to the thigh along the tube.

V. INDICATIONS FOR USE

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

VI. COMPARISON OF INTENDED USE AND TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Attribute	**K201199 Subject Device: Jada® System**	**K170622 Predicate Device: Bakri® Postpartum Balloon** **Bakri® Postpartum Balloon with Rapid Instillation Components**	**Comparison**
Manufacturer	Alydia Health	Cook Incorporated	N/A
Product Code	OQY	OQY	Same
Indications for Use	The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.	Bakri® Postpartum Balloon is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted. Bakri® Postpartum Balloon with Rapid	Different

		Instillation Components is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.	
Principle of Action	Inserted into the uterus and establishes a vacuum to cause the uterine walls to press against one another, producing a tamponade of the bleeding vessels	Inserted into the uterus and is inflated to press outward on the uterine walls, producing tamponade of the bleeding vessels	Different
Design	Inflatable cervical seal and intrauterine loop with vacuum pore	Inflatable uterine balloon and a single drainage side port	Different
Rx/OTC	Rx	Rx	Same
Materials	Silicone, Polyvinylchloride (PVC), Acrylonitrile-Butadiene-Styrene (ABS)	Silicone	Different
Sterile	SAL 10^{-6}	SAL 10^{-6}	Same
Single-use	Yes	Yes	Same

The Indications for Use statement for the Jada® System is not identical to the predicate device; however, the differences do not alter the intended use of the device. Both the subject and predicate devices have the same intended use for the treatment of abnormal uterine bleeding when conservative management is warranted.

The following technological differences exist between the subject and predicate devices:

- Principle of Operation: The subject device utilizes vacuum to affect tamponade on uterine walls, whereas the predicate device utilizes the fluidic pressure of an expanding balloon to affect tamponade
- Design: The subject device's intrauterine loop has a looped (drain) tube with a series of Vacuum Pores on the inside surface. The intrauterine loop features an elliptical pattern that lays flat on the uterine tissue bed, whereas the

predicate device has a single opening drain tube protruding out of the middle of the inflated balloon

- Materials: The patient contacting portions of both devices are made of silicone. However, the subject device includes a seal valve and vacuum connector made of ABS and PVC, respectively. All patient contacting devices are made of silicone for the subject and predicate device.

These differences in technological characteristics do not raise different questions of safety and effectiveness. Non-clinical and clinical data provided by Alydia Health were used to address the differences related to design and principle of operation to demonstrate substantial equivalence to the predicate device.

VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Mechanical Testing

The following mechanical tests were performed:

- Cervical Seal and Tube Dimensions: Verification of tube and seal dimensions
- Intrauterine Loop Portion Dimensional Test – Verification of intrauterine loop dimensions
- Removal of Intrauterine Portion Test – Verification that intrauterine loop and shield remain intact during removal
- Vacuum Pore Diameter – Verification of vacuum pore size
- No Sharp Edges – Verification of smooth edges and surfaces of device
- Attaining Pressure Drop – Verification that cervical seal withstands pressure differential of 180 mmHg vacuum
- Static Load Test – Verification that the cervical seal withstands a static load of 1 lb. applied axially along the tube without failure
- Overfill Capacity – Verification that cervical seal does not fail when filled with 180 mL water.
- Cervical Seal Inflation – Verification that cervical seal can be filled with 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Impact Load Test – Verification that the cervical seal withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Connection Tube Junction Impact Load Test - Verification that the intrauterine loop withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Flow Rate – Verification that the device with vacuum is able to evacuate 400 mL of simulated blood in 1 minute or less
- Device Integrity Leak Test – Verification that the joints of the device do not leak when 180 mmHg of vacuum is applied

- Integration to Hospital Vacuum Line – Verification that the device connects to a vacuum tube
- Inflation Tube Geometry – Verification that the cervical seal inflation lumen is functional
- Syringe Accommodation – Verification that a luer tapered syringe can be attached to the seal valve
- Cervical Seal Deflation – Verification that cervical seal can be emptied of 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Cervical Seal Diameter and Bond Stability – Verification that the seal maintains a diameter of 70 mm and maintains integrity after 48 hours
- Clotted Blood Test – Verification that the device can evacuate simulated blood in the presence of clotted blood without occluding
- Vacuum Connector Bond Test – Verification that the vacuum connector withstands a tensile load of 8.8 lbf
- Seal Valve Bond Test – Verification that the seal valve withstands a tensile load of 3.7 lbf

Biocompatibility Testing

The Jada® System is a surface device in contact with a breached surface, with limited duration (≤ 24 hours).

The biocompatibility evaluation for the Jada® System was conducted in accordance with the FDA June 2016 guidance *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process", Guidance for Industry and Food and Drug Administration Staff*. The battery of testing included the following tests:

- Cytotoxicity (ISO 10993-5:2009)
- Maximization Sensitization (ISO 10993-10:2010)
- Vaginal Irritation (ISO 10993-10:2010)
- Systemic toxicity (ISO 10993-11:2017)
- Material Mediated Pyrogenicity (ISO 10993-11:2017)

Sterilization and Shelf-Life Testing

The Jada® System is sterilized using gamma radiation to a SAL = 10^{-6}, according to ISO 11137-2: 2013. A shelf-life of 4 years has been established based on real-time aging.

Clinical Studies

Clinical testing of the Jada® System included an initial pilot study of 10 women in Indonesia, an initial phase of the pivotal study of 13 women in Uganda, and an IDE pivotal study of 107 women in the U.S. Substantial equivalence was based in part on the pivotal study, as described below.

Pivotal Study

The pivotal study was a prospective, multicenter, single-arm, open label, literature-controlled study at 12 sites in the U.S. A total of 107 subjects were enrolled into the study, of which 106 subjects were evaluable. Study entrance criteria included the following estimated blood loss (EBL) ranges:

Vaginal delivery: 500 – 1500 mL EBL or
C-section delivery: 1000 – 1500 mL EBL

Primary Effectiveness Endpoint

The primary effectiveness endpoint was as follows:
Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line or surgical intervention to control uterine hemorrhage after the use of the Jada® System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada® System use is standard of care and does not constitute failure of the primary effectiveness endpoint.

Primary Safety Endpoint

The primary safety endpoint was the incidence, severity and seriousness of device-related adverse events.

Effectiveness Results

The analysis of effectiveness was based on the 106 subjects in the ITT Cohort. Results from the 104 subjects in the mITT and 97 subjects in the PP Cohort are also presented. The treatment success rate in the ITT Cohort was 94.3% (100/106, $p<0.001$), with a lower bound 95% confidence limit of 88.1%. The success rate performance goal was 82.0% (95% CI: 73.4% to 89.2%), based on a meta-analysis of data from literature assessing the performance of the Bakri Postpartum Balloon. The treatment success rate in the mITT Cohort was 96.2% (100/104; 95% CI: 90.4%, 98.9%). The treatment success rate in the PP Cohort was 99% (96/97; 95% CI: 94.4% to 100%).

Safety Results

There were no adverse events judged definitely related to the device or the procedure and there was a low rate of possibly related adverse events, all of which were anticipated in this patient population and with introduction of an intrauterine device. Five possibly device-related adverse events were rated as “mild” and three were rated as “moderate” without any event in this group rated “severe”. The three moderate events were cases of endometritis, which is a known risk of long labor, vaginal exam, and postpartum hemorrhage.

Summary

In summary, the pivotal trial of the Jada® System demonstrates the device's safety and effectiveness in the treatment of abnormal postpartum uterine bleeding and hemorrhage.

VIII. CONCLUSIONS

The nonclinical and clinical performance data described above demonstrate that the Jada® System is as safe and effective as the predicate device and supports a determination of substantial equivalence.

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Principal
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(b)(4)

July 10, 2020

(b)(4)

(b)(4) Clinical Studies

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(650) 343-4813 (office)

(650) 773-3445 (cell)

On Aug 28, 2020, at 9:15 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

<image001.png><http://www.fda.gov/>

<image002.jpg><https://www.facebook.com/FDA>
<image003.jpg><https://twitter.com/US_FDA>
<image004.jpg><http://www.youtube.com/user/USFoodandDrugAdmin>
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>

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From: Cindy Domecus
<domecusconsulting@comcast.net<mailto:domecusconsulting@comcast.net>>

Sent: Thursday, August 27, 2020 6:36 PM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello Cindy,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

<image001.png><http://www.fda.gov/>

<image002.jpg><https://www.facebook.com/FDA>

<image003.jpg><https://twitter.com/US_FDA>
<image004.jpg><http://www.youtube.com/user/USFoodandDrugAdmin>
<image005.jpg><http://www.flickr.com/photos/fdaphotos/>
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>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus
<DomecusConsulting@comcast.net<mailto:DomecusConsulting@comcast.net>>

Sent: Thursday, August 27, 2020 10:41 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: **(b)(4) Deficiencies** (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

On Aug 27, 2020, at 4:47 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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<image009.jpg><https://twitter.com/US_FDA>
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>

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus
<DomecusConsulting@comcast.net<mailto:DomecusConsulting@comcast.net>>

Sent: Thursday, August 27, 2020 12:50 AM

To: Avery, Reginald <Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>>

Cc: K201199@docs.fda.gov<mailto:K201199@docs.fda.gov>

Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald
<Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,

Reginald

Reginald Avery, Ph.D.

Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices

OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices

OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152

Reginald.Avery@fda.hhs.gov<mailto:Reginald.Avery@fda.hhs.gov>

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<image002.jpg><https://www.facebook.com/FDA>
<image003.jpg><https://twitter.com/US_FDA>
<image004.jpg><http://www.youtube.com/user/USFoodandDrugAdmin>
<image005.jpg><http://www.flickr.com/photos/fdaphotos/>
<image006.jpg><http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm
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(b)(4) Deficiencies

CLINICAL STUDY REPORT

APPENDIX 9.6

(b)(4) Clinical Studies

(b)(4) Clinical Studies

U.S. FOOD & DRUG ADMINISTRATION

August 28, 2020

Alydia Health
% Cindy Domecus, R.A.C.
Principal
Domecus Consulting Services LLC
1171 Barroilhet Drive
Hillsborough, CA 94010

Re: K201199
Trade/Device Name: Jada® System
Regulation Number: 21 CFR§ 884.4530
Regulation Name: Obstetric-gynecologic specialized manual instrument
Regulatory Class: II
Product Code: OQY
Dated: July 27, 2020
Received: July 29, 2020

Dear Cindy Domecus:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies.

You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Monica D. Garcia -S

Monica D. Garcia, Ph.D.
Acting Assistant Director
DHT3B: Division of Reproductive,
Gynecology and Urology Devices
OHT3: Office of GastroRenal, ObGyn,
General Hospital and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

U.S. FOOD & DRUG ADMINISTRATION

Food and Drug Administration
CDRH/OPEQ/OHT3/DHT3B
WO66 RM2646
10903 New Hampshire Ave
Silver Spring, MD 20993-0002
301-796-7048

Premarket Notification 510(k) Review

Date: June 29, 2020

Reviewer: Poulomi Nandy

Subject: Traditional 510(k)# K201199

Applicant: Alydia Health	**Device Trade Name:** Jada System
Contact Name: Cindy Domecus	**Contact Title:** Principal
Correspondent Firm: Domecus Consulting Services LLC	**Phone:** (650) 343-4813 **Email:** domecusconsulting@comcast.net
Received Date: May 4, 2020	**Due Date:** August 2, 2020
Pro Code(s): OQY **Class:** II **Reg #:** 884.4530	**Reg Name:** Obstetric-Gynecologic Specialized Manual Instrument

Predicate Devices:

Submission #	Pro Code	Device Trade Name	Applicant
K170622	OQY	Bakri Postpartum Balloon, Bakri Postpartum Balloon with Rapid	Cook Incorporated

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(b)(5) FDA Reviewer Notes

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Digital Signature Concurrence Table (Doc ID: 04500.14.01)	
This document represents a high-level summary of the Agency's determination on whether the applicant's device is substantially equivalent to a legally marketed predicate device. In determining whether the subject device is substantially equivalent to a predicate device, we carefully considered the relevant regulatory and statutory criteria for Agency decision-making under 21 CFR part 807 and section 513(i) of the Federal Food, Drug and Cosmetic Act (FD&C Act). We considered the burden that may be incurred by the applicant's attempt to follow the premarket notification process. The deficiencies provided in this review, if any, represent the required minimum information necessary to support a substantial equivalence determination. Therefore, we believe that we have considered the least burdensome requirements, under section 513(i)(1)(D) of the FD&C Act, for a 510(k) determination of substantial equivalence.	
Reviewer Sign-Off	Poulomi Nandy -S 2020.07.01 22:27:26 -04'00'

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From: Zhang, Qin
To: Bailey, Michael T; Nandy, Poulomi (CDRH); Colden, Kelly; Garcia, Monica
Subject: RE: FYI (b)(5)
Date: Thursday, April 16, 2020 11:00:46 AM
Attachments: image001.png
image007.png

(b)(5)

Qin

From: Bailey, Michael T <Michael.Bailey@fda.hhs.gov>
Sent: Thursday, April 16, 2020 10:44 AM
To: Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov>; Colden, Kelly <Kelly.Colden@fda.hhs.gov>; Garcia, Monica <Monica.Garcia@fda.hhs.gov>
Cc: Zhang, Qin <Qin.Zhang@fda.hhs.gov>
Subject: RE: FYI (b)(5)

Poulomi,

(b)(5)

Michael T. Bailey, Ph.D.
Team Lead, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, Ob/Gyn, General Hospital and Urology Devices
CDRH | Food and Drug Administration
White Oak, Bldg. 66, Rm. 2666 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 301-796-6530
michael.bailey@fda.hhs.gov

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From: Nandy, Poulomi (CDRH)
Sent: Thursday, April 16, 2020 10:15 AM
To: Colden, Kelly <Kelly.Colden@fda.hhs.gov>; Bailey, Michael T <Michael.Bailey@fda.hhs.gov>; Garcia, Monica <Monica.Garcia@fda.hhs.gov>
Subject: FYI - (b)(5)

Hi All,

(b)(5)

Thanks,
Poulomi.

From: Colden, Kelly <Kelly.Colden@fda.hhs.gov>
Sent: Monday, April 6, 2020 12:29 PM
To: Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov>; Bailey, Michael T <Michael.Bailey@fda.hhs.gov>; Garcia, Monica <Monica.Garcia@fda.hhs.gov>
Subject: RE: (b)(5)

Poulomi,

(b)(5)

Thanks,

Kelly

Kelly Colden MD, MPH
Medical Officer
Obstetrical and Reproductive Health Devices Team
Division of Reproductive, Gynecology, and Urology Devices (DHT3B)
FDA/CDRH/OPEQ/OHT3

WO 66, 2660B
Silver Spring, MD 20993
Phone: 240-402-5341
kelly.colden@fda.hhs.gov

From: Nandy, Poulomi (CDRH) <Poulomi.Nandy@fda.hhs.gov>
Sent: Monday, April 6, 2020 11:19 AM
To: Colden, Kelly <Kelly.Colden@fda.hhs.gov>; Bailey, Michael T <Michael.Bailey@fda.hhs.gov>; Garcia, Monica <Monica.Garcia@fda.hhs.gov>
Subject (b)(5)

Hi All,

(b)(5)

(b)(5)

Thanks,
Poulomi.

Poulomi Nandy
Microbiologist, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices | OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
Office of Product Evaluation and Quality

CDRH | Food and Drug Administration
White Oak, Bldg. 66, Rm. G246 |10903 New Hampshire Avenue | Silver Spring, MD 20993

Phone: (301) 796-7048
poulomi.nandy@fda.hhs.gov
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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K201199

Device Name
Jada® System

Indications for Use *(Describe)*
The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Hello Reginald,

Would you mind confirming receipt of my below email sent on Saturday? I have received a temporary delivery failure notice for the K number email address, but not yours. Nevertheless, I wanted to make sure you received it. Since the beginning of COVID, I have noticed that emails to FDA don't always get through on first attempt. I imagine that your servers are overloaded with pandemic-related communications.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

Begin forwarded message:

From: Cindy Domecus <domecusconsulting@comcast.net>
Subject: Re: **Request for information for Jada System (K201199/S001)**
Date: August 22, 2020 at 7:06:42 PM PDT
To: "Avery, Reginald" <Reginald.Avery@fda.hhs.gov>
Cc: "K201199@docs.fda.gov" <K201199@docs.fda.gov>

Hello Reginald,

(b)(4) Deficiencies

Thank you for your continued reivew of our file.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

SECTION 6: 510(k) SUMMARY (21 CFR § 807.92(a))

The 510(k) Summary is provided in this section. The 510(k) Summary complies with 807.92(a) and has been prepared in accordance with the formatting in Appendix C of FDA's July 28, 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

510(k) Summary

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510(k) Summary – K201199

I. SUBMITTER

510(k) Owner
Colby Holtshouse
Alydia Health
3495 Edison Way
Menlo Park, CA 94025
Phone: 650-275-3772
Fax: 415-354-3473
Email: colby@alydiahealth.com

Submission Correspondent
Cindy Domecus, R.A.C. (US & EU)
Domecus Consulting Services LLC
Phone: (650) 343-4813
Fax: (650) 343-7822
Email: DomecusConsulting@comcast.net

Date Prepared
August 28, 2020

II. DEVICE

Name of Device:	Jada® System
Common or Usual Name:	Vacuum-induced Hemorrhage Control
Regulation Name:	Obstetric-Gynecologic Specialized Manual Instrument
Regulation Number:	21 CFR § 884.4530
Regulatory Class:	II
Product Code:	OQY (Intrauterine Tamponade Balloon)

III. PREDICATE DEVICE

The predicate device is the Bakri® Postpartum Balloon, Bakri® Postpartum Balloon with Rapid Instillation Components, K170622. The predicate device has not been subject to a design-related recall.

IV. DEVICE DESCRIPTION

The Jada® System is a 41 cm long intrauterine device primarily made of silicone. The vacuum connector and seal valve are made of polyvinylchloride and acrylonitrile-butadiene-styrene. The device consists of an intrauterine loop on the distal end of a translucent tube. The proximal end of the tube has a vacuum connector for connection to a vacuum tube. Proximal to the connection of the Intrauterine Loop is

a donut-shaped cervical seal. The cervical seal is filled with and emptied of 60-120 mL of sterile fluid by attaching a syringe to the seal valve. The intrauterine loop has 20 vacuum pores oriented toward its inside diameter. The outer surface of the intrauterine loop is a silicone shield which overhangs the vacuum pores to protect tissue from vacuum and to prevent the vacuum pores from plugging with tissue and blood clots.

Before placing the Jada® System device inside the uterus, the intrauterine loop is compressed. The compressed loop is inserted into the uterus transvaginally. The cervical seal is placed within the vagina, at the external cervical os, and inflated. Vacuum is then applied to a maximum value of 90 mmHg until bleeding is controlled. The device should be fixed to the thigh along the tube.

V. INDICATIONS FOR USE

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.

VI. COMPARISON OF INTENDED USE AND TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Attribute	**K201199 Subject Device: Jada® System**	**K170622 Predicate Device: Bakri® Postpartum Balloon** **Bakri® Postpartum Balloon with Rapid Instillation Components**	**Comparison**
Manufacturer	Alydia Health	Cook Incorporated	N/A
Product Code	OQY	OQY	Same
Indications for Use	The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.	Bakri® Postpartum Balloon is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted. Bakri® Postpartum Balloon with Rapid	Different

		Instillation Components is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.	
Principle of Action	Inserted into the uterus and establishes a vacuum to cause the uterine walls to press against one another, producing a tamponade of the bleeding vessels	Inserted into the uterus and is inflated to press outward on the uterine walls, producing tamponade of the bleeding vessels	Different
Design	Inflatable cervical seal and intrauterine loop with vacuum pore	Inflatable uterine balloon and a single drainage side port	Different
Rx/OTC	Rx	Rx	Same
Materials	Silicone, Polyvinylchloride (PVC), Acrylonitrile-Butadiene-Styrene (ABS)	Silicone	Different
Sterile	SAL 10^{-6}	SAL 10^{-6}	Same
Single-use	Yes	Yes	Same

The Indications for Use statement for the Jada® System is not identical to the predicate device; however, the differences do not alter the intended use of the device. Both the subject and predicate devices have the same intended use for the treatment of abnormal uterine bleeding when conservative management is warranted.

The following technological differences exist between the subject and predicate devices:

- Principle of Operation: The subject device utilizes vacuum to affect tamponade on uterine walls, whereas the predicate device utilizes the fluidic pressure of an expanding balloon to affect tamponade
- Design: The subject device's intrauterine loop has a looped (drain) tube with a series of Vacuum Pores on the inside surface. The intrauterine loop features an elliptical pattern that lays flat on the uterine tissue bed, whereas the

predicate device has a single opening drain tube protruding out of the middle of the inflated balloon

- Materials: The patient contacting portions of both devices are made of silicone. However, the subject device includes a seal valve and vacuum connector made of ABS and PVC, respectively. All patient contacting devices are made of silicone for the subject and predicate device.

These differences in technological characteristics to not raise different questions of safety and effectiveness. Non-clinical and clinical data provided by Alydia Health were used to address the differences related to design and principle of operation to demonstrate substantial equivalence to the predicate device.

VII. PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Mechanical Testing

The following mechanical tests were performed:

- Cervical Seal and Tube Dimensions: Verification of tube and seal dimensions
- Intrauterine Loop Portion Dimensional Test – Verification of intrauterine loop dimensions
- Removal of Intrauterine Portion Test – Verification that intrauterine loop and shield remain intact during removal
- Vacuum Pore Diameter – Verification of vacuum pore size
- No Sharp Edges – Verification of smooth edges and surfaces of device
- Attaining Pressure Drop – Verification that cervical seal withstands pressure differential of 180 mmHg vacuum
- Static Load Test – Verification that the cervical seal withstands a static load of 1 lb. applied axially along the tube without failure
- Overfill Capacity – Verification that cervical seal does not fail when filled with 180 mL water.
- Cervical Seal Inflation – Verification that cervical seal can be filled with 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Impact Load Test – Verification that the cervical seal withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Connection Tube Junction Impact Load Test - Verification that the intrauterine loop withstands an impact test of dropping a 1 lb. weight 2 ft axially along the tube without failure
- Flow Rate – Verification that the device with vacuum is able to evacuate 400 mL of simulated blood in 1 minute or less
- Device Integrity Leak Test – Verification that the joints of the device do not leak when 180 mmHg of vacuum is applied

- Integration to Hospital Vacuum Line – Verification that the device connects to a vacuum tube
- Inflation Tube Geometry – Verification that the cervical seal inflation lumen is functional
- Syringe Accommodation – Verification that a luer tapered syringe can be attached to the seal valve
- Cervical Seal Deflation – Verification that cervical seal can be emptied of 60 mL of water within 30 seconds with 10 lbs. of force on syringe
- Cervical Seal Diameter and Bond Stability – Verification that the seal maintains a diameter of 70 mm and maintains integrity after 48 hours
- Clotted Blood Test – Verification that the device can evacuate simulated blood in the presence of clotted blood without occluding
- Vacuum Connector Bond Test – Verification that the vacuum connector withstands a tensile load of 8.8 lbf
- Seal Valve Bond Test – Verification that the seal valve withstands a tensile load of 3.7 lbf

Biocompatibility Testing

The Jada® System is a surface device in contact with a breached surface, with limited duration (≤ 24 hours).

The biocompatibility evaluation for the Jada® System was conducted in accordance with the FDA June 2016 guidance *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process", Guidance for Industry and Food and Drug Administration Staff*. The battery of testing included the following tests:

- Cytotoxicity (ISO 10993-5:2009)
- Maximization Sensitization (ISO 10993-10:2010)
- Vaginal Irritation (ISO 10993-10:2010)
- Systemic toxicity (ISO 10993-11:2017)
- Material Mediated Pyrogenicity (ISO 10993-11:2017)

Sterilization and Shelf-Life Testing

The Jada® System is sterilized using gamma radiation to a SAL = 10^{-6}, according to ISO 11137-2: 2013. A shelf-life of 4 years has been established based on real-time aging.

Clinical Studies

Clinical testing of the Jada® System included an initial pilot study of 10 women in Indonesia, an initial phase of the pivotal study of 13 women in Uganda, and an IDE pivotal study of 107 women in the U.S. Substantial equivalence was based in part on the pivotal study, as described below.

Pivotal Study

The pivotal study was a prospective, multicenter, single-arm, open label, literature-controlled study at 12 sites in the U.S. A total of 107 subjects were enrolled into the study, of which 106 subjects were evaluable. Study entrance criteria included the following estimated blood loss (EBL) ranges:

Vaginal delivery: 500 – 1500 mL EBL or
C-section delivery: 1000 – 1500 mL EBL

Primary Effectiveness Endpoint

The primary effectiveness endpoint was as follows:
Control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line or surgical intervention to control uterine hemorrhage after the use of the Jada® System per the Instructions for Use.

Non-surgical, second line procedures include uterine balloon therapy, uterine packing, or uterine artery embolization. Surgical intervention includes procedures such as uterine arterial ligation, uterine compression sutures or hysterectomy.

Note: Continuation of the administration of uterotonics concomitant with and post Jada® System use is standard of care and does not constitute failure of the primary effectiveness endpoint.

Primary Safety Endpoint

The primary safety endpoint was the incidence, severity and seriousness of device-related adverse events.

Effectiveness Results

The analysis of effectiveness was based on the 106 subjects in the ITT Cohort. Results from the 104 subjects in the mITT and 97 subjects in the PP Cohort are also presented. The treatment success rate in the ITT Cohort was 94.3% (100/106, $p<0.001$), with a lower bound 95% confidence limit of 88.1%. The success rate performance goal was 82.0% (95% CI: 73.4% to 89.2%), based on a meta-analysis of data from literature assessing the performance of the Bakri Postpartum Balloon. The treatment success rate in the mITT Cohort was 96.2% (100/104; 95% CI: 90.4%, 98.9%). The treatment success rate in the PP Cohort was 99% (96/97; 95% CI: 94.4% to 100%).

Safety Results

There were no adverse events judged definitely related to the device or the procedure and there was a low rate of possibly related adverse events, all of which were anticipated in this patient population and with introduction of an intrauterine device. Five possibly device-related adverse events were rated as “mild” and three were rated as “moderate” without any event in this group rated “severe”. The three moderate events were cases of endometritis, which is a known risk of long labor, vaginal exam, and postpartum hemorrhage.

Summary

In summary, the pivotal trial of the Jada® System demonstrates the device's safety and effectiveness in the treatment of abnormal postpartum uterine bleeding and hemorrhage.

VIII. CONCLUSIONS

The nonclinical and clinical performance data described above demonstrate that the Jada® System is as safe and effective as the predicate device and supports a determination of substantial equivalence.

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

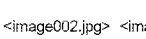
Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality

CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov



Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received: https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

SECTION 14: LABELING

This section includes the proposed labeling for the Jada System. The proposed labeling is comprised of the following:

- Instructions for Use (PN-030), provided in **Exhibit 14.A**
- Package labels: (Pouch Label PN-032 and Carton Label PN-033), provided in **Exhibit 14.B**
- Quick Reference Guide (PN-031), provided in **Exhibit 14.C**

The Indications for Use stated in the labeling are identical to the Indications for Use form (Form 3881) provided in **Section 5** and the 510(k) Summary provided in **Section 6**.

The Jada System is a prescription device, so qualifies for exemption per 21 CFR 801 Subpart D. The labeling includes the prescription statement/symbol per 21 CFR 801.109(b)(1).

Per 21 CFR 801.1, the labeling includes the name and place of business of the manufacturer.

There is no device-specific guidance document, special controls document or requirements in a device-specific classification regulation regarding labeling that is applicable to the subject device.

21 CFR 809.10 does not apply to the subject device, as the Jada System is not an in vitro diagnostic device.

TEST FACILITY

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SPONSOR

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STUDY TITLE

ISO Systemic Toxicity Study in Mice

TEST ARTICLE NAME

Postpartum Hemorrhage Intrauterine Suction Device

TEST ARTICLE IDENTIFICATION

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SECTION 6: 510(k) SUMMARY (21 CFR § 807.92(a))

The 510(k) Summary is provided in this section. The 510(k) Summary complies with 807.92(a) and has been prepared in accordance with the formatting in Appendix C of FDA's July 28, 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

510(k) Summary

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From: Stephens, Nicholas * [Nicholas.Stephens@fda.hhs.gov]
Sent: 7/29/2020 6:20:16 PM
To: domecusconsulting@comcast.net
Subject: K201199/S001 Acknowledgement Notification
Attachments: K201199.S001- Letter.pdf

Acknowledgment Letter

7/29/2020

Cindy Domecus, Principal
Domecus Consulting Services LLC
1171 Barroilhet Drive
Hillsborough, CA 94010
UNITED STATES

Dear Cindy Domecus:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has received your submission. This submission has been assigned the unique document control number below. All future correspondence regarding this submission should be identified prominently with the number assigned and should be submitted to the Document Control Center at the above letterhead address. Failure to do so may result in processing delays. If you believe the information identified below is incorrect, please notify the Program Operations Staff at (301) 796-5640.

Submission Number: K201199/S001
Received: 7/29/2020
Applicant: Alydia Health
Device: Jada System

We will notify you when the review of this document has been completed or if any additional information is required. If you are submitting new information about a submission for which we have already made a final decision, please note that your submission will not be re-opened. For information about CDRH review regulations and policies, please refer to http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm.

Sincerely yours,

Center for Devices and Radiological Health

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SECTION 6: 510(k) SUMMARY (21 CFR § 807.92(a))

The 510(k) Summary is provided in this section. The 510(k) Summary complies with 807.92(a) and has been prepared in accordance with the formatting in Appendix C of FDA's July 28, 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

510(k) Summary

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U.S. FOOD & DRUG ADMINISTRATION

K201199
Alydia Health
Trade/Device Name: Jada System
Contact Name: Cindy Domecus

This document is being communicated via e-mail as an attachment. The date on which FDA sent this e-mail is the official date of this correspondence.

We have reviewed your submission K201199 and have determined that additional information is required. Your file is being placed on hold pending a complete response to the attached deficiencies.

Please submit your response, referencing the submission number K201199 to:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Please refer to the eCopy guidance at https://www.fda.gov/media/83522/download for current information on eCopy requirements.

Your response is due within 180 days from the date of this request, which is the hold date plus 180 days. If a complete response is not received in CDRH's Document Control Center by this date, we will consider this submission to be withdrawn, and we will delete it from our review system.

You may not market this device until you have received a letter from FDA allowing you to do so. If you market the device without FDA clearance, you will be in violation of the Federal Food, Drug, and Cosmetic Act.

If you would like a meeting or teleconference with the review team and management to discuss your planned approach for responding to the attached deficiencies, please submit your request for feedback as a Submission Issue Q-Submission (Q-Sub). Please note that a Submission Issue Q-Sub does not take the place of a formal response to this email notification. As noted above, FDA will consider this submission to be withdrawn if FDA does not receive, in a submission to the Document Control Center, a complete response to all of the attached deficiencies within 180 calendar days of the date of this request.

This request for additional information has undergone supervisory review to ensure that the deficiencies cited are least burdensome and relevant to the marketing decision. Please see the revised guidance "Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions" issued

on September 29, 2017 (https://www.fda.gov/media/71735/download) for clarification regarding major and minor deficiencies.

MAJOR DEFICIENCY LIST

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FDA is offering a teleconference within 10 calendar days from the date on this letter to address any clarification questions you may have pertaining to the deficiencies. If you are interested in a teleconference, please provide (1) proposed dates and (2) a list of your clarification questions via email at least 48 hours before the teleconference to the contact information listed below. We would like to emphasize that the purpose of the meeting is to address specific clarification questions. The teleconference is not intended for review of new information, test methods or data; these types of questions could be better addressed via a Submission Issue Q-Submission (Q-Sub). For additional information regarding Q-Subs, please refer to the Guidance for Industry and FDA Staff on Medical Devices: Requests for Feedback and Meetings for Medical Device Submissions at https://www.fda.gov/media/114034/download.

Least Burdensome (LB) Flag

The LB flag is an approach to allow 510(k) submitters the opportunity for the informal review by or on behalf of Division management of an issue raised in an FDA request for additional information (i.e., a deficiency letter). The goal of the LB flag is to quickly address FDA requests that submitters do not believe

are least burdensome or when submitters believe they are being held to a different standard than their legally marketed predicate device. The LB flag is not intended to clarify deficiencies, is not an appeal under 21 CFR 10.75, and is not intended to provide a review of a proposed response to deficiencies.

If you would like to throw the LB flag, FDA has several criteria that should be met before you submit your request:

- You should have tried to address your concern by discussing it with Division management before attempting to throw the LB flag. This discussion with Division management may take place as part of a teleconference (such as the voluntary teleconference held within 10 days following transmission of an Additional Information letter to clarify deficiencies), email, or a Q-Submission Submission Issue Request.
- Your flag should generally be limited to two topic areas. Topic areas are common premarket review deficiency categories that apply to many device types across multiple reviewing Divisions. Examples of topic areas include biocompatibility, sterility, reprocessing, software, electromagnetic compatibility, wireless, electrical safety, clinical, and non-clinical performance testing.
- If you would like to discuss issues pertaining to more than two topic areas, you should contact 510K_Program@fda.hhs.gov for more information.
- You should throw the LB flag within 60 calendar days of the date that FDA sent the deficiency letter.

Upon meeting the criteria, you should send a short email (e.g., 1-2 page) that includes: 1) a summary of the deficiencies under disagreement, 2) a summary of relevant communications with Division management, and 3) a proposed path forward. The LB flag should be sent to the lead reviewer and their Assistant Director. You should also copy 510K_Program@fda.hhs.gov on your LB flag email request. Within two business days of your email, your request will be acknowledged by the reviewing Division. If you do not meet the criteria for the LB flag, you will be notified in this acknowledgement email.

Your LB flag should contain sufficient information to determine whether the deficiency letter was not least burdensome, or you are being held to a different standard than your predicate device. FDA may request a phone call with you to discuss your concern further and intends to communicate feedback from Division management on LB flags through email no later than 21 calendar days of their receipt. Please note that the LB flag does not change the deadline for your response to the Document Control Center. If you have any questions, please contact 510K_Program@fda.hhs.gov.

DEPARTMENT OF HEALTH AND HUMAN SERVICES **M E M O R A N D U M**

Food and Drug Administration
Office of Device Evaluation

DATE: June 12, 2023

FROM: Reginald Avery, PhD, Biomedical Engineer
CDRH/OPEQ/OHT3/DHT3B/THT3B1
(240) 402-6152

TO: Poulomi Nandy, Microbiologist
CDRH/OPEQ/OHT3/DHT3B/THT3B1

RE: Mechanical Engineering Consult
K201199 (CON2011147)
Jada System
Alydia Health

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Clinical Evaluation Report: InPress Postpartum Hemorrhage Vacuum Device

Prepared for:

InPress Technologies, Inc.
955 Morro Street
San Luis Obispo, CA 93401 USA

Prepared by:

(b)(4)

November 19, 2015

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SECTION 9: CLINICAL TRIAL INFORMATION

This submission is supported by the following clinical performance data:

1. Pilot study in Indonesia
2. Cases enrolled under earlier version of pivotal study protocol in Uganda
3. PEARLE IDE Pivotal Study

The required information regarding these clinical trials is provided below.

A. Financial Certification/Disclosure

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Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 28, 2020, at 10:16 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
OPEQ: Office of Product Evaluation and Quality
CDRH | Food and Drug Administration

White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Friday, August 28, 2020 1:10 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

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From: Cindy Domecus <domecusconsulting@comcast.net>
Sent: Thursday, August 27, 2020 6:36 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 27, 2020, at 9:12 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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<image002.jpg> <image003.jpg> <image004.jpg> <image005.jpg> <image006.jpg>

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 10:41 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies n (K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 27, 2020, at 4:47 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello Cindy,

Please send me a Word version of your 510(k) Summary. This will help us to track and share any proposed changes we make with you as we finalize the submission.

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re: (b)(4) Deficiencies (K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) 5 (cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

DHT3B: Division of Reproductive, Gynecology and Urology Devices
OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
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White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993

Ph: 240-402-6152
Reginald.Avery@fda.hhs.gov

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(b)(4) Deficiencies

MEMORANDUM FOR STATISTICAL CONSULT

Date: August 24, 2020

Yanping Qu -S
Digitally signed by Yanping Qu -S
Date: 2020.08.24 15:24:33 -04'00'

From: Yanping Qu, Ph.D., CDRH/OCEA/DCEA2/TCEA2A

Subject: Statistical Review of 510(k) Supplement K201199/S001
Jada® System
Alydia Health, Inc.

To: Reginald Avery, CDRH/OHT3/DHT3B/THT3B1

(b)(5)

(b)(5) FDA Reviewer Notes

(b)(5) FDA Reviewer Notes

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Clinical Investigation Report

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Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

*WOMAN Trial Collaborators**

Summary

Background Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces deaths due to bleeding in trauma patients. We aimed to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

Methods In this randomised, double-blind, placebo-controlled trial, we recruited women aged 16 years and older with a clinical diagnosis of post-partum haemorrhage after a vaginal birth or caesarean section from 193 hospitals in 21 countries. We randomly assigned women to receive either 1 g intravenous tranexamic acid or matching placebo in addition to usual care. If bleeding continued after 30 min, or stopped and restarted within 24 h of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given. Patients were assigned by selection of a numbered treatment pack from a box containing eight numbered packs that were identical apart from the pack number. Participants, care givers, and those assessing outcomes were masked to allocation. We originally planned to enrol 15 000 women with a composite primary endpoint of death from all-causes or hysterectomy within 42 days of giving birth. However, during the trial it became apparent that the decision to conduct a hysterectomy was often made at the same time as randomisation. Although tranexamic acid could influence the risk of death in these cases, it could not affect the risk of hysterectomy. We therefore increased the sample size from 15 000 to 20 000 women in order to estimate the effect of tranexamic acid on the risk of death from post-partum haemorrhage. All analyses were done on an intention-to-treat basis. This trial is registered with ISRCTN76912190 (Dec 8, 2008); ClinicalTrials.gov, number NCT00872469; and PACTR201007000192283.

Findings Between March, 2010, and April, 2016, 20 060 women were enrolled and randomly assigned to receive tranexamic acid (n=10 051) or placebo (n=10 009), of whom 10 036 and 9985, respectively, were included in the analysis. Death due to bleeding was significantly reduced in women given tranexamic acid (155 [1·5%] of 10 036 patients *vs* 191 [1·9%] of 9985 in the placebo group, risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045), especially in women given treatment within 3 h of giving birth (89 [1·2%] in the tranexamic acid group *vs* 127 [1·7%] in the placebo group, RR 0·69, 95% CI 0·52–0·91; p=0·008). All other causes of death did not differ significantly by group. Hysterectomy was not reduced with tranexamic acid (358 [3·6%] patients in the tranexamic acid group *vs* 351 [3·5%] in the placebo group, RR 1·02, 95% CI 0·88–1·07; p=0·84). The composite primary endpoint of death from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] deaths or hysterectomies in the tranexamic acid group *vs* 546 [5·5%] in the placebo group, RR 0·97, 95% CI 0·87-1·09; p=0·65). Adverse events (including thromboembolic events) did not differ significantly in the tranexamic acid versus placebo group.

Interpretation Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no adverse effects. When used as a treatment for postpartum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.

Funding London School of Hygiene & Tropical Medicine, Pfizer, UK Department of Health, Wellcome Trust, and Bill & Melinda Gates Foundation.

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April 26, 2017
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See Online/Editorial
http://dx.doi.org/10.1016/S0140-6736(17)31111-X

*Collaborators listed at end of the report

Correspondence to:
Clinical Trials Unit, London School of Hygiene & Tropical Medicine, London, UK
thewomantrial@LSHTM.AC.UK

Introduction

Primary post-partum haemorrhage, usually defined as a blood loss of more than 500 mL within 24 h of giving birth, is the leading cause of maternal death worldwide, responsible for about 100 000 deaths every year.[1–3] Most of the deaths occur soon after giving birth and almost all (99%) occur in low-income and middle-income countries.[4,5]

Tranexamic acid reduces bleeding by inhibiting the enzymatic breakdown of fibrinogen and fibrin by plasmin.[6] Findings of a systematic review of clinical trials of tranexamic acid in surgery showed that the drug

Research in context

Evidence before this study

Before the WOMAN trial, there was evidence that antifibrinolytics reduced surgical blood loss and re-operation to control bleeding. To assess the effects of anti-fibrinolytics in post-partum haemorrhage, we did a systematic review of randomised trials published in any language. We searched the following databases up to November, 2008: MEDLINE, PubMed, Embase, Cochrane Central Register of Controlled trials, Web of Science, metaRegister of controlled trials, LILACS, Reproductive Health Library, African Health-line, POPLINE, MedCarib, CINAHL, Clinicaltrials.gov, and the reference lists of eligible trials. Search terms have been published previously (Ferrer P, 2009). We found no trials of antifibrinolytics in post-partum haemorrhage. In 2010, while the WOMAN trial was underway, findings of an international multicentre randomised trial of 20 211 bleeding trauma patients (the CRASH-2 trial) showed that tranexamic acid reduced death due to bleeding with no apparent increase in vascular occlusive events. Subgroup analyses showed that tranexamic acid was only effective when given within 3 h of injury. In 2012, WHO guidelines recommended that tranexamic acid should be used for the treatment of post-partum haemorrhage when uterotonics fail to control the bleeding or when the bleeding is thought to be due to trauma. The evidence for this recommendation was extrapolated from trials in surgery and trauma showing that tranexamic acid was a safe option for the treatment of trauma-related bleeding.

Added value of this study

The WOMAN trial results show that the effect of tranexamic acid in post-partum haemorrhage is consistent with the effects recorded in surgery and trauma. There was a significant reduction in death due to bleeding and laparotomy to control bleeding with tranexamic acid and no evidence of any increased risk of thromboembolic events. With regards to time to treatment, when set in the context of results from trauma, early treatment also seems to be more effective. There is no evidence that the effect of tranexamic acid varies by cause of bleeding or type of birth. Tranexamic acid did not prevent hysterectomy possibly because this is done so soon after the onset of primary post-partum haemorrhage that there is little time for tranexamic acid to have an effect.

Implications of all the available evidence

Our results support the inclusion of tranexamic acid in WHO treatment guidelines for primary post-partum haemorrhage but suggest that treatment should be given as soon as possible after onset. Future research should assess the bioavailability of tranexamic acid after alternative (non-intravenous) routes of administration because this might facilitate its use in primary health-care settings.

reduces blood loss by about one third.[7,8] Tranexamic acid reduces death due to bleeding in patients with trauma. The CRASH-2 trial,[9] which recruited 20 211 adults with acute traumatic bleeding, showed that tranexamic acid reduced death due to bleeding, with no apparent increase in vascular occlusive events. Planned subgroup analysis of the effect of tranexamic acid by time from injury to the start of treatment showed that early treatment is essential. In patients given treatment within 3 h of injury, tranexamic acid reduced death due to bleeding by nearly one third. However, when given after 3 h, there was no benefit.[10] Early activation of fibrinolysis is common after trauma and is associated with increased mortality.[11] Trauma triggers the release of tissue plasminogen activator, the enzyme that converts plasminogen to the fibrinolytic enzyme plasmin.[12,13]

Early activation of fibrinolysis is also recorded after childbirth. Within 1 h of giving birth, the serum concentration of tissue plasminogen activator doubles, possibly because of tissue damage during childbirth;[14] thereafter, the concentration falls.[14] On the basis of results of clinical trials in surgery and trauma, tranexamic acid is recommended for the treatment of primary post-partum haemorrhage if uterotonics fail to control the bleeding or if the bleeding is thought to be due to trauma.[1] However, further trials of tranexamic acid in primary post-partum haemorrhage are needed.[1] Here we aimed to address this research gap and assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

For the **protocol** see http://www.txacentral.org/

Methods

Study design and participants

The WOMAN (World Maternal Antifibrinolytic) trial is an international, randomised, double-blind placebo-controlled trial of women aged 16 years and older with a clinical diagnosis of post-partum haemorrhage after a vaginal birth or caesarean section done in 193 hospitals in 21 countries. Although the diagnosis was clinical, we specified that diagnosis of primary post-partum haemorrhage could be based on clinically estimated blood loss of more than 500 mL after vaginal birth or 1000 mL after caesarean section or any blood loss sufficient to compromise haemodynamic stability. The fundamental eligibility criterion was the clinician's uncertainty about whether to use tranexamic acid in a particular woman with post-partum haemorrhage. Patients received all usual care but were also randomly allocated to receive tranexamic acid or placebo.

The trial was done in accordance with the good clinical practice guidelines by the International Conference on Harmonisation.[15] The consent procedures are described in detail in the protocol.[16] The procedure at each site was approved by the relevant ethics committee and regulatory agencies. In summary, consent was obtained from

women if their physical and mental capacity allowed (as judged by the treating clinician). If a woman was unable to give consent, proxy consent was obtained from a relative or representative. If a proxy was unavailable, then if permitted by local regulation, consent was deferred or waived. When consent was deferred or given by a proxy, the woman was informed about the trial as soon as possible, and consent was obtained for ongoing data collection, if needed.

Randomisation and masking

After eligibility was confirmed and consent procedures completed, baseline information was collected on the entry form. Patients were then randomly allocated to receive tranexamic acid or placebo by selection of the lowest numbered treatment pack from a box containing eight numbered packs that were identical apart from the pack number. The randomisation codes were generated and held by an independent statistical consultant from Sealed Envelope Ltd (UK). The codes were given to the drug packers so that treatment packs could be prepared in accordance with the randomisation list. Once the treatment pack was opened and the ampoules were confirmed as intact, the patient was considered to be randomly assigned. After randomisation, outcome data were obtained for every participant even if the treatment was not given. Participants, caregivers, and study staff (site investigators and trial coordinating centre staff) were masked to treatment allocation. An emergency unblinding service was available via Sealed Envelope Ltd.

The tranexamic acid (cyklokapron injection) used in the trial was manufactured by Pfizer Ltd, Sandwich, UK. The matching placebo (sodium chloride 0·9%) was prepared by South Devon Healthcare NHS Trust, Devon, UK. Ampoules and packaging were identical in appearance. The masking was done by Brecon Pharmaceuticals Limited, Hereford, UK and involved the removal of the original manufacturer's label and replacement with the clinical trial label bearing the randomisation number, which was used as the pack identification. Apart from the randomisation number, all pack label texts were identical for tranexamic acid and placebo. Correct masking and coding of ampoules was checked by independent random testing of each batch by high-performance liquid chromatography to confirm the contents of the ampoules.

Procedures

Patients were randomly allocated to receive 1 g tranexamic acid or placebo by slow intravenous injection. Investigators were advised to give 1 g (10 mg/mL) of tranexamic acid intravenously at an approximate rate of 1 mL per min. If bleeding continued after 30 min or stopped and restarted within 24 h of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given. Every patient was assigned a uniquely numbered treatment pack, containing four ampoules of 500 mg tranexamic acid or placebo, two syringes and needles, stickers with the trial details and randomisation number (for attaching to data forms and medical records) and instructions. Every box had information leaflets for participants and their representatives, consent forms, and data collection forms. The stickers, instructions, leaflets, and forms were translated into local languages. Outcome data were collected at death, discharge or 6 weeks (42 days) after randomisation (whichever occurred first). Adverse events were reported up to day 42.

Outcomes

The primary outcome was a composite of death from all causes or hysterectomy within 42 days of randomisation. Death was also assessed separately. Participating clinicians were requested to record the immediate cause of death (the final pathophysiological process leading to death) rather than the underlying cause of death and were trained accordingly. In the event that there was more than one cause, clinicians were asked to record the main cause. Because there was no reason to believe that tranexamic acid can reduce deaths from causes unrelated to bleeding, we planned to assess the effect of tranexamic acid on cause-specific mortality with death due to bleeding as the key secondary outcome. Other secondary outcomes were thromboembolic events (deep-vein thrombosis, pulmonary embolism, myocardial infarction, and stroke), surgical interventions (intrauterine tamponade, embolisation, brace sutures, arterial ligation, hysterectomy, and laparotomies done after randomisation to control bleeding and achieve haemostasis), complications (renal failure, cardiac failure, respiratory failure, hepatic failure, sepsis, and seizures), other untoward medical events (adverse events), quality of life measured using the EQ5D and status of any thromboembolic events in breastfed babies (assessed as per normal clinical practice with no special tests done). Outcomes were measured at hospital discharge or on day 42 if still in hospital. Data were sent to the trial coordinating centre by direct entry into an electronic database or by using encrypted data forms (which were sent by fax, email, or uploaded to a secure server). We monitored data quality using a combination of centralised consent monitoring, statistical data checking, and site visits at which patient data forms were compared with clinical case notes.

Statistical analysis

We published a statistical analysis plan before the allocation was unblinded.[18] This plan included details of a protocol amendment to increase the sample size. Before the trial started, we anticipated a baseline event rate of 2·5% for death and 2·5% for hysterectomy. Assuming a control group event rate of 2·5% for death and 2·5% for hysterectomy and that 1% of women die after hysterectomy, we originally estimated that a trial with 15 000 women would have 90% power to detect a 25% reduction (from 4–3%) in the composite primary endpoint death or

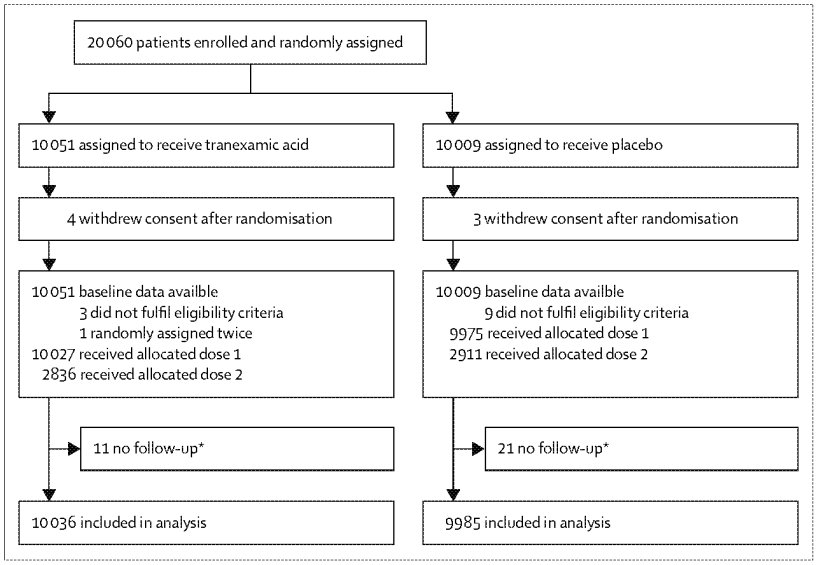

Figure 1: **Trial profile**
*Patients for whom there is no information about the primary endpoint.

	Tranexamic acid group (n=10 051)	Placebo group (n=10 009)
Age at randomisation (years)		
<16	1 (<1%)	3 (<1%)
16–25	3445 (34%)	3407 (34%)
26–33	4580 (46%)	4608 (46%)
≥34	2022 (20%)	1987 (20%)
Unknown	3 (<1%)	4 (<1%)
Baby delivered in the randomising hospital		
Yes	8869 (88%)	8756 (88%)
No	1181 (12%)	1251 (13%)
Unknown	1 (<1%)	2 (<1%)
Type of delivery		
Vaginal	7093 (71%)	7126 (71%)
Caesarean section	2957 (29%)	2879 (29%)
Unknown	1 (<1%)	4 (<1%)
Time between delivery and randomisation (h)		
≤1	4852 (48%)	4733 (47%)
>1 to ≤3	2678 (27%)	2691 (27%)
>3	2517 (25%)	2574 (26%)
Unknown	4 (<1%)	11 (<1%)
Placenta fully delivered		
Yes	9089 (90%)	9016 (90%)
No	962 (10%)	990 (10%)
Primary cause of haemorrhage		
Uterine atony	6437 (64%)	6347 (63%)
Placenta praevia or accreta	943 (9%)	935 (9%)
Surgical trauma or tears	1834 (18%)	1857 (19%)
Other	720 (7%)	737 (7%)
Unknown	117 (1%)	133 (1%)
Systolic blood pressure (mm Hg)		
≥90	8138 (81%)	8065 (81%)
<90	1908 (19%)	1929 (19%)
Unknown	5 (<1%)	15 (<1%)
Estimated volume of blood lost (mL)		
≤500	295 (3%)	313 (3%)
>500 to ≤1000	4949 (49%)	4861 (49%)
>1000 to ≤1500	2832 (28%)	2882 (29%)
>1500	1973 (20%)	1953 (20%)
Unknown	2 (<1%)	0
Uterotonic prophylaxis given		
Yes	9687 (96%)	9618 (96%)
No	131 (1%)	139 (1%)
Unknown	233 (2%)	252 (3%)
Clinical signs of haemodynamic instability		
Yes	5961 (59%)	5898 (59%)
No	4090 (41%)	4110 (41%)

Table 1: **Baseline characteristics of participants before randomisation**

hysterectomy at the 5% significance level. However, during the trial it became apparent that the decision to conduct a hysterectomy was often made at the same time as randomisation. For example, in response to life-threatening bleeding during caesarean section, a clinician might decide to do a hysterectomy, and while the hysterectomy is underway, the woman is enrolled into the trial. Although tranexamic acid could affect the risk of death in these cases, it could not affect the risk of hysterectomy. To protect against the possibility that the effect of tranexamic acid on death and hysterectomy was different, the sample size was increased from 15 000 to 20 000 women. We estimated that a trial with 20 000 women should have sufficient power to detect a 25% reduction in mortality at the 5% significance level (3–2·25%). We hoped that the increased sample size might compensate for the dilution of the treatment effect from hysterectomies that were done at the same time as randomisation. We also refined the study hypothesis in view of new evidence that had become available since the trial was initiated. In particular, findings of the CRASH-2 trial[10] had shown that tranexamic acid reduces death due to bleeding in trauma patients and that early treatment was more effective, with strong evidence of an interaction by time to treatment. In response, we pre-specified an analysis of cause-specific mortality with death due to bleeding as the main outcome. We also pre-specified subgroup analyses by time to treatment. These changes were made before un-blinding and without any knowledge of the trial results.

All analyses were done on an intention-to-treat basis. For each binary outcome, we calculated risk ratios and 95% CIs and two-sided p values. We did a complete case analysis with no imputation for missing data. To mitigate the risk that a chance imbalance in prognostic factors could affect the results, for the primary endpoint (death or hysterectomy) and the most important secondary endpoint (death due to bleeding), we pre-specified an analysis adjusted for baseline risk. The safety of trial participants was overseen by an independent data safety and monitoring committee, which reviewed seven un-blinded interim analyses.

We planned to report the effects of treatment on the primary outcome subdivided by three baseline characteristics: hours from giving birth to randomisation (<1, 1–3, >3 h); type of birth (vaginal or caesarean section); and primary cause of haemorrhage (uterine atony *vs* all others). To examine the hypothesis that tranexamic acid would be most effective when given soon after birth and less effective (possibly even harmful) when given several hours after giving birth, we pre-specified a subgroup analysis of the effect of tranexamic acid on death due to bleeding according to the time interval between giving birth and tranexamic acid treatment. The main analysis for the pre-specified subgroups was an unadjusted test of interaction in a logistic regression model to assess evidence for whether the effect of treatment differs across subgroup categories. Unless there was strong evidence against the null hypothesis of homogeneity of effects (ie, p<0·001), the overall relative risk was regarded as the most reliable guide to the approximate relative risks in all subgroups. However, because there was strong prior evidence to expect a time to treatment interaction, we pre-specified that we would set the results of this analysis in the context of all available data on the time to treatment interaction.[18]

After publication of the planned primary and secondary analyses, the trial data will be made available via our data sharing portal, The Free Bank of Injury and Emergency Research Data (freeBIRD) website. This will allow for maximum utilisation of the data to improve patient care and advance medical knowledge.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between March, 2010, and April, 2016, 20 060 women were enrolled and randomly assigned to receive tranexamic acid (n=10 051) or placebo (n=10 009), of whom 20 002 (99·7%) received the first dose of the allocated treatment (10 037 received tranexamic acid and 9975 received placebo; figure 1). Seven women withdrew their consent after randomisation and we excluded their data from the analyses (four in the tranexamic acid group and three in the placebo group). We were unable to obtain primary outcome data for 32 women and 12 patients did not fulfil the trial eligibility criteria. One patient in the tranexamic acid group was randomly assigned twice. The primary analysis includes data for 20 021 (99·8%) women. The baseline characteristics were similar between the treatment groups (table 1).

There were 483 maternal deaths of which 374 (77%) were within 24 h of randomisation and 43 (9%) were within 1 h of randomisation (figure 2). The appendix shows the distribution of deaths from hours since childbirth (appendix p 1). 346 (72%) deaths were due to bleeding. Table 2 shows the effect of tranexamic acid on maternal death. The risk of death due to bleeding was significantly reduced in patients who received tranexamic acid (155 [1·5%] of 10 036 *vs* 191 [1·9%] in the placebo group; risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045). After adjusting for baseline risk, the risk ratio for death due to bleeding with tranexamic acid was 0·78 (95% CI 0·62–0·98; p=0·03). Deaths from pulmonary embolism, organ failure, sepsis, eclampsia and other causes did not differ significantly between the tranexamic acid and the placebo group (table 2). We recorded fewer deaths from all causes with tranexamic acid but the reduction was not significant

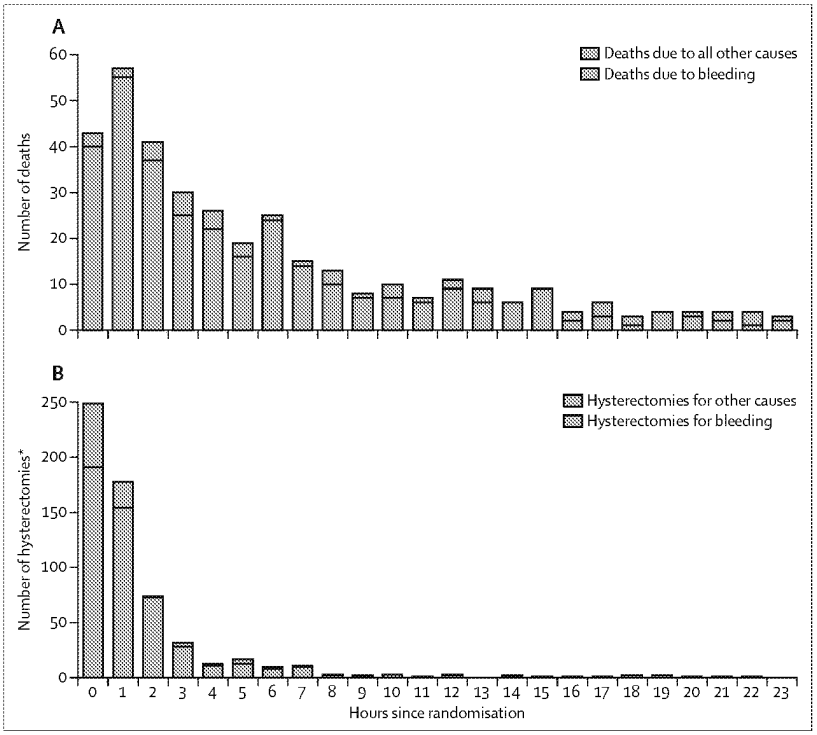

Figure 2: **Cause of death by hours since randomisation (A) and cause of hysterectomy by hours since randomisation (B)**

*Excludes data for 311 women who had a hysterectomy before randomisation.

	Tranexamic acid group (n=10 036)	Placebo group (n=9985)	RR (95% CI)	p value (two-sided)
Bleeding	155 (1·5%)	191 (1·9 %)	0·81 (0·65–1·00)	0·045
Pulmonary embolism	10 (0·1%)	11 (0·1)	0·90 (0·38–2·13)	0·82
Organ failure	25 (0·3%)	18 (0·2%)	1·38 (0·75–2·53)	0·29
Sepsis	15 (0·2%)	8 (0·1%)	1·87 (0·79–4·40)	0·15
Eclampsia	2 (0·02%)	8 (0·1%)	0·25 (0·05–1·17)	0·057
Other	20 (0·2%)	20 (0·2%)	0·99 (0·54–1·85)	0·99
Any cause of death	227 (2·3%)	256 (2·6%)	0·88 (0·74–1·05)	0·16

Data are n (%), unless otherwise indicated. RR=risk ratio.

Table 2: **Effect of tranexamic acid on maternal death**

To **access data at freeBIRD** see http://freebird.lshtm.ac.uk

See Online for appendix

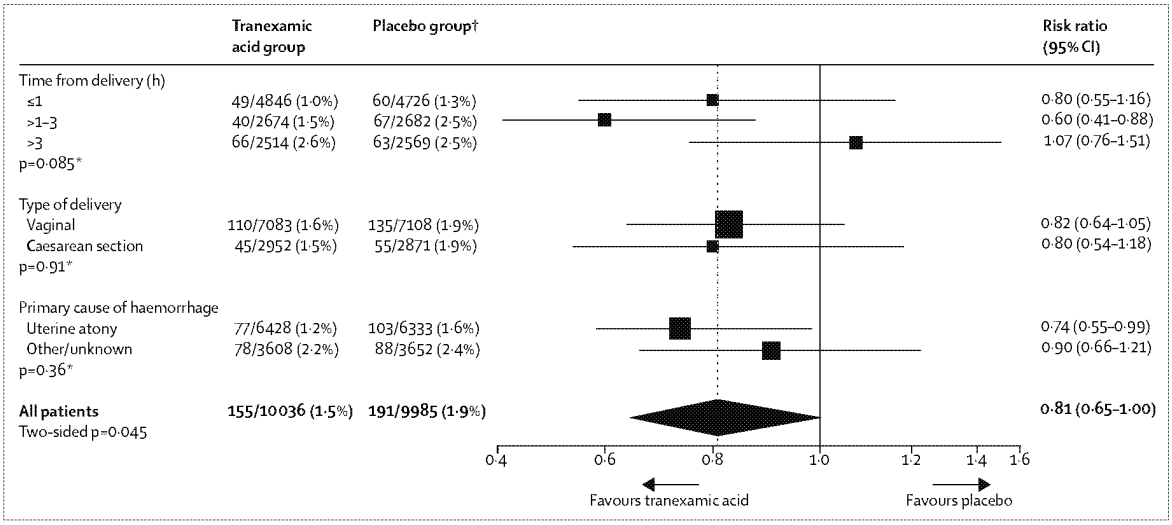

Figure 3: **Death from bleeding by subgroup**
*Heterogeneity p value. †One patient excluded from subgroup analysis because of missing baseline data.

	Tranexamic acid group	Placebo group	Risk ratio (95% CI)
Time from delivery (h)			
≤1	253/4844 (5·2%)	229/4726 (4·9%)	1·08 (0·91–1·28)
>1–≤3	122/2672 (4·6%)	154/2682 (5·7%)	0·80 (0·63–1·00)
>3	159/2514 (6·3%)	161/2569 (6·3%)	1·01 (0·82–1·25)
p=0·11*			
Type of delivery			
Vaginal	255/7080 (3·6%)	288/7108 (4·1%)	0·89 (0·75–1·05)
Caesarean section	279/2951 (9·5%)	257/2873 (9·0%)	1·06 (0·90–1·24)
p=0·15*			
Primary cause of haemorrhage			
Uterine atony	249/6426 (3·9%)	274/6333 (4·3%)	0·90 (0·76–1·06)
Other or unknown	285/3606 (7·9%)	272/3652 (7·5%)	1·06 (0·90–1·24)
p=0·15*			
All patients	534/10 032 (5·3%)	546/9985 (5·5%)	0·97 (0·87–1·09)
Two-sided p=0·65			

Data are n (%) unless otherwise indicated. *p value from likelihood ratio test.

Table 3: **Effect of tranexamic acid on composite primary endpoint (death or hysterectomy) by subgroup**

(227 [2·3%] in the tranexamic acid group *vs* 256 [2·6%] in the placebo group; RR 0·88, 95% CI 0·74–1·05; p=0·16).

In women given tranexamic acid within 3 h of giving birth, tranexamic acid substantially reduced the risk of death due to bleeding (89 [1·2%] women died in the tranexamic acid group *vs* 127 [1·7%] in the placebo group, RR 0·69, 95% CI 0·52–0·91; p=0·008). There was no apparent reduction when tranexamic acid was given after 3 h (66 [2·6%] tranexamic acid group *vs* 63 [2·5%] placebo group, RR 1·07, 95% CI 0·76–1·51; p=0·70).There was no heterogeneity in the effect by type of birth or cause of bleeding (figure 3).

709 women had hysterectomies of which 608 (86%) were on the day of randomisation and 191 (27%) were within 1 h of randomisation (figure 2). The appendix shows the distribution of hysterectomy from hours since childbirth (appendix p 1). 578 (81%) of 709 hysterectomies were done to control bleeding. The risk of hysterectomy was not reduced with tranexamic acid (358 [3·6%] done in the tranexamic acid group *vs* 351 [3·5%] in the placebo group, RR 1·02, 95% CI 0·88–1·07; p=0·84). The risk of hysterectomy to control bleeding was not significantly reduced with tranexamic acid (283 [2·8%] tranexamic acid group *vs* 295 [3·0%] placebo group, RR 0·95, 95% CI 0·81–1·12; p=0·57).

The primary endpoint of death from all causes or hysterectomy within 42 days of giving birth occurred in 1080 women. Of these, 371 (34%) women died without undergoing a hysterectomy, 112 (10%) died after hysterectomy, and 597 (55%) survived after hysterectomy. The risk of death from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] tranexamic acid group *vs* 546 [5·6%] placebo group, RR 0·97, 95% CI 0·87–1·09; p=0·65). After adjusting for baseline risk, the risk ratio for death from all causes or hysterectomy was 0·98 (95% CI 0·87–1·10; p=0·75). There was no significant heterogeneity in the effect of tranexamic acid by time to treatment, type of birth or cause of bleeding (table 3).

The use of intrauterine tamponade, embolisation, manual removal of the placenta, and arterial ligation did not differ significantly between the tranexamic acid and the placebo group (table 4). Brace sutures were used more often in the tranexamic group (300 [3·0%] tranexamic acid group *vs* 250 [2·5%] placebo group; RR 1·19, 95% CI 1·01–1·41; p=0·035). 209 laparotomies were done after randomisation to control bleeding and achieve haemostasis of which 114 (55%) followed caesarean section births and 95 (45%) followed vaginal

	All women				Women who gave birth vaginally				Women who gave birth by caesarean section			
	Tranexamic acid group (n=10 032)	Placebo group (n=9985)	RR (95% CI)	p value	Tranexamic acid group (n=7080)	Placebo (n=7108)	RR (95% CI)	p value	Tranexamic acid group (n=2951)	Placebo (n=2873)	RR (95% CI)	p value
Intrauterine tamponade	705 (7·0%)	729 (7·3%)	0·96 (0·87–1·06)	0·45	519 (7·3%)	547 (7·7%)	0·95 (0·85–1·07)	0·41	186 (6·3%)	182 (6·3%)	0·99 (0·82–1·21)	0·96
Manual removal of placenta	918 (9·2%)	961 (9·6%)	0·95 (0·87–1·04)	0·25	745 (10·5%)	779 (11·0%)	0·96 (0·87–1·06)	0·40	173 (5·9%)	182 (6·3%)	0·93 (0·76–1·13)	0·45
Embolisation	10 (0·1%)	13 (0·1%)	0·77 (0·34–1·75)	0·52	4 (0·06%)	7 (0·1%)	0·57 (0·17–1·96)	0·37	6 (0·2%)	6 (0·2%)	0·97 (0·31–3·02)	0·96
Brace sutures	300 (3·0%)	250 (2·5%)	1·19 (1·01–1·41)	0·035	50 (0·7%)	50 (0·7%)	1·00 (0·68–1·48)	0·98	250 (8·5%)	200 (7·0%)	1·22 (1·02–1·46)	0·031
Arterial ligation	225 (2·2%)	254 (2·5%)	0·88 (0·74–1·05)	0·16	57 (0·8%)	65 (0·9%)	0·88 (0·62–1·25)	0·48	168 (5·7%)	189 (6·6%)	0·87 (0·71–1·06)	0·16
Laparotomy for bleeding	82 (0·8%)	127 (1·3%)	0·64 (0·49–0·85)	0·002	37 (0·5%)	58 (0·8%)	0·64 (0·42–0·97)	0·032	45 (1·5%)	69 (2·4%)	0·63 (0·44–0·92)	0·016

Data are n (%), unless otherwise indicated. RR=relative risk. p values from Pearson's χ^2 test.

Table 4: **Effect of tranexamic acid on need for surgical intervention**

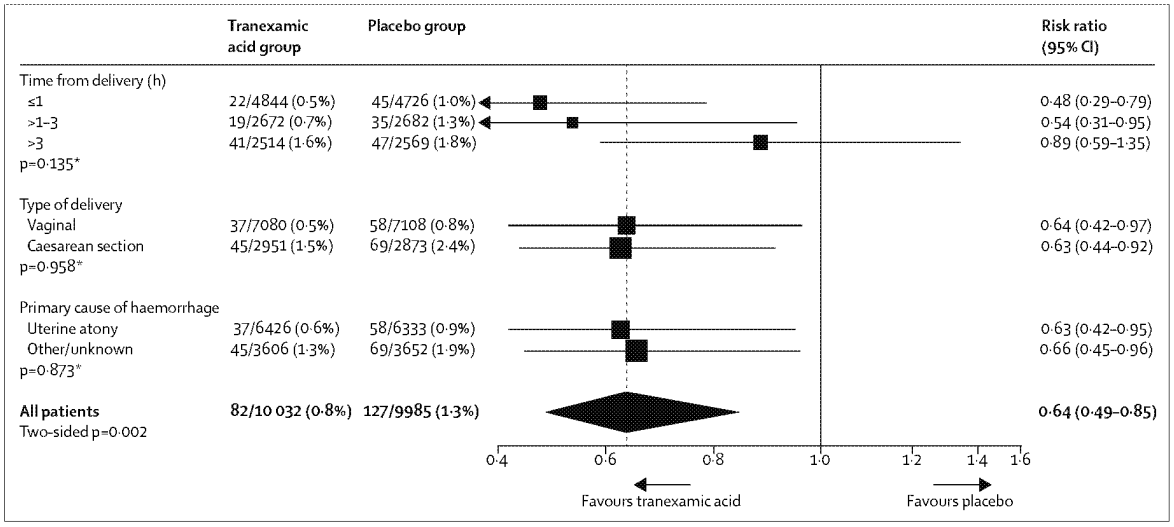

Figure 4: **Laparotomy for bleeding by subgroup**

*Heterogeneity p value.

births. There was a significant reduction in laparotomy to control bleeding with tranexamic acid (82 [0·8%] tranexamic acid group *vs* 127 [1·3%] placebo group; RR 0·64, 95% CI 0·49-0·85; p=0·002). We recorded no significant heterogeneity in the effect of tranexamic acid on laparotomy to control bleeding by time since giving birth, type of birth, or cause of bleeding (figure 4). Blood product transfusions were given to 5461 (54%) of 10 036 patients allocated to tranexamic acid and 5426 (54%) of 9985 women allocated to placebo. Among women who were transfused, the mean number of blood units received did not differ significantly between patients in the tranexamic acid and placebo groups. Of the women who died, 37 (7·7%) did not receive any blood products. Of these, 18 (48·7%) were in the tranexamic acid group and 19 (51·4%) were in the placebo group.

The incidence of thromboembolic events (pulmonary embolism, deep-vein thrombosis, myocardial infarction, and stroke) did not differ significantly in the tranexamic acid versus the placebo group (table 5). The risk of organ failure (renal, cardiac, respiratory, and hepatic) and sepsis did not differ significantly between the tranexamic acid and the placebo group. 33 (0·33%) women in the tranexamic acid group had a seizure versus 43 (0·43%) in the placebo group. Eight women in the tranexamic acid group suffered the death of a breast-fed baby compared with seven women in the placebo group. No thromboembolic events were reported in breast-fed babies in either group. Of women who survived, there were no significant differences in quality of life measures. Of the women who survived, four (<1%) did not have a quality of life

	Tranexamic acid group	Placebo group	RR (95% CI)	p value
Thromboembolic events*	10033	9985	..	
Any event	30 (0·3%)	34 (0·3%)	0·88 (0·54–1·43)	0·603
Venous events	20 (0·2%)	25 (0·3%)	0·80 (0·44–1·43)	0·446
Deep vein thrombosis	3 (0·03%)	7 (0·07%)	0·43 (0·11–1·65)	0·203
Pulmonary embolism	17 (0·2%)	20 (0·2%)	0·85 (0·44–1·61)	0·611
Arterial events	10 (0·1%)	9 (0·09%)	1·11 (0·45–2·72)	0·827
Myocardial infarction	2 (0·02%)	3 (0·03%)	0·66 (0·11–3·97)	0·651
Stroke	8 (0·08%)	6 (0·06%)	1·33 (0·46–3·82)	0·599
Complications*	10033	9985	..	..
Renal failure	129 (1·3%)	118 (1·2%)	1·09 (0·85–1·39)	0·505
Cardiac failure	110 (1·1%)	115 (1·2%)	0·95 (0·73–1·23)	0·710
Respiratory failure	108 (1·1%)	124 (1·2%)	0·87 (0·67–1·12)	0·274
Hepatic failure	29 (0·3%)	30 (0·3%)	0·96 (0·58–1·60)	0·882
Sepsis	180 (1·8%)	185 (1·9%)	0·97 (0·79–1·19)	0·756
Seizure	33 (0·3%)	43 (0·4%)	0·76 (0·49–1·20)	0·242
Use of uterotonics	10034	9984	..	..
Received at least one type	9996 (99·6%)	9930 (99·5%)	1·00 (1·00–1·00)	0·090
Oxytocin	9940 (99·1%)	9865 (98·8%)	1·00 (1·00–1·01)	0·079
Ergometrine	4326 (43·1%)	4314 (43·2%)	1·00 (0·97–1·03)	0·891
Misoprostol	6707 (66·8%)	6717 (67·3%)	0·99 (0·97–1·01)	0·513
Prostaglandin	689 (6·9%)	722 (7·2%)	0·95 (0·86–1·05)	0·313
ED-5Q+	9805	9728	..	..
Mobility	30 (0·3%)	31 (0·3%)	0·96 (0·58–1·58)	0·874
Self-care	39 (0·4%)	31 (0·3%)	1·25 (0·78–2·00)	0·355
Usual activities	38 (0·4%)	44 (0·5%)	0·86 (0·56–1·32)	0·484
Pain/discomfort	13 (0·1%)	18 (0·2%)	0·72 (0·35–1·46)	0·357
Anxiety/depression	30 (0·3%)	29 (0·3%)	1·03 (0·62–1·71)	0·920

Data are n (%), unless otherwise indicated. *Fatal or non-fatal. RR=relative risk.

Table 5: **Effect of tranexamic acid on thromboembolic events, complications, use of uterotonics, and quality of life**

measure completed. 57 additional adverse events were reported (appendix p 2).

Discussion

The administration of tranexamic acid to women with post-partum haemorrhage reduces deaths due to bleeding and laparotomy to control bleeding with no evidence of any adverse effects or complications. When given soon after delivery, tranexamic acid reduces death due to bleeding by nearly one third.

Our study had several strengths but also some limitations. The randomisation method ensured that participating doctors had no foreknowledge of the treatment allocation. Baseline prognostic factors were well balanced and results adjusted for baseline risk were similar to the unadjusted analyses. Because almost all randomly assigned patients were followed up there is little potential for bias. We originally planned to enrol 15 000 women to assess the effect of tranexamic acid on a composite primary endpoint of death from all-causes or hysterectomy within 42 days of giving birth. However, during the trial it became apparent that the decision to conduct a hysterectomy was often made at the same time as the decision to enrol a women into the trial. Although we excluded hysterectomies done before randomisation, we could not exclude those in which the decision to conduct a hysterectomy was made at the same time as the decision to randomise or before the trial treatment had been received. We predicted that this would dilute the effect of tranexamic acid on the risk of hysterectomy. There would also be dilution from hysterectomies done several days after birth for reasons other than to prevent life-threatening bleeding. With these concerns in mind, we increased the sample size from 15 000 to 20 000 patients in the hope that the trial would have enough power to detect a reduction in post-partum haemorrhage death.[17]

There was a statistically significant reduction in death due to bleeding with tranexamic acid with no significant increase or decrease in any other cause of death. Because more than one quarter of deaths were not due to bleeding, the reduction in all-cause mortality with tranexamic acid, which is a weighted average of its effect on bleeding and non-bleeding deaths, was not statistically significant. Indeed, considering that one quarter of deaths after post-partum haemorrhage are not bleeding related, it would require trials many times larger than ours to show a statistically significant reduction in all-cause mortality.[18] Nevertheless, because the relative contributions of bleeding and non-bleeding (eg, sepsis) deaths to all-cause mortality will vary by region or between hospitals, the effect on all-cause mortality is not generalisable. For example, tranexamic acid will have a larger effect on all-cause mortality in hospitals where sepsis death is rare than in hospitals where sepsis death is common. The effect of tranexamic acid on death due to bleeding is the generalisable measure.

Although tranexamic acid did not prevent hysterectomy, it substantially reduced the number of laparotomies to control bleeding. While hysterectomy might be a last resort to control bleeding in high-income settings, in Africa and Asia where many women are anaemic and blood supplies are limited,[19–21] hysterectomy is often an early intervention to prevent death from exsanguination. Furthermore, there would probably have been a delay between randomisation and the administration of the trial treatment, so that even though the decision to randomise might have preceded the decision to do a hysterectomy, in some cases the trial treatment would not have been received when the hysterectomy decision was made. On the other hand, laparotomies which often involve re-operation to control bleeding following caesarean section, are more commonly done after other interventions including the trial treatment have been given. This might have allowed sufficient time for tranexamic acid to affect the risk of laparotomy. Randomised trials in elective surgery also show large reductions in the need for re-operation to control bleeding with tranexamic acid.[22]

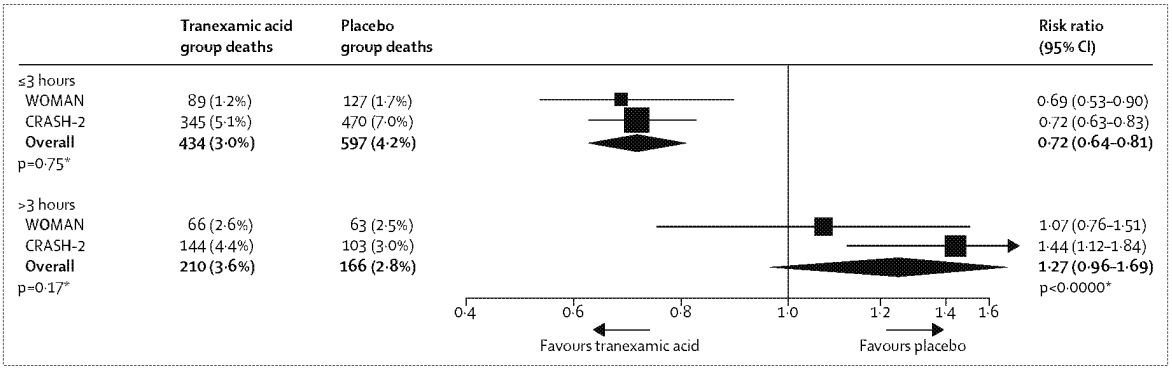

Figure 5: **Time to treatment**
*Heterogeneity p value.

The dilution of the effect of tranexamic acid arising from interventions that were initiated prior to receipt of the trial treatment is likely to apply to other surgical interventions and blood transfusion. Considering that there may only be a few hours from onset of primary post-partum haemorrhage to maternal death, it is not surprising that other interventions were given concurrently with the trial treatment. Given the urgency, clinicians cannot wait and see if the trial treatment has an effect before giving other treatments, not least because half of the women received placebo. The only outcome that invariably follows randomisation is death. This may explain why in this trial, and in the CRASH-2 trial of tranexamic acid in significant traumatic bleeding, there was a reduction in death due to bleeding with tranexamic acid despite no reduction in transfusion.[9]

The WOMAN trial began before the results of the CRASH-2 trial of tranexamic acid in bleeding trauma patients were available. The CRASH-2 trial recruited 20 211 adults with traumatic bleeding and showed that tranexamic acid reduces death due to bleeding and all-cause mortality with no increase in vascular occlusive events. There was strong evidence of a time to treatment interaction. In patients treated within 3 h of injury, tranexamic acid reduced death due to bleeding by around one third, but when given after 3 h, it seemed to increase the risk.[9,10] Early activation of fibrinolysis is common after trauma and is associated with increased mortality.[11] Because similar temporal changes in fibrinolysis have been observed after childbirth,[23] we expected that early treatment with tranexamic acid would also be more effective after post-partum haemorrhage and planned to set the WOMAN trial results in the context of all available clinical data on the time to treatment interaction. Bearing in mind that even a large trial such as ours would have limited power to detect a time to treatment interaction for death due to bleeding, setting the trial results in the context of the totality of the available evidence seemed to be the most sensible approach. Although there are ongoing trials of tranexamic acid in life threatening bleeding, the CRASH-2 trial is the only trial to date that provides such evidence.[24,25] Figure 5 shows the results of the WOMAN trial in the context of the CRASH-2 results. There is a strong suggestion that early treatment is most effective and late treatment is unlikely to be beneficial.

On the basis of clinical trials of tranexamic acid in surgery and trauma, WHO guidelines recommended tranexamic acid in post-partum haemorrhage if uterotonics fail to stop the bleeding or if it is thought that the bleeding may be due to trauma.[1] Our results suggest that if tranexamic acid is used in the treatment of post-partum haemorrhage it should be given soon after the onset of post-partum haemorrhage alongside uterotonics. First, our findings show that a significant proportion of mothers die within hours of post-partum haemorrhage onset. In such circumstances, waiting to see if uterotonics fail to stop the bleeding could put some mothers' lives at risk. We found no evidence of adverse effects with tranexamic acid and it has also been shown to be safe and effective in trauma and surgery. Second, our data suggest that early administration is most effective. Treatment within 3 h of birth significantly reduced death due to bleeding and the need for laparotomy to control bleeding, an observation consistent with results of trials of tranexamic acid in traumatic bleeding. Although we did not see a monotonic decrease in the risk of death due to bleeding with decreasing time to treatment, as seen in trauma, this is more likely to reflect the imprecision of the estimates rather than the underlying biological relationship. We did observe such a monotonic decrease in the risk of laparotomy to control bleeding as time to treatment decreased. Finally, the temporal changes in fibrinolytic activation after childbirth are similar to those in trauma with an early (within one hour) increase in levels of tissue plasminogen activator.[14] However, in the light of our results, further research into the timecourse of the changes in coagulation and fibrinolysis after childbirth are needed.

In the WOMAN trial, tranexamic acid was given by intravenous injection. However, in low-income and middle-income countries, many deaths from post-partum bleeding occur at home or settings where

intravenous injections might not be feasible. Therefore, bioavailability of tranexamic acid after non-intravenous routes of administration needs to be assessed.

WOMAN Trial Collaborative Group

Writing Committee: Haleema Shakur (chair), Ian Roberts (chair), Bukola Fawole (Nigeria), Rizwana Chaudhri (Pakistan), Mohamed El-Sheikh (Sudan), Adesina Akintan (Nigeria), Zahida Qureshi (Kenya), Hussein Kidanto (Tanzania), Bellington Vwalika (Zambia), Abdulfetah Abdulkadir (Ethiopia), Saturday Etuk (Nigeria), Shehla Noor (Pakistan), Etienne Asonganyi (Cameroon), Zarko Alfirevic (UK), Danielle Beaumont (UK), Carine Ronsmans (UK), Sabaratnam Arulkumaran (UK). *Steering Committee*: Sabaratnam Arulkumaran (Chair, from 2014), Adrian Grant (Chair, 2009–2014) who died as the trial was ongoing, Kaosar Afsana, Metin Gülmezoglu (2009–2015), Beverley Hunt, Oladapo Olayemi, Ian Roberts. *Data Monitoring and Ethics Committee*: Iain Chalmers (chair), Pisake Lumbiganon, Gilda Piaggio, Tony Brady (independent statistician). *Protocol Committee*: Haleema Shakur, Ian Roberts, Zarko Alfirevic, Diana Elbourne, Metin Gülmezoglu, Carine Ronsmans. *Trial coordinating team*: Eni Balogun (trial manager), Tracey Pepple (data manager), Danielle Prowse (data assistant), Nigel Quashi (data manager), Lin Barneston (data manager 2010-2012), Collette Barrow (trial administrator), Danielle Beaumont (senior trial manager), Lisa Cook (assistant trial manager 2010–2011), Lauren Frimley (assistant trial manager), Daniel Gilbert (data assistant 2012–2013), Catherine Gilliam (administrator), Rob Jackson (data manager 2012–2015), Taemi Kawahara (trial manager 2010–2015), Hakim Miah (IT manager), Sergey Kostrov (systems officer), Maria Ramos (project administator 2010–2015), Ian Roberts (chief investigator), Haleema Shakur (project director), Phil Edwards (statistician), Tom Godec and Sumaya Huque (statisticial support). *Nigeria coordinating team*: Bukola Fawole (coordinating centre director), Olujide Okunade (assistant trial coordinator), Olusade Adetayo (assistant trial coordinator). *Pakistan coordinating team*: Rizwana Chaudhri (coordinating centre director), Aasia Kayani (research coordinator), Kiran Javaid (assistant research coordinator). *National Coordinators*: Bukola Fawole (Nigeria), Rizwana Chaudhri (Pakistan), Chrstine Biryabarema (Uganda), Zahida Qureshi (Kenya), Robert Tchounzou (Cameroon), Mohamed El-Sheikh (Sudan), Hussein Kidanto (Tanzania), Mohan Regmi (Nepal), Bellington Vwalika (Zambia), Kastriot Dallaku (Albania), Mateus Sahani (Democratic Republic of Congo), Sayeba Akhter (Bangladesh), Abdulfetah Abdulkadir (Ethiopia), Nicolas Meda (Burkina Faso), Anthony Kwame Dah (Ghana).

Trial sites and investigators

Nigeria (5711): Mother & Child Hospital, Akure (875): Adesina Akintan, Olufemi Odekunle, Oluwabusola Monehin, Austin Ojo, Grace Akinbinu, Ifeoma Offiah; University of Calabar Teaching Hospital (555): Saturday Etuk, Ubong Akpan, Uduak Udofia, Useneno Okon, Ezukwa Omoronyia, Okpe James; University College Hospital, Ibadan (310): Oladapo Olayemi, Nike Bello, Blessed Adeyemi, Chris Aimakhu; Federal Medical Centre Owo (268): Olufemi Akinsanya, Bamidele Adeleye, Oluwaseun Adeyemi, Kayode Oluwatosin; University of Ilorin Teaching Hospital (228): Abiodun Aboyeji, Abiodun Adeniran, Adebayo Adewale, Noah Olaomo; Delta State University Teaching Hospital (198): Lawrence Omo-Aghoja, Emmanuel Okpako, Lucky Oyeye; Maitama District Hospital (188): Francis Alu, John Ogudu, Ezekiel Ladan; Federal Medical Centre Katsina (163): Ibrahim Habib, Babasola Okusanya; University of Abuja Teaching Hospital (160): Olatunde Onafowokan, David Isah, Abalaka Aye; Irrua Specialist Teaching Hospital (157): Felix Okogbo, Egbaname Aigere, Mark Ogbiti; Federal Medical Centre Lokoja (153): Temitope Onile, Olaide Salau, Yinka Amode; Federal Medical Centre Gusau (142): Kamil Shoretire, Adebola Owodunni, Kehinde Ologunde; Adeoyo Maternity Hospital (141): Akintunde Ayinde; Federal Medical Centre Abeokuta (136): Moses Alao, Olalekan Awonuga, Babatunde Awolaja; Lagos University Teaching Hospital (131): Omololu Adegbola, Fatimah Habeebu-Adeyemi, Adeyemi Okunowo; Nyanya General Hospital (124): Hadiza Idris, Ola Okike, Nneka Madueke; Jos University Teaching Hospital (112): Josiah Mutihir, Nankat Joseph, Babatunde Adebudo; Ladoke Akintola University of Technology Teaching Hospital - Osogbo Site (104): Adeniyi Fasanu, Olugbenga Akintunde, Olufemi Abidoye; Seventh Day Adventist Hospital (104): Owigho Opreh, Sophia Udonwa, Gladys Dibia; Lagos Island Maternity Hospital (103): Simeon Bazuaye, Arafat Ifemeje; University of Uyo Teaching hospital (97): Aniefiok Umoiyoho, Emmanuel Inyang-Etoh; Federal Medical Centre Birnin-Kebbi (95): Sununu Yusuf, Kayode Olayinka; Obafemi Awolowo University Teaching Hospital (92): Babalola Adeyemi, Olusegun Ajenifuja; Federal Medical Centre Azare (89): Umar Ibrahim, Yusuf Baffah Adamu; Lagos State University Teaching Hospital (71): Oluwarotimi Akinola, Grace Adekola-Oni; Braithwaite Memorial Specialist Hospital (70): Paul Kua, Roseline Iheagwam; University of Maiduguri Teaching Hospital (65): Audu Idrisa, Ado Geidam; Federal Medical Centre Makurdi (62): Andrea Jogo, Joseph Agulebe; Nnamdi Azikiwe University Teaching Hospital (57): Joseph Ikechebelu, Onyebuchi Udegbunam; Ekiti State University Teaching Hospital (56): Jacob Awoleke, Oluseyi Adelekan; Ahmadu Bello University Teaching Hospital (53): Hajaratu Sulayman, Nkeiruka Ameh; Ajeromi General Hospital (53): Nurudeen Onaolapo, Affiss Adelodun; Plateau State Specialist Hospital (53): William Golit, Dachollom Audu; Ladoke Akintola University of Technology Teaching Hospital - Ogbomoso Site (52): Adetunji Adeniji, Folasade Oyelade; Abubakar Tafawa Balewa University Teaching Hospital (51): Lamaran Dattijo, Palmer Henry; Wesley Guild Hospital (OAUTH) (49): Babalola Adeyemi, Olabisi Loto; Federal Teaching Hospital Abakaliki (38): Odidika Umeora, Abraham Onwe; Federal Medical Centre Owerri (36): Emily Nzeribe, Bartthy Okorochukwu; Federal Medical Centre Ido-Ekiti (34): Augustine Adeniyi; Kogi State Specialist Hospital (30): Emmanuel Gbejegbe, Akpojaro Ikpen; Federal Medical Centre Bida (28): Ikemefuna Nwosu, Abdulrasaq Sambo; National Hospital Abuja (23): Olubunmi Ladipo, Sola Abubakar; Karshi General Hospital (16): Ola Nene Okike; Federal Medical Centre Umuahia (14): Enyinnaya Chikwendu Nduka; University of Nigeria Teaching Hospital, Enugu (14): Eziamaka Pauline Ezenkwele; Federal Medical Center Asaba (11): Daniel Onwusulu; State Specialist Hospital Akure (11): Theresa Azonima Irinyenikan; Usmanu Danfodiyo University Teaching Hospital (11): Swati Singh; Federal Medical Centre Yenagoa (10): Amaitari Bariweni; Aminu Kano Teaching Hospital (7): Hadiza Galadanci; Federal Medical Centre Keffi (7): Peter Achara; Gwarimpa General Hospital (3): Osagie Osayande; General Hospital Minna (1): Mohammed Gana.

Pakistan (5282): Holy Family Hospital, Gyn & Obs Unit 1 (478): Rizwana Chaudhri, Kiran Jabeen, Ayesha Mobeen, Sadaf Mufti, Maliha Zafar; Ayub Teaching Hospital (420): Shehla Noor, Basharat Ahmad, Maimoona Munawar, Jeharat Gul, Naseema Usman; Holy Family Hospital, Gyn & Obs Unit 2 (303): Fehmida Shaheen, Mariam Tariq, Nadia Sadiq, Rabia Batool; Ziauddin University Kemari Campus (280): Habiba Sharaf Ali, Manahil Jaffer, Asma Baloch, Noonari Mukhtiar; Bolan Medical Complex Hospital Unit II (267): Tasneem Ashraf, Raheela Asmat, Salma Khudaidad, Ghazala Taj; Liaquat University Hospital LUMHS Gynae Unit I (230): Roshan Qazi, Saira Dars, Faryal Sardar, Sanobar Ashfaq; Rehman Medical Institute Private Limited (223): Saeeda Majeed; Lady Reading Hospital (222): Sadaqat Jabeen, Rukhsana Karim, Farzana Burki, Syeda Rabia Bukhari; Liaquat Memorial Women & Children Hospital Kohat (215): Fouzia Gul, Musarrat Jabeen, Akhtar Sherin, Qurratul Ain; Nishtar Hospital Unit III (182): Shahid Rao, Uzma Shaheen, Samina Manzoor; Fatima Bai Hospital (159): Shabeen Masood, Shabana Rizvi, Anita Ali; Lady Aitchison Hospital (143): Abida Sajid, Aisha Iftikhar, Shazia Batool; Shalamar Hospital (128): Lubna Dar, Shahenzad Sohail, Shazia Rasul; Sir Ganga Ram Hospital Lahore (111): Shamsa Humayun, Rashida Sultana, Sofia Manzoor; MCH Centre PIMS, Obs and Gynae Unit I (109): Syeda Mazhar, Afshan Batool, Asia Nazir; MCH Centre PIMS, Obs and Gynae Unit II (107): Nasira Tasnim; Nishtar Hospital Unit I (104): Hajira Masood; People's University of Medical and Health Sciences (104): Razia Khero, Neelam Surhio, Samana Aleem; Federal Government Services Hospital (FGSH) Unit III (101): Naila Israr, Saba Javed, Lubna Bashir; Sobhraj Maternity Hospital KMC (96): Samina Iqbal, Faiza Aleem; Services Hospital Lahore Unit II (91): Rubina Sohail, Saima Iqbal; Patel Hospital (89): Samina Dojki, Alia Bano; Dera Ismail Khan District Teaching Hospital (87): Naseem Saba; Sharif Medical & Dental City (85): Maimoona Hafeez,

Nishat Akram; Federal Government Poly Clinic (FGPC) Hospital Unit I Islamabad (84): Naila Israr, Riffat Shaheen; Liaquat National Hospital (83): Haleema Hashmi, Sharmeen Arshad; Ziauddin University Hospital Clifton Campus (81): Rubina Hussain, Sadia Khan; CGH Cantonment General Hospital (Rawalpindi) (65): Nighat Shaheen, Safia Khalil; Isra University Hospital (61): Pushpa Sachdev, Gulfareen Arain; Jinnah Hospital Lahore (59): Amtullah Zarreen, Sara Saeed; Fatima Memorial Hospital (58): Shamayela Hanif; Shifa International Hospital (50): Nabia Tariq, Mahwish Jamil; Ziauddin University Hospital Nazimabad Campus (47): Shama Chaudhry, Hina Rajani; Services Hospital Lahore Unit III (43): Tayyiba Wasim, Summera Aslam; Combined Military Hospital (CMH) Lahore (40): Nilofar Mustafa; Nishtar Hospital Unit II (40): Huma Quddusi, Sajila Karim; Ziauddin University Hospital North Nazimabad Campus (40): Shazia Sultana, Misbah Harim; Lady Willingdon Hospital OBGYN Unit II (34): Mohd Chohan; Nescom Hospital (33): Nabila Salman; Pakistan Railway Hospital (26): Fareesa Waqar, Shamsunnisa Sadia; DHQ Hospital Rawalpindi (24): Lubna Kahloon, Shehla Manzoor; Zainab Panjwani Memorial Hospital (23): Samar Amin; Combined Military Hospital (CMH) Kharian (18): Umbreen Akram; Mian Mohammad Trust Hospital (16): Ambreen Ikram; Punjab Medical College (11): Samina Kausar; Kahota Research Laboratory (KRL) General Hospital (10): Tahira Batool; Military Hospital (MH) Rawalpindi (2): Brigadier Naila Tahir Kyani.

Uganda (2235): Mulago Hospital (1065): Christine Biryabarema, Ruth Bulime, Regina Akello, Bernadette Nakawooya Lwasa, Joselyn Ayikoru, Christine Namulwasira; Mubende Regional Referral Hospital (260): Patrick Komagum, Isabirye Rebecca, Nayiga Annet, Nakirigya Nuulu; St Francis Hospital Buluba (254): Elizabeth Nionzima, Rose Bwotya, Margret Nankya, Sarah Babirye (RIP); Mbarara Hospital (239): Joseph Ngonzi, Cesar Sanchez, Nkonwa Innocent, Kusasira Anitah; Entebbe General Hospital (143): Ayiko Jackson, Elizabeth Ndagire, Christine Nanyongo; Adjumani Hospital (103): Dominic Drametu; Angal St Luke Hospital (64): Grace Meregurwa; Church of Uganda Kisiizi Hospital (63): Francis Banya, Rita Atim; Uganda Martyrs, Ibanda Hospital (37): Emmanuel Byaruhanga; Nyakibale Hospital (7): Lema Felix.

Kenya (1031) Garissa Provincial General Hospital (317): Hussein Iman, Vincent Oyiengo, Peninah Waigi, Rose Wangui; Coast Provincial General Hospital (238): Faiza Nassir, Musimbi Soita, Rophina Msengeti, Zeinab Zubier; Moi Teaching and Referral Hospital (162): Hillary Mabeya, Antony Wanjala, Henry Mwangi; AIC Kijabe Hospital (147): Brian Liyayi, Evelyn Muthoka, Alfred Osoti; Nakuru Provincial General Hospital (85): Amos Otara, Veronicah Ongwae; Kenyatta National Hospital, University of Nairobi (53): Zahida Qureshi, Victor Wanjohi; Mwingi District Hospital (14): Bonface Musila; Bungoma District Hospital (8): Kubasu Wekesa; The Nairobi Hospital (7): Alex Nyakundi Bosire.

Cameroon (893): Kumba District Referral Hospital (271): Etienne Asonganyi, Alice Ntem, Angeline Njoache, Alice Ashu; Regional Hospital Limbe (152): André Simo, Robert Tchounzou, Dorothy Keka; Dschang District Hospital (120): Kenfack Bruno, Amadou Ndouoya, Martin Saadio; Hopital Laquintinie de Douala (120): Mesack Tchana, Odel Gwan, Pauline Assomo; St Theresa's Catholic Hospital (99): Venantius Mutsu, Nji Eric; Yaounde Gynaeco-Obstetric and Paediatric Hospital (67): Pascal Foumane, Philemon Nsem; Yaounde Central Hospital (22): Jeanne Fouedjio, Ymele Fouelifack; Centre Hospitalier et Universitaire Yaounde (20): Pierre Marie Tebeu; Sa'a District Hospital (14): Georges Nko'ayissi; Banyo District Hospital (8): Eta Ngole Mbong.

Sudan (860): Khartoum North Teaching Hospital (311): Wisal Nabag, Riham Desougi, Hadia Mustafa, Huida Eltaib; Omdurman Maternity Hospital (199): Taha Umbeli, Khalid Elfadl, Murwan Ibrahim; Kassala New Hospital (Al Saudi) (97): Abdalla Mohammed, Awadia Ali; Wad Medani Teaching Hospital of Obstetrics and Gynaecology (77): Somia Abdelrahiem, Mohammed Musa; El-Obeid Teaching Hospital (74): Khidir Awadalla, Samirra Ahmed; Kosti Hospital (34): Mahdi Bushra, Omer Babiker; Soba University Hospital (33): Hala Abdullahi, Mohamed Ahmed; Gadarif Obstetrics and Gynaecology Hospital (28): Dr. Elhassan Safa, Dr. Huida Almardi; Khartoum Teaching Hospital (6): Duria Rayis; Elmek Nimir University Hospital (1): Saeed Abdelrahman Abdelgabar.

United Kingdom (569): Liverpool Women's Hospital, Liverpool Women's NHS Foundation Trust (128): Zarko Alfirevic, Gillian Houghton, Andrew Sharpe; City Hospital Nottingham, Nottingham University Hospitals Trust (106): Jim Thornton, Nick Grace, Carys Smith; Sunderland Royal Hospital, City Hospitals Sunderland NHS Trust (96): Kim Hinshaw, Dawn Edmundson; The Royal Victoria Infirmary, Newcastle Upon Tyne Hospitals NHS Trust (92): Paul Ayuk, Alison Bates; Queen's Medical Centre, Nottingham University Hospitals Trust (91): George Bugg, Joanne Wilkins; St Mary's Hospital, Central Manchester University Hospitals NHS Foundation Trust (38): Clare Tower, Alysha Allibone; St Thomas' Hospital, Guy's and St Thomas' NHS Foundation Trust (18): Eugene Oteng-Ntim.

Tanzania (538) Muhimbili National Hospital (221): Hussein Kidanto, Ahmad Kazumari, Anna Danford, Matilda Ngarina; Temeke Municipal Hospital (118): Muzdalifat Abeid, Khadija Mayumba, Magreth Zacharia; Hospitali Teule Muheza Designated District Hospital (91): George Mtove, Leonard Madame; Bugando Medical Centre (83): Anthony Massinde, Berno Mwambe; Sekou Toure Regional Hospital (16): Rwakyendela Onesmo; Mwananyamala Municipal Hospital (9): Sebastian Kitengile Ganyaka

Nepal (533): BP Koirala Institute of Health Sciences (364): Mohan Regmi, Shyam Gupta, Rabindra Bhatt, Ajay Agrawal; Nepal Medical College Teaching Hospital (132): Pramila Pradhan, Nikita Dhakal, Punita Yadav; Birat Hospital and Research Centre (23): Gyanendra Karki; Mid Western Regional Hospital (14): Bhola Ram Shrestha.

Zambia (496): University Teaching Hospital Lusaka (362): Bellington Vwalika, Mwansa Lubeya, Jane Mumba, Willies Silwimba; Livingstone General Hospital (55): Isaiah Hansingo, Noojiri Bopili; St Francis Hospital Katete (30): Ziche Makukula; Kabwe General Hospital (20): Alexander Kawimbe; Kafue District Hospital (16): Mwansa Ketty Lubeya; Saint Paul's Mission Hospital (11): Willard Mtambo; Chipata General Hospital (2): Mathew Ng'ambi.

Albania (485) Obstetric Gynaecology University Hospital "K Gliozheni" (385): Kastriot Dallaku, Saimir Cenameri, Ilir Tasha, Aferdita Kruja; Regional Hospital Fier (72): Besnik Brahimaj; Regional Hospital Elbasan (20): Armida Tola; Lezha Regional Hospital (8): Leon Kaza.

Democratic Republic of Congo (457): Hope Medical Center (112): Mateus Sahani, Desire Tshombe, Elizabeth Buligho; Centre Medical ADEBECO (96): Roger Paluku-Hamuli, Charles Kacha; CSR Carmel (69): Kato Faida; Centre de Sante de Reference Albert Barthel (48): Badibanga Musau; Centre Medical VUHE (48): Herman Kalyana; Virunga General Hospital (40): Phanny Simisi; GESOM (Groupe d'entraide et de Solidarite Medicale) (24): Serge Mulyumba; Centre de Sante de Reference Kahembe (8): Nzanzu Kikuhe Jason; Centre Hospitalier Notre Dame d'Afrique (8): Jean Robert Lubamba; Provincial Hospital Goma (4): Willis Missumba.

Bangladesh (325): Dhaka Medical College Hospital (102): Ferdousi Islam, Nazneen Begum; Ad-din Women's Medical College & Hospital (99): Sayeba Akhter, Ferdousi Chowdhury; Chittagong Medical College Hospital (64): Rokeya Begum, Farjana Basher; Ibn Sina Medical College Hospital (30): Nazlima Nargis, Abu Kholdun; Rajshahi Medical College Hospital (30): Shahela Jesmin, Shrodha Paul.

Ethiopia (302): Jimma University Hospital (158): Hailemariam Segni, Getachew Ayana, William Haleke; St. Paul's Hospital Millennium Medical College (144): Abdulfetah Abdulkadir, Hassen Hussien, Fikre Geremew.

Burkina Faso (142): Centre Hospitalier Universitaire Souro Sanou (129): Moussa Bambara, Adolphe Somé, Amadou Ly; Centre Hospitalier Regional de Dedougou (13): Roamba Pabakba.

Jamaica (73): University Hospital of the West Indies (73): Horace Fletcher, Leslie Samuels.

Ghana (41): Komfo Anokye Teaching Hospital (39): Henry Opare-Addo, Roderick Larsen-Reindorf; Ashanti Mampong Municipal Hospital (2): Kwadwo Nyarko-Jectey.

Papua New Guinea (38): Port Moresby General Hospital (38): Glen Mola, Malts Wai.

Egypt (33): Mataria Teaching Hospital (33): Magdy El Rahman, Wafaa Basta, Hussein Khamis.

Colombia (8): Fundacion Valle del Lili (8): Maria Fernanda Escobar, Liliana Vallecilla.

Cote d'Ivoire (8): Hopital General Abobo Nord (8): Gabriel Essetchi Faye.

Contributors

Haleema Shakur and Ian Roberts conceived the study, reviewed the scientific literature, and were responsible for study design, data collection, data analysis, data interpretation, writing, and reviewing the report; they take overall responsibility for this report. Bukola Fawole, Rizwana Chaudhri, Moharned El-Sheikh, Adesina Akintan, Zahida Qureshi, Hussein Kidanto, Bellington Vwalika, Abdulfetah Abdulkadir, Saturday Etuk, Shehla Noor, Etienne Asonganyi, and Danielle Beaumont contributed to data collection, data interpretation, and reviewing the report. Zarko Alfirevic contributed to the study design, data collection, data interpretation, and reviewing the report, Carine Ronsmans contributed to the study design, data interpretation, and reviewing the report, and Sabaratnam Arulkumaran contributed to reviewing the report.

Declaration of interests

We declare no competing interests.

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Hello Reginald,

Thanks for the update! Did Dr. Nandy leave FDA (just curious)?

Cindy Domecus, R.A.C. (US & EU)

Principal

Domecus Consulting Services LLC

(650) 343-4813 (office)

(b)(6) (cell)

> On Aug 21, 2020, at 2:04 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:
>
> Hello Cindy,
>
> I am replacing Dr. Nandy as the lead reviewer for this file and will complete the review for the Jada System. I have discussed the file with Dr. Nandy to ensure our review is consistent. Please let me know if you have any questions.
>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
> OPEQ: Office of Product Evaluation and Quality
> CDRH | Food and Drug Administration
>
> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
> Ph: 240-402-6152
> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>
> <image001.png> <http://www.fda.gov/>
>
> <image003.jpg> <https://www.facebook.com/FDA> <image005.jpg>
<https://twitter.com/US_FDA> <image007.jpg>
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>

> From: Cindy Domecus <DomecusConsulting@comcast.net
<mailto:DomecusConsulting@comcast.net>>

> Sent: Friday, August 21, 2020 4:20 PM

> To: Avery, Reginald <Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>>

> Cc: K201199@docs.fda.gov <mailto:K201199@docs.fda.gov>

> Subject: Re: Request for information for Jada System (K201199/S001)

>

> Hello Reginald,

>

> Thank you for your reivew of our file. I am writing to confirm receipt of your below request and that we will respond by the requested date. We stand ready to respond to any further questions FDA may have as the review team completes its review of our file.

>

> Can you please clarify if you are replacing Poulomi as the lead reviewer for this file or is she just on vacation at this time? Thanks.

>

> Have a nice weekend.

>

> Cindy Domecus, R.A.C. (US & EU)

> Principal

> Domecus Consulting Services LLC

> (650) 343-4813 (office)

> (b)(6) (cell)

>

>

>

>

>

>

> On Aug 21, 2020, at 12:23 PM, Avery, Reginald <Reginald.Avery@fda.hhs.gov
<mailto:Reginald.Avery@fda.hhs.gov>> wrote:

>

> Hello,

>

> I am reviewing your 510(k) supplement for the Jada System. Could you please address the following questions? If possible, please provide a response by noon on Tuesday, August 25, 2020.

(b)(4) Deficiencies

(b)(4) Deficiencies

> Do not hesitate to contact me if you have any questions or concerns.
>
> Thanks,
> Reginald
>
> Reginald Avery, Ph.D.
> Biomedical Engineer, Obstetrical and Reproductive Health Devices Team
>
> DHT3B: Division of Reproductive, Gynecology and Urology Devices
> OHT3: Office of Gastrorenal, ObGyn, General Hospital and Urology Devices
> OPEQ: Office of Product Evaluation and Quality
> CDRH | Food and Drug Administration
>
>
> White Oak, Bldg. 66, Rm. 2647 | 10903 New Hampshire Avenue | Silver Spring, MD 20993
> Ph: 240-402-6152
> Reginald.Avery@fda.hhs.gov <mailto:Reginald.Avery@fda.hhs.gov>
> <image013.png> <http://www.fda.gov/>
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> <image014.jpg> <https://www.facebook.com/FDA> <image015.jpg>
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<http://www.youtube.com/user/USFoodandDrugAdmin> <image017.jpg>
<http://www.flickr.com/photos/fdaphotos/> <image018.jpg>
<http://www.fda.gov/AboutFDA/ContactFDA/StayInformed/RSSFeeds/default.htm>
>
> Excellent customer service is important to us. Please take a moment to provide feedback regarding the customer service you have received:
https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E
<https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E>

TEST FACILITY

(b)(4)

SPONSOR

(b)(4)

STUDY TITLE

ISO Guinea Pig Maximization Sensitization Test

TEST ARTICLE NAME

Postpartum Hemorrhage Intrauterine Suction Device

TEST ARTICLE IDENTIFICATION

(b)(4)

(b)(4)

(b)(4) Testing

(b)(4) Testing

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(b)(4) Testing

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(b)(4) Testing

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(b)(4) Deficiencies

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Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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Reginald.Avery@fda.hhs.gov


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https://www.research.net/s/cdrhcustomerservice?ID=1521&S=E

From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 10:41 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies [K201199/S001)

Hello Reginald,

Attached is a Word version of the most recent 510(k) Summary, submitted under S001. We will look for any changes FDA might request. Thanks.

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Principal
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(b)(6) (cell)

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Reginald

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From: Cindy Domecus <DomecusConsulting@comcast.net>
Sent: Thursday, August 27, 2020 12:50 AM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: R[(b)(4) Deficiencies]K201199/S001)

Hello Reginald,

Attached is our response to your below request and the accompanying 4 exhibits. Please let me know if you need anything further as you complete your reivew. Thank you again for your continued reivew of our application!

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
[(b)(6)] (office)
(cell)

On Aug 26, 2020, at 7:32 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

(b)(4) Deficiencies

(b)(4) Deficiencies

Thanks,
Reginald

Reginald Avery, Ph.D.
Biomedical Engineer, Obstetrical and Reproductive Health Devices Team

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U.S. FOOD & DRUG ADMINISTRATION

Food and Drug Administration
CDRH/OPEQ/OHT3/DHT3B
WO66 RM2647
10903 New Hampshire Ave
Silver Spring, MD 20993-0002
240-402-6152

Premarket Notification 510(k) Review

Date: August 28, 2020

Reviewer: Reginald Avery

Subject: Traditional 510(k)# K201199/S001

Applicant: Alydia Health	**Device Trade Name:** Jada System
Contact Name: Cindy Domecus	**Contact Title:** Principal
Correspondent Firm: Domecus Consulting Services LLC	**Phone:** (650) 343-4813 **Email:** domecusconsulting@comcast.net
Received Date: May 4, 2020	**Due Date:** August 2, 2020
Pro Code(s): OQY **Class:** II **Reg #:** 884.4530	**Reg Name:** Obstetric-Gynecologic Specialized Manual Instrument

Predicate Devices:

Submission #	Pro Code	Device Trade Name	Applicant
K170622	OQY	Bakri Postpartum Balloon, Bakri Postpartum Balloon with Rapid Instillation Component	Cook Incorporated

(b)(5)

(b)(5) FDA Reviewer Notes

(b)(5) FDA Reviewer Notes

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(b)(5) FDA Reviewer Notes

Digital Signature Concurrence Table (Doc ID: 04500.14.01)	
This document represents a high-level summary of the Agency's determination on whether the applicant's device is substantially equivalent to a legally marketed predicate device. In determining whether the subject device is substantially equivalent to a predicate device, we carefully considered the relevant regulatory and statutory criteria for Agency decision-making under 21 CFR part 807 and section 513(i) of the Federal Food, Drug and Cosmetic Act (FD&C Act). We considered the burden that may be incurred by the applicant's attempt to follow the premarket notification process. The deficiencies provided in this review, if any, represent the required minimum information necessary to support a substantial equivalence determination. Therefore, we believe that we have considered the least burdensome requirements, under section 513(i)(1)(D) of the FD&C Act, for a 510(k) determination of substantial equivalence.	
Reviewer Sign-Off	Reginald K. Avery -S 2020.08.28 13:29:07 -04'00'

SECTION 5: INDICATIONS FOR USE

Provided in this section is the Indications for Use Statement (Form 3881) for the subject device.

Hello Reginald,

(b)(4) Deficiencies

Cindy Domecus, R.A.C. (US & EU)
Principal
Domecus Consulting Services LLC
(650) 343-4813 (office)
(b)(6) (cell)

On Aug 28, 2020, at 9:15 AM, Avery, Reginald <Reginald.Avery@fda.hhs.gov> wrote:

Hello,

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Thanks,
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Sent: Thursday, August 27, 2020 6:36 PM
To: Avery, Reginald <Reginald.Avery@fda.hhs.gov>
Cc: K201199@docs.fda.gov
Subject: Re (b)(4) Deficiencies K201199/S001)

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(b)(4) Deficiencies

SECTION 13: SUBSTANTIAL EQUIVALENCE

(b)(4)

PREDICATE DEVICE

The subject device, the Jada System, is substantially equivalent to the predicate device described below in **Table 13-1**:

Table 13-1. Predicate Device

Device Name	Company	K #	Classification Regulation and Product Code
Bakri® Postpartum Balloon	Cook Incorporated	K170622	21 CFR § 884.4530 Product Code: OQY

This identified predicate device is consistent throughout the submission. A copy of the predicate device labeling is provided in **Exhibit 13.A**.

(b)(4)

INDICATIONS FOR USE

The Indications for Use for the subject and predicate devices are presented in **Table 13-2** below.

Table 13-2. Indications for Use Comparison

Jada System **SUBJECT DEVICE**	**Bakri® Postpartum Balloon** **PREDICATE DEVICE**
The Jada System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.	Bakri® Postpartum Balloon is intended to provide temporary control or reduction of postpartum uterine bleeding when conservative management is warranted.

The differences between the subject and predicate Indications for Use do not alter the intended therapeutic use of the device nor do they affect the safety and effectiveness of the device relative to the predicate. Both the subject and predicate devices have the same intended use, which is for the treatment of abnormal postpartum uterine bleeding when conservative management is warranted.

(b)(4)

In summary, the differences in the Indications for Use for the subject device do not raise different questions of safety and effectiveness and therefore, do not preclude a meaningful comparison with the predicate device.

TECHNOLOGICAL CHARACTERISTICS

Provided below in **Table 13-3** is a comparison of the technological characteristics of the subject and predicate devices. Following **Table 13-3** is a discussion of why the differences do not raise different questions of safety and effectiveness. The substantial equivalence analysis is concluded with a discussion of each of the decision points noted in FDA's July 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

Table 13-3. Technological Characteristics Comparison

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Both the subject and predicate devices are intended to treat abnormal uterine bleeding through tamponade. At a high level, the subject and predicate devices are based on the following same technological elements:

- Tamponade of the blood vessels in the uterine walls
- In-dwelling treatment within the uterus and genital tract ≤24 hours
- Drain tube (Intrauterine Loop with Vacuum Pores) to remove blood and fluid from postpartum uterus
- All patient contacting materials are medical grade silicone

The following technological differences exist between the subject and predicate devices:

- (b)(4)
-

- (b)(4)

Discussion of Differences in Technological Characteristics

(b)(4)

FDA'S SUBSTANTIAL EQUIVALENCE DECISION MAKING GUIDANCE

Below we address each of the decision points in FDA's substantial equivalence decision-making process, as identified in FDA's July 2014 guidance *The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)], Guidance for Industry and Food and Drug Administration Staff*.

Decision 1: Is the predicate device legally marketed?

Yes, the predicate device is legally marketed under K170622.

Decision 2: Do the devices have the same intended use?

Yes, the subject and predicate devices have the same intended use, which is for the treatment of abnormal postpartum uterine bleeding when conservative management is warranted.

Decision 3: Do the devices have the same technological characteristics?

No, the devices have similar technological characteristics, but they are not identical.

Decision 4: Do the different technological characteristics of the devices raise different questions of safety and effectiveness?
No, the safety and effectiveness questions are the same for the subject and predicate device:

- Has the mechanical performance of the device been demonstrated?
- Has biocompatibility of the device materials been demonstrated?
- Has sterilization been validated?
- Can the device be safely inserted into the uterus?
- Can the device safely remain in the uterus for the required treatment period?
- Does the device effectively treat postpartum abnormal bleeding?

Decision 5a: Are the methods acceptable?
Yes, test methods were used in the nonclinical evaluation of the subject device. Recognized standards were followed for biocompatibility, sterilization and packaging qualifications. Nonclinical bench testing of the subject device was performed using predetermined test methods utilizing calibrated instruments and equipment. The clinical evaluation of the device was conducted per an approved IDE application, G150265.

Decision 5b: Do the data demonstrate substantial equivalence?
Yes, the subject device has been demonstrated to be safe and effective for its intended use through both nonclinical and clinical testing. The results of the testing support a conclusion that the subject device does not raise different questions of safety or effectiveness as compared to the predicate device.

CONCLUSION
In summary, the intended use of the subject and predicate devices is identical, which is for the treatment of abnormal postpartum uterine bleeding when conservative management is warranted. The differences between the subject and predicate Indications for Use do not alter the intended therapeutic use of the device nor do they affect the safety and effectiveness of the device relative to the predicate.

(b)(4)

Also, the clinical performance data on the Jada System provided in this 510(k) submission (see **Section 21. Performance Data: Clinical**) support use of the subject device for both abnormal postpartum uterine bleeding and hemorrhage.

The differences in technological characteristics also do not raise different questions of safety and effectiveness. The subject device has been demonstrated to be safe

and effective for its intended use through both nonclinical and clinical testing. The results of the testing support a conclusion that the subject device does not raise different questions of safety or effectiveness as compared to the predicate device.

(b)(4)

Contains Nonbinding Recommendations

Print Form

Acceptance Checklist for Traditional 510(k)s

(Should be completed within 15 days of DCC receipt)

The following information is not intended to serve as a comprehensive review.
FDA recommends that the submitter include this completed checklist as part of the submission.

510(k) #: K201199 Date Received by DCC: May 4, 2020

Lead Reviewer: Poulomi Nandy

Center: CDRH Office: OHT 3 Division: DHT3B

Decision:

◉ Accept. If Accept, notify submitter.

○ Refuse to Accept. If Refuse to Accept, notify submitter electronically and include a copy of this checklist.

Is an Addendum attached?: ○ Yes ◉ No Click paperclip icon on the left panel if Addendum is attached.

Note: If an element is left blank on the checklist, it does not mean the checklist is incomplete; it means the reviewer did not assess the element during the RTA review and that the element will be assessed during substantive review.

IMPORTANT - Many checklist elements include additional details regarding information to address the element that can be seen by hovering over the element (Example - Element 4 in Section A of the checklist).

Preliminary Questions

Answers in the shaded blocks indicate consultation with a Center advisor is needed. (Boxes checked in this section represent FDA's preliminary assessment of these questions at the time of administrative review.)	Yes	No	N/A
1 Is the product a device (per section 201(h) of the FD&C Act) or a combination product (per 21 CFR 3.2(e)) with a device constituent part subject to review in a 510(k)? If it appears not to be a device (per section 201(h) of the FD&C Act) or such a combination product (per 21 CFR 3.2(e)), or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action, and inform management. *Provide a summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* If the product does not appear to be a device or such a combination product, mark "No."	☒	☐	
Comments:			
2 Is the submission with the appropriate Center? If the product is a device or a combination product with a device constituent part, is it subject to review by the Center in which the submission was received? If you believe the submission is not with the appropriate Center or you are unsure, consult with the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide a summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* If submission should not be reviewed by your Center mark "No."	☒	☐	
Comments:			

3 If a Request for Designation (RFD) was submitted for the device or combination product with a device constituent part and assigned to your center, identify the RFD # and confirm the following: **a) Is the device or combination product the same (e.g., design, formulation) as that presented in the RFD submission?** **b) Are the indications for use for the device or combination product identified in the 510(k) the same as those identified in the RFD submission?** If you believe the product or the indications presented in the 510(k) have changed from the RFD, or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide a summary of Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* If the answer to either question above is no, mark "No." If there was no RFD, mark "N/A."	☐	☐	☒
Comments:			
4 Is the submission for a combination product that contains as a constituent part a drug that has the same active moiety as an approved drug with exclusivity as described in 21 USC 503(g)(5)(C)(ii)-(v) (section 503(g)(5)(C)(ii)-(v) of the FD&C Act)? If "Yes," then contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide the summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.*	☐	☐	☒
Comments:			
5 Is this device type eligible for a 510(k) submission? If a 510(k) does not appear to be appropriate (e.g., Class III type and PMA required, or Class I or II type and 510(k)-exempt), consult with the appropriate CDRH or CBER staff during the acceptance review, provide a summary of the discussion with them, and indicate their recommendation/action in the comment section below. If 510(k) is not the appropriate regulatory submission, mark "No."	☒	☐	
Comments:			
6 Is there a pending PMA for the same device with the same indications for use? If "Yes," consult your management and CDRH Office of Product Evaluation and Quality/Office of Regulatory Programs/Division of Regulatory Programs 1 (Submission Support) (OPEQ/ORP/DRP1) or appropriate CBER staff to determine the appropriate action.	☐	☒	
Comments:			
7 If clinical studies have been submitted, is the submitter the subject of an Application Integrity Policy (AIP)? If "Yes," consult with the CDRH Office of Product Evaluation and Quality/ Office of Clinical Evidence and Analysis/Division of Clinical Science and Quality (OPEQ/OCEA/DCEA1) or CBER Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Bioresearch Monitoring Branch (OCBQ/DIS/BMB) to determine the appropriate action, provide a summary of the discussion with them, and indicate their recommendation/action. If no clinical studies have been submitted, mark "N/A." Check on the AIP list at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/application-integrity-policy/application-integrity-policy-list.	☐	☒	☐
Comments:			

- If the answer to 1 or 2 appears to be "No," then stop review of the 510(k) and contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.
- If the answer to 3a or 3b appears to be "No," then stop the review and contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.
- If the answer to 4 is "Yes," then contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer, provide a summary of the discussion with them, and indicate their recommendation/action.
- If the answer to 5 is "No," the lead reviewer should consult management and other Center resources to determine the appropriate action.
- If the answer to 6 is "Yes," then stop review of the 510(k), contact the CDRH/OPEQ/ORP/DRP1, or appropriate CBER staff.
- If the answer to 7 is "Yes," then contact CDRH/OPEQ/OCEA/DCEA1 or CBER/OCBQ/DIS/BMB, provide a summary of the discussion with DCEA1 or BMB Staff, and indicate their recommendation/action.

Organizational Elements

Failure to include these items should not result in an RTA designation.

*Submitters including the checklist with their submission should identify the page numbers where requested information located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	*Page #
1) Submission contains a Table of Contents	☒	☐	
2) Each section is labeled (e.g., headings or tabs designating Device Description section, Labeling section, etc.)	☒	☐	
3) All pages of the submission are numbered. *All pages should be numbered in such a manner that information can be referenced by page number. This may be done either by consecutively numbering the entire submission, or numbering the pages within a section (e.g., 12-1, 12-2…).*	☒	☐	
4) Type of 510(k) is identified (i.e., Traditional, Abbreviated, or Special). *If type of 510(k) is not designated, review as a Traditional 510(k).*	☒	☐	
Comments:			

Elements of a Complete Submission (RTA Items)
(21 CFR 807.87 unless otherwise indicated)

Submission should be designated RTA if not addressed.

- Any "No" answer will result in a "Refuse to Accept" decision; however, FDA staff has discretion to determine whether missing items are needed to ensure that the submission is administratively complete to allow the submission to be accepted or to request missing checklist items interactively from submitters during RTA review.
- Each element on the checklist should be addressed within the submission. The submitter may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criterion is considered present (Yes). An assessment of the rationale will be considered during the review of the submission.

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
A. Administrative					
1) All content used to support the submission is written in English (including translations of test reports, literature articles, etc.)	☒	☐		☐	
2) Submission identifies the following (FDA recommends use of the CDRH Premarket Review Submission Cover Sheet form (Form 3514, available at https://www.fda.gov/media/72421/download)):				☐	
a) Device trade/proprietary name	☒	☐			
b) Device class and panel OR Classification regulation OR Statement that device has not been classified with rationale for that conclusion	☒	☐			
3) Submission contains an Indication for Use Statement with Rx and/or OTC designated (see also 21 CFR 801.109, and FDA's guidance "Alternative to Certain Prescription Devices Labeling Requirements," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/alternative-certain-prescription-device-labeling-requirements.) *See recommended* format (https://www.fda.gov/media/86323/download).	☒	☐		☐	
4) Submission contains a 510(k) Summary or 510(k) Statement.	☒	☐		☐	
5) Submission contains a Truthful and Accuracy Statement per 21 CFR 807.87(l) *See recommended format (https://www.fda.gov/medical-devices/premarket-notification-510k/premarket-notification-truthful-and-accurate-statement).*	☒	☐		☐	
6) Submission is a Class III 510(k) device.	☐		☒	☐	
7) Submission contains clinical data	☒		☐	☐	
a) Submission includes completed Financial Certification (FDA Form 3454, available at https://www.fda.gov/media/70465/download) or Disclosure (FDA Form 3455, available at https://www.fda.gov/media/69872/download) information for each covered clinical study included in the submission. *Select "N/A" if the submitted clinical data is not a "covered clinical study" as defined in the guidance entitled "Financial Disclosures by Clinical Investigators", available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/financial-disclosure-clinical-investigators.*	☒	☐	☐		
b) Submission includes completed Certification of Compliance with requirements of ClinicalTrials.gov Data Bank (FDA Form 3674, available at https://www.fda.gov/media/69901/download) (42 U.S.C. 282(j)(5)(B)) for each applicable device clinical trial included in the submission. *Select "N/A" if the submitted clinical data is not an "applicable device clinical trial" as defined in Title VIII of FDAAA, Sec. 801(j)*	☒	☐	☐		

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
c) Statements of Compliance for Clinical Investigations *Select "N/A" if the submission does not contain any clinical data from investigations (as defined in 21 CFR 812.3(h)) to demonstrate substantial equivalence.* *For multicenter clinical investigations involving both United States (US) and outside United States (OUS) sites, part (i) should be addressed for the US sites and part (ii) should be addressed for the OUS sites. 21 CFR 812.28 applies to all OUS clinical investigations that enroll the first subject on or after February 21, 2019.* *Please refer to the guidance document entitled "Acceptance of Clinical Data to Support Medical Device Applications and Submissions - Frequently Asked Questions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-clinical-data-support-medical-device-applications-and-submissions-frequently-asked for more information.*	☒		☐		
i) For each clinical investigation conducted in the US, the submission includes a statement of compliance with 21 CFR parts 50, 56, and 812. **OR** The submission includes a brief statement of the reason for noncompliance with 21 CFR parts 50, 56, and 812.	☒	☐	☐		
ii) For each clinical investigation conducted OUS, the submission includes a statement that the clinical investigations were conducted in accordance with good clinical practice (GCP) as described in 21 CFR 812.28(a)(1). **OR** The submission includes a waiver request in accordance with 21 CFR 812.28(c). **OR** The submission includes a brief statement of the reason for not conducting the investigation in accordance with GCP and a description of steps taken to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of subjects have been adequately protected.	☒	☐	☐		
8) The submission identifies prior submissions for the same device included in the current submission (e.g., submission numbers for a prior not substantially equivalent [NSE] determination, prior deleted or withdrawn 510(k), Q-Submission, IDE, PMA, etc.). **OR** States that there were no prior submissions for the subject device.	☒	☐		☐	
a) If there were prior submissions, the submitter has identified where in the current submission any issues related to a determination of substantial equivalence from prior submissions for this device are addressed.	☒	☐	☐		
9) The submission utilizes voluntary consensus standard(s) (See section 514(c) of the FD&C Act). *This includes both FDA-recognized and non-recognized consensus standards.*	☒		☐	☐	
a) The submission cites FDA-recognized voluntary consensus standard(s).	☒		☐		

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
i) The submission includes a Declaration of Conformity (DOC) as outlined in FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices. **OR** If citing general use of a standard as noted in FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," the basis of such use is included along with the underlying information or data that supports how the standard was used.	☒	☐			
b) The submission cites non-FDA-recognized voluntary consensus standard(s).	☐		☒		
Combination Product Provisions - Per 503(g) of the FD&C Act. Select "N/A" if the product is not a combination product. 21 CFR 3.2(e). The remaining criteria in this section will be omitted from the checklist if "N/A" is selected. If you are unsure if the product is a combination product, consult with the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.			☒		
B. Device Description					
12) The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding the device description that is applicable to the subject device.	☐		☒	☐	
13) Descriptive information is present and consistent within the submission (e.g., the device description section is consistent with the device description in the labeling).	☒	☐		☐	
14) The submission includes descriptive information for the device, including the following:				☐	
a) A description of the principle of operation or mechanism of action for achieving the intended effect.	☒	☐			
b) A description of proposed conditions of use, such as surgical technique for implants; anatomical location of use; user interface; how the device interacts with other devices; and/or how the device interacts with the patient.	☒	☐	☐		
c) A list and description of each device for which clearance is requested.	☒	☐	☐		
d) Submission contains representative engineering drawing(s), schematics, illustrations, photos and/or figures of the device. **OR** Submission includes a statement that engineering drawings, schematics, etc. are not applicable to the device (e.g., device is a reagent and figures are not pertinent to describe the device).	☒	☐			
15) Device is intended to be marketed with accessories and/or as part of a system.	☐		☒	☐	
C. Substantial Equivalence Discussion					
16) Submitter has identified a predicate device(s), including the following information:				☐	

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
a) Predicate device identifier provided (e.g., 510(k) number, De Novo number, reclassified PMA number, classification regulation reference, if exempt (e.g., 21 CFR 872.3710), or statement that the predicate is a preamendment device). For predicates that are preamendments devices, information is provided to document preamendments status. *Information regarding documenting preamendment status is available online (https://www.fda.gov/medical-devices/quality-and-compliance-medical-devices/preamendment-status).*	☒	☐			
b) The identified predicate(s) is consistent throughout the submission (e.g., the predicate(s) identified in the Substantial Equivalence section is the same as that listed in the 510(k) Summary (if applicable) and that used in comparative performance testing).	☒	☐			
17) Submission includes a comparison of the following for the predicate(s) and subject device and a discussion why any differences between the subject and predicate(s) do not impact safety and effectiveness [see section 513(i)(1)(A) of the FD&C Act and 21 CFR 807.87(f)] *See the FDA guidance document "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k for more information on comparing intended use and technological characteristics.*				☐	
a) Indications for Use	☒	☐			
b) Technology, including technical specifications, features, materials, and principles of operation	☒	☐			
D. Proposed Labeling (see also 21 CFR part 801 and 809 as applicable)					
18) Submission includes proposed package labels and labeling (e.g., instructions for use, package insert, operator's manual).	☒	☐		☐	
a) Indications for use are stated in labeling and are identical to Indications for Use form and 510(k) Summary (if 510(k) Summary provided).	☒	☐			
b) Labeling includes: - Statements of conditions, purposes or uses for which the device is intended (e.g., hazards, warnings, precautions, contraindications) (21 CFR 801.5) **AND** - Includes adequate directions for use (see 21 CFR 801.5) **OR** - Submission states that device qualifies for exemption per 21 CFR 801 Subpart D	☒	☐			
19) Labeling includes name and place of business of the manufacturer, packer, or distributor (21 CFR 801.1).	☒	☐		☐	
20) Labeling includes the prescription statement [see 21 CFR 801.109(b)(1)] or Rx Only symbol (see also Section 502(a) of the FD&C Act and FDA's guidance "Alternative to Certain Prescription Device Labeling Requirements," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/alternative-certain-prescription-device-labeling-requirements.	☒	☐	☐	☐	
21) The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding labeling that is applicable to the subject device.	☐		☒		

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
22) If the device is an in vitro diagnostic device, provided labeling includes all applicable information required per 21 CFR 809.10.	☐	☐	☒	☐	
E. Sterilization					
If an *in vitro* diagnostic (IVD) device and sterilization is not applicable, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected.			☐		
☒ Provided sterile, intended to be single-use					
☐ Requires processing during its use-life					
☐ Non-sterile when used (and no processing required)					
☐ Information regarding the sterility status of the device is not provided. (If this box is checked, please also check one of the two boxes below.)					
☐ Sterility status not needed for this device (e.g., software-only device)					
☐ Sterility status needed or need unclear					
This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination. *Please refer to the FDA guidance document "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/reprocessing-medical-devices-health-care-settings-validation-methods-and-labeling, for additional information.*					
23) Assessment of the need for cleaning and subsequent disinfection or sterilization information				☐	
a) Identification of device and/or accessories, if applicable, that are provided sterile.	☒	☐	☐		
b) Identification of device and/or accessories, if applicable, that are end user sterilized or disinfected.	☐	☐	☒		
c) Identification of device, and/or accessories, if applicable, that are reusable.	☐	☐	☒		
24) If the device and/or accessories, if applicable, are provided sterile:			☐	☒	
a) Sterilization method is stated for each device (including dose for radiation sterilization).	☒	☐			
b) A description of method to validate the sterilization parameters is provided for each proposed sterilization method (e.g., half-cycle method and full citation of FDA-recognized standard, including date).	☒	☐			
c) For devices sterilized using chemical sterilants such as ethylene oxide (EO) and hydrogen peroxide, submission states maximum levels of sterilant residuals remaining on the device and sterilant residual limits.	☐	☐	☒		
d) Sterility Assurance Level (SAL) is stated.	☒	☐			
e) Submission includes description of packaging.	☒	☐			
f) For products labeled "non-pyrogenic," a description of the method used to make the determination stated (e.g., limulus amebocyte lysate [LAL]).	☐	☐	☒		
Comments: for 24 f) product not labelled non-pyrogenic, however test data provided under biocompatibility section.					

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
25) If the device and/or accessory, if applicable, is reusable or end user sterilized or disinfected:			☒	☐	
a) Cleaning method is provided in labeling for each device and/or accessory, if applicable.	☐	☐	☒		
b) Disinfection method is provided in labeling for each device and/or accessory, if applicable.	☐	☐	☒		
c) Sterilization method is provided in labeling for each device and/or accessory, if applicable.	☐	☐	☒		
d) Device types in this submission are listed in the Federal Register (FR) Notice entitled "Validated Instructions for Use and Validation Data Requirements for Certain Reusable Medical Devices in Premarket Notifications" (Reprocessing FR Notice, available at https://www.federalregister.gov / documents/2017/06/09/2017-12007/medical-devices-validated-instructions-for-use-and-validation-data-requirements-for-certain-reusable).	☐		☒		
i) If device types in this submission are included in the Reprocessing FR Notice, the submission includes protocols and test reports for validating the reprocessing instructions.	☐	☐	☒		
26) The device has a device-specific guidance document, special controls, and/or requirement in a device-specific regulation regarding sterility and/or reprocessing that is applicable to the subject device.	☐		☒	☐	
F. Shelf Life					
27) Proposed shelf life/expiration date stated **OR** Statement that shelf-life is not applicable because of low likelihood of time-dependent product degradation	☒	☐	☐	☐	
28) For a sterile device, submission includes summary of methods used to establish that device packaging will maintain a sterile barrier for the entirety of the proposed shelf life.	☒	☐	☐	☐	
29) Submission includes summary of methods used to establish that device performance is maintained for the entirety of the proposed shelf-life (e.g., mechanical properties, coating integrity, pH, osmolality, etc.). **OR** Statement why performance data is not needed to establish maintenance of device performance characteristics over the shelf-life period.	☒	☐		☐	
G. Biocompatibility					
If an vitro diagnostic (IVD) device, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected.			☐		
Submission states that there: (one of the below must be checked)		☐		☐	
☒ Are direct or indirect tissue-contacting components.					
☐ Are no direct or indirect tissue-contacting components.					
☐ Information regarding tissue contact status of the device is not provided (if this box checked, please also check one of the two boxes below).					
☐ Tissue contact information not needed for this device (e.g., software-only device)					
☐ Tissue contact information needed or need unclear					

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.					
30) Submission includes a list identifying each of tissue-contacting device component (e.g., implant, delivery catheter) and associated materials of construction for each component, including identification of color additives, if present.	☒	☐		☐	
31) Submission identifies contact classification (e.g., surface-contacting, less then 24 hour duration) for each tissue-contacting device component (e.g., implant, delivery catheter)	☒	☐		☐	
32) For a biocompatibility assessment of tissue-contacting components, submission includes: – Each relevant endpoint for the device (as identified in device-specific guidance, or Attachment A of the FDA guidance document entitled "Use of International Standard ISO 10993-1, `Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'" available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and), has been addressed. - For any testing performed, test protocol (including identification and description of test article including whether the test article is the device in its final finished form using the recommended approach in Attachment F of "Use of International Standard ISO 10993-1, `Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'" methods, and pass/fail criteria), and analysis of results (including tables with data points and statistical analyses, where appropriate), as described in Attachment E of the guidance document entitled "Use of International Standard ISO 10993-1, `Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'" provided for each completed test. **OR** A statement that biocompatibility testing is not needed with a rationale that considers all relevant endpoints (e.g., materials and manufacturing/processing are identical to the predicate).	☒	☐		☐	
H. Software					
Submission states that the device: (one of the below must be checked)		☐		☐	
☐ Does contain software/firmware					
☒ Does not contain software/firmware					
☐ Information on whether device contains software/firmware is not provided. (If this box is checked, please also check one of the two boxes below.)					
☐ Software/firmware information not needed for this device (e.g., surgical suture, condom)					
☐ Software/firmware information is needed or need unclear					
This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.					
I. Cybersecurity					
Submission states that the device: *(one of the below must be checked)*		☐		☐	
☐ Does contain any external wired and/or wireless communication interfaces (Wired: USB, ethernet, SD, CD, RGA, etc. or Wireless: Wi-Fi, Bluetooth, RF, inductive, Cloud, etc.)					
☒ Does not contain external interfaces as described above					

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
☐ Information on whether device has external interfaces is not provided. (If this box is checked, please also check one of the two boxes below.)					
☐ Cybersecurity information not needed for this device (e.g., surgical suture, condom)					
☐ Cybersecurity information is needed or need unclear					
This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.					
J. Electrical Safety and EMC					
Electrical Safety Submission states that the device: *(one of the below must be checked)*		☐		☐	
☐ Does require electrical safety evaluation					
☒ Does not require electrical safety evaluation					
☐ Information on whether device requires electrical safety evaluation is not provided. (If this box is checked, please also check one of the two boxes below.)					
☐ Electrical safety information not needed for this device (e.g., surgical suture, condom)					
☐ Electrical safety information is needed or need unclear					
This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.					
EMC Submission states that the device: (one of the below must be checked)		☐		☐	
☐ Does require EMC evaluation					
☒ Does not require EMC evaluation					
☐ Information on whether device requires EMC evaluation is not provided. (If this box is checked, please also check one of the two boxes below.)					
☐ EMC information not needed for this device (e.g., surgical suture, condom)					
☐ EMC information is needed or need unclear					
This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.					
K. Performance Data - General					
If an in vitro diagnostic (IVD) device, select "N/A." The criteria in this section will be omitted from checklist if "N/A" is selected. Performance data criteria relating to IVD devices is addressed in Section K.			☐		

Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed. *Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.	Yes	No	N/A	Comment	*Page #
38) Summaries of the non-clinical laboratory studies and full test reports* are provided. *Summary and full test report content recommendations can be found in FDA's guidance "Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket. If a submitter chooses to declare conformity to a voluntary consensus standard that FDA has recognized, submission of a full test report may not be necessary. Refer to 9a. See FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices.	☒	☐	☐	☐	
a) Submission includes an explanation of how the data generated from each test supports a finding of substantial equivalence (e.g., comparison to predicate device testing, dimensional analysis, etc.).	☒	☐	☐		
39) The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding performance data that is applicable to the subject device.	☐		☒	☐	
40) If literature is referenced in the submission, submission includes:			☒		
41) For each completed animal study, the submission provides the following:			☒	☐	
L. Performance Characteristics - In Vitro Diagnostic Devices Only **(Also see 21 CFR 809.10(b)(12))**					
Submission states that the device: (one of the below must be checked)				☐	
☐ is an in vitro diagnostic device.					
☒ is not an in vitro diagnostic device.					
If "is not" is selected, the performance data-related criteria below are omitted from the checklist.					

Digital Signature Concurrence Table

Reviewer Sign-Off	Poulomi Nandy -S 2020.05.11 10:16:58 -04'00'
Management Sign-Off (digital signature optional)*	

* Management review of checklist and concurrence with decision required.

Clinical Investigation Report

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FDA U.S. FOOD & DRUG ADMINISTRATION

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
OFFICE OF PRODUCT EVALUATION AND QUALITY
OFFICE OF CLINICAL EVIDENCE AND ANALYSIS
DIVISION OF CLINICAL EVIDENCE AND ANALYSIS 2

MEMORANDUM FOR STATISTICAL CONSULT

Yanping Qu -S

Digitally signed by Yanping Qu -S
Date: 2020.06.23 09:53:32 -04'00'

Date: June 23, 2020

From: Yanping Qu, Ph.D., CDRH/OCEA/DCEA2/TCEA2A

Subject: Statistical Review of 510(k) K201199
Jada® System
Alydia Health, Inc.

To: Poulomi Nandy, CDRH/OHT3/DHT3B/THT3B1

(b)(5)

(b)(5) FDA Reviewer Notes

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Yanping Qu

CC:

Kelly Colden, Clinical Reviewer, CDRH/OHT3/DHT3B/THT3B1
Li Ming Dong, Ph.D., Team Leader, CDRH/OCEA/DCEA2/TCEA2A
Xu (Sherry) Yan, Ph.D., Assistant Director, CDRH/OCEA/DCEA2/TCEA2A
DBS Reviews

SECTION 19: ELECTRICAL SAFETY AND EMC

The subject device does not include any electrical components, so this element of FDA's 510(k) Acceptance Checklist is not applicable.

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