



Memorandum

Date . SEP 30 1996

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Kensey Nash Corporation
Angio-Seal™ Hemostatic Puncture Closure Device - ACTION

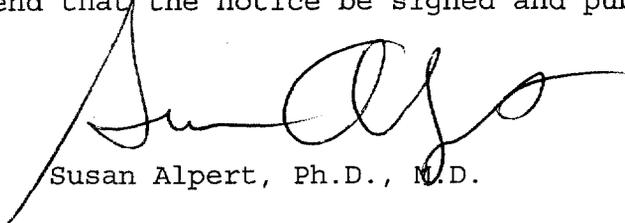
To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

- (1) a premarket approval order for the above referenced medical device (Tab B); and
- (2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.



Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

Prepared by Christopher M. Sloan, CDRH, HFZ-450, 9/12/96, 443-8243

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food And Drug Administration

[DOCKET NO. _____]

KENSEY NASH CORP.; PREMARKET APPROVAL OF The Angio-Seal™

Hemostatic Puncture Closure Device

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Kensey Nash Corp., Exton, PA, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the Angio-Seal™ Hemostatic Puncture Closure Device. After reviewing the recommendation of the Circulatory System Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter of September 30, 1996, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review, to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Christopher M. Sloan,
Center for Devices and Radiological Health (HFZ-450),
Food and Drug Administration,
9200 Corporate Blvd.,
Rockville, MD 20850,
301-443-8243.

SUPPLEMENTARY INFORMATION: On October 28, 1993, Kensey Nash Corp., Exton, PA 19341, submitted to CDRH an application for premarket approval of the Angio-Seal™ Hemostatic Puncture Closure Device. The device is a vascular hemostasis device and is indicated for use in closing and in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8F or smaller procedure sheath.

On May 8, 1995, the Circulatory System Devices Panel of the Medical Devices Advisory Committee, an FDA advisory committee, reviewed and recommended approval of the application.

On September 30, 1996, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's

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action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.



This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated: _____.





Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

SEP 30 1996

Ms. Julie N. Broderick
Director of Clinical and
Regulatory Affairs
Kensey Nash Corporation
55 East Uwchlan Avenue
Exton, Pennsylvania 19341

Re: P930038
Angio-Seal™ Hemostatic Puncture Closure Device
Filed: October 28, 1993
Amended: February 1, May 20, September 19, October 5,
November 25, and December 1 and 5, 1994, January 4,
10, 13 and 17, March 17, April 20, May 11, June 6,
July 6 and 13, September 19 and 22, November 1, 13,
and 13, and December 5 and 11, 1995, and January 11
and 30, February 12, March 25, April 1, May 10,
July 1, and September 12, 1996

Dear Ms. Broderick:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Angio-Seal™ Hemostatic Puncture Closure Device. This device is indicated for use in closing and in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8 French or smaller procedural sheath. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

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Expiration dating for this device has been established and approved at six months. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

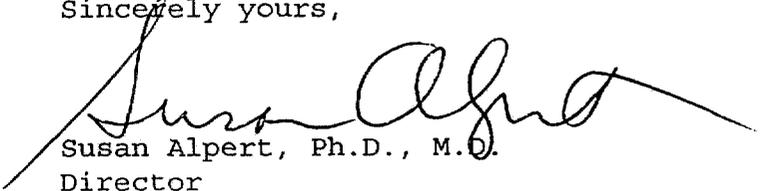
You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have questions concerning this approval order, please contact Christopher Sloan at (301) 443-8243.

Sincerely yours,


Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the **addition** of, but **not the replacement** of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. **This procedure is not applicable to changes**

in device design, composition, specifications, circuitry, software or energy source.

Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

- (1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).
- (2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:
 - (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and

- (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

- (1) A mixup of the device or its labeling with another article.
- (2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and
 - (a) has not been addressed by the device's labeling or
 - (b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.
- (3) Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

- (1) may have caused or contributed to a death or serious injury or
- (2) has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, 340
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name: Vascular Hemostasis Device

Device Trade Name: Angio-Seal* Hemostatic Puncture Closure Device

Applicant's Name and Address: Kensey Nash Corporation
55 East Uwchlan Avenue
Exton, Pennsylvania 19341

PMA Number: P930038

Date of Panel Recommendation: May 8, 1995

Date of Notice of Approval to the Applicant: SEP 30 1996

II. Indications for Use

The Angio-Seal* device is indicated for use in closing and in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8 French or smaller procedural sheath.

III. Device Description

The Angio-Seal* Hemostatic Puncture Closure Device consists of the Angio-Seal* device, an 8F insertion sheath, an arteriotomy locator (modified dilator), a 0.038" guidewire, and a post-placement tension spring. The Angio-Seal* device is composed of a plug of collagen sponge and a specially designed absorbable polymer anchor that are connected by an absorbable positioning suture. The device seals and sandwiches the arteriotomy between its two primary members, the anchor and the collagen plug. Hemostasis is achieved primarily by the mechanical means of the anchor-arteriotomy-collagen sandwich, which is supplemented by the coagulation-inducing properties of the collagen. The device is contained in a delivery system that stores and then delivers the absorbable components to the arterial puncture.

IV. Contraindications

The Angio-Seal* device is contraindicated in patients with arteriotomies in which sheaths or devices larger than 8F have been used.

V. Warnings

Do not use if temperature indicator dot on package has changed from light grey to dark grey or black.

Use of this device where bacterial contamination of the procedure sheath or surrounding tissues may have occurred may cause infection.

Do not use the Angio-Seal* device if there is suspicion that the introducer has been placed through the superficial femoral artery and into the profunda femoris. Collagen deposition into the superficial femoral artery could result.

If the puncture site is at the bifurcation of the superficial femoral and profunda femoris arteries, the Angio-Seal* device should not be used due to the risk of the anchor catching on the bifurcation and collagen being deposited into the vessel.

VI. Precautions

Special Patient Populations

The safety and effectiveness of the Angio-Seal* device has not been established in the following patient populations:

- Patients who have known allergies to beef products, collagen and/or collagen products, or polyglycolic or polylactic acid polymers.
- Patients with pre-existing autoimmune disease.
- Patients undergoing therapeutic thrombolysis.
- Patients punctured through a vascular graft.
- Patients with clinically significant peripheral vascular disease.
- Patients with uncontrolled hypertension (>180 mm Hg systolic).
- Patients with a bleeding disorder, including thrombocytopenia (<100,000 platelet count), thrombasthenia, von WilleBrand's disease, or anemia (Hgb<10 mg/dl, Hct<30).
- Pediatric patients or others with small femoral artery size (< 4 mm in diameter). Small femoral artery size may prevent the Angio-Seal* anchor from deploying properly in these patients.
- Patients who are pregnant or lactating.

The safety of early ambulation (<6 hours) after Angio-Seal* device use has not been studied in a controlled clinical trial

The Angio-Seal* device should only be used by physicians possessing adequate instruction in the use of the device, e.g., participation in an Angio-Seal* physician instruction program or equivalent

Use a single wall puncture technique. Do not puncture the posterior wall of the artery.

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- If a patient has had a procedure sheath left in place for longer than 8 hours, consideration should be given to the use of prophylactic antibiotics before insertion of the Angio-Seal* device.

The Angio-Seal* device should be used within one hour of opening the foil pouch. The biodegradable components will begin to deteriorate upon exposure to ambient conditions.

Observe sterile technique at all times when using the Angio-Seal* device.

The Angio-Seal* device contains materials that are degraded by heat and moisture; therefore, the device must not be resterilized.

The Angio-Seal* device is for single use only and should not be reused in any manner.

When a venous sheath has been placed in the same leg as the arterial sheath, the venous sheath should be removed and hemostasis obtained prior to use of the Angio-Seal* device.

The Angio-Seal* device must be inserted only through the insertion sheath provided in the kit. Do not substitute any other sheath.

If the Angio-Seal* device does not anchor in the artery due to improper orientation of the anchor or patient vascular anatomy, the entire absorbable plug and delivery system should be withdrawn from the patient. Hemostasis can then be achieved by applying manual pressure.

Leave the tension spring in place for at least 20 minutes, but not more than 45 minutes, following placement of the Angio-Seal* device. Anchor deformation could occur if the tension spring is allowed to remain in place for longer than 45 minutes.

Repuncture at the same location of previous Angio-Seal* device use has not been studied in humans and is not recommended for 90 days.

VII. Alternative Practices and Procedures

The alternative practice to achieve hemostasis post-catheterization is manual compression, including supplemental use of mechanical compression devices or pressure dressings. In addition, there is a legally marketed vascular hemostasis device consisting of two collagen plugs which are placed in the extra-arterial puncture tract that is available for hemostasis post-catheterization.

VIII. Marketing History

The 8F Angio-Seal* device has been marketed in Europe and Canada by Sherwood-Davis & Geck (St. Louis, MO) since December, 1994. The device has not been subject to regulatory action in any of these countries due to adverse patient safety or effectiveness issues. However, Sherwood-Davis & Geck voluntarily recalled two lots of product from the European market in December, 1995. Although these two lots passed all quality control testing, two subsequent lots were found to have a below-specification characteristic in pre-release testing. The two lots were recalled from the market as a precaution. The manufacturing process was modified to correct the problem. No below-specification lots have been detected since the modified manufacturing process was implemented.

IX. Adverse Effects of the Device on Health

The Angio-Seal* device was evaluated in three independent, randomized, controlled clinical trials involving 1,241 patients (N=481, N=435, and N=325). The studies compared the Angio-Seal* device (A-S) to manual pressure (MP); the third study also compared two versions of the device, each containing a different type of collagen. Of the 699 patients treated with the Angio-Seal* device, 442 (63%) were post diagnostic angiography, 158 (23%) were post PTCA, and 99 (14%) had undergone another procedure

Of all patients enrolled in the three trials, eight patients (5 A-S and 3 MP) died within one month of the procedure. No deaths, however, were considered to be related to use of the device.

Table 1 reports the adverse events as a percentage of patients exposed to the Angio-Seal* device in the three clinical investigations. Patients receiving the different collagen types in the third trial are combined into a single A-S group. Patients who underwent a procedure other than diagnostic angiography or PTCA are not included in the following table.

Table 1: Percentage of Patients Experiencing Adverse Events
(All diagnostic angiography and PTCA patients
enrolled in Angio-Seal* clinical studies; N=1029)[^]

Procedure:	Diagnostic Angiography				PTCA			
	A-S (N=441)		MP (N=304)		A-S (N=157)		MP (N=127)	
	N	%	N	%	N	%	N	%
Device malfunction	25	5.7%	N/A		11	7.0%	N/A	
Device failure (anchor/suture failure)	0	0%	N/A		1	0.6%	N/A	
Vascular repair†	2	0.5%	1	0.3%	1	0.6%	1	0.8%
Transfusion	0	0%	0	0%	0	0%	0	0%
Infection Extending Hospitalization	0	0%	0	0%	1	0.6%	0	0%
Deep Vein Thrombosis	0	0%	0	0%	0	0%	0	0%
Hematoma >6 cm	7	1.6%	3	1.0%	2	1.3%	2	1.6%
Hematoma <6 cm	12	2.7%	8	2.6%	5	3.2%	7	5.5%
Late bleeding	16	3.6%	6	2.0%	7	4.5%	1	0.8%
Pseudoaneurysm	8	1.8%	2	0.7%	1	0.6%	2	1.6%
Late pain	4	0.9%	0	0%	1	0.6%	0	0%
Vagal response	1	0.2%	1	0.3%	3	1.9%	2	1.6%
AV fistula	0	0%	2	0.7%	1	0.6%	0	0%
Retro-peritoneal bleeding	1	0.2%	0	0%	0	0%	0	0%
Thrombus formation	1	0.2%	0	0%	0	0%	0	0%
Irritation/swelling	1	0.2%	0	0%	0	0%	0	0%
Low grade fever	1	0.2%	0	0%	0	0%	0	0%
Cerebral embolus	0	0%	1	0.3%	0	0%	0	0%
Any complication‡	50	11.3%	20	6.6%	22	14.0%	14	11.0%
No major complication	439	99.5%	303	99.7%	156	99.4%	126	99.2%

[^] Excludes patients who were disqualified from the study following randomization but prior to sheath removal. Some patients may have experienced more than one complication.

† In all but one case, the "vascular repair" consisted of ultrasound guided compression of a pseudoaneurysm.

‡ Not including device malfunction or failure.

Based on experience in the clinical trials, the following describes possible treatments for several risks or situations which are associated with use of the Angio-Seal* device or vascular access procedures.

- *Bleeding or hematoma* - Apply digital or manual pressure to puncture site. If necessary, pressure devices, such as a clamp or pressure bandage, may be used to provide supplemental compression.
- *AV fistula or pseudoaneurysm* - If suspected, the condition may be evaluated with duplex ultrasound. When indicated, ultrasound guided compression of a pseudoaneurysm may be used after the Angio-Seal* device has been placed.
- *Device non-deployment* - Follow instructions for use if anchor does not catch at tip of sheath during deployment procedure. If device pulls out with sheath upon withdrawal, apply manual or mechanical pressure per standard procedure. Examine device to ensure all absorbable components have been withdrawn.
- *Anchor fracture or embolism* - Examine device to determine if anchor has been withdrawn. If bleeding occurs, apply manual or mechanical pressure to the puncture site per standard procedures. If anchor is not attached to the device, monitor patient (for at least 24 hours) for signs of vascular occlusion. Clinical

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- experience to date indicates that tissue ischemia from an embolized anchor is unlikely. Should ischemic symptoms appear, treatment options include thrombolysis, percutaneous extraction of the anchor or fragments, or surgical intervention.
- *Infection* - Any sign of infection at the puncture site should be taken seriously and the patient monitored carefully. Surgical removal of the device should be given careful consideration whenever an access site infection is suspected.
 - *Collagen deposition into the artery or thrombosis at puncture site* - If this condition is suspected, the diagnosis can be confirmed by duplex ultrasound. Treatment of this event may include thrombolysis, percutaneous thrombectomy, or surgical intervention.
 - *Very thin patients* - Collagen may protrude from the skin after tamping has been completed. Attempt to push the collagen under the skin using the tamper or a sterile hemostat. DO NOT cut off the excess collagen, as the suture woven through the collagen may be cut and the integrity of the anchor/collagen sandwich could be compromised.
 - *Obese patients* - The tamper tube may not be long enough to be exposed or grasped at the skin. Place fingers on either side of the suture, compress the surrounding tissue, and attempt to expose the tamper tube. If necessary, a sterile hemostat may be used to grasp the tamper tube so the collagen can be tamped adequately.

The following potential adverse reactions or conditions may also be associated with one or more Angio-Seal* device components (i.e., collagen, synthetic absorbable suture, and/or synthetic absorbable polymer):

- allergic reaction
- foreign body reaction
- potentiation of infection
- inflammation
- edema

X. Summary of Non-Clinical Studies

A. In Vitro (Laboratory) Studies

1. Biocompatibility Studies

The biocompatibility of the Helistat® collagen (a legally marketed collagen hemostat), anchor polymer, suture (a legally marketed polyglycolic acid suture), and delivery system components contacting the body was evaluated in accordance with the *Tripartite Biocompatibility Guidance for Medical Devices*. Information supporting the biocompatibility of the alternate collagen material (P1076) was presented in a Device Master File (MAF-723) and is incorporated by reference into this PMA for the Angio-Seal* device. Depending on the degree and duration of body contact for each device

component, all (or a subset of) the following tests were conducted: cytotoxicity, sensitization, acute systemic toxicity, mutagenicity, hemolysis, pyrogenicity, implantation, and subchronic toxicity. All device materials were demonstrated to be nonhemolytic, nonpyrogenic, nontoxic, nonmutagenic, and biocompatible for their intended use

2. Anchor Qualification Studies

The anchor component was qualified through a series of tests, including: a maximum pull strength test at high strain rate; a constant load to failure test at a clinical strain rate; a notched anchor test simulating a low-load failure and an *in vivo* strength test. *In vitro* degradation testing of the anchor was also conducted. The anchor qualification testing demonstrated that the anchor meets its specifications and has sufficient strength throughout device deployment and subsequent absorption.

3. Studies of the Absorbable Unit

In vitro testing was also performed on the absorbable unit of Angio-Seal*. This testing included verification of the design of the collagen-suture knot attachment, the weave pattern of the positioning suture through the collagen plug, and the post-placement security of the anchor-artery-collagen sandwich. Testing demonstrated that the collagen-suture attachment is secure, the weave pattern ensures consistent collagen deployment, and the absorbable unit is sufficiently secure post-placement.

4. Delivery System Studies

The Angio-Seal* device tensioner and suture storage mechanisms were validated using *in vitro* testing, which was verified by use of the device in animals. The tensioner testing evaluated a number of variables likely to affect tensioner performance, including radiation effects from sterilization and the presence of blood in the tensioner. The testing demonstrated that, under a number of different conditions, the tensioner mechanism consistently meets its specification to provide enough force to deploy the absorbable plug without applying enough force to cause the anchor or suture to fail.

5. Shelf Life Studies

Product stability testing performed for the Angio-Seal* device demonstrated that functionality and sterility of the device was maintained for a minimum of 6 months. Based on these results, a shelf life of 6 months for the Angio-Seal* device has been established.

B. In Vivo (Animal) Studies

A series of animal studies were conducted during the development of the Angio-Seal* device. Several animal models were studied including swine distal aorta and proximal iliac arteries, canine distal aorta and femoral arteries, and the goat carotid artery. Acute studies evaluated the deployability of the anchor and its effectiveness in anchoring against the intraarterial wall, the effectiveness of the device in causing hemostasis, and the thrombogenicity of the anchor. For chronic studies, animals were sacrificed at various intervals from one to 90 days post device placement and encapsulation of the anchor and resorption of the device were assessed by gross pathology and histopathology.

The animal studies showed that the Angio-Seal* device is easy to use, deploys reliably and consistently, and causes rapid hemostasis of the puncture site. The polymer anchor is encapsulated and absorbed without causing either thrombus formation or stenosis in the arterial lumen. The entire device is absorbed with minimal tissue inflammation within 60-90 days. The studies supported the initiation of the clinical trials with the Angio-Seal*.

XI. Summary of Clinical Studies

Three randomized, controlled, clinical studies [U.S. Phase II Study (N=481); European Phase II Study (N=435); and a collagen comparison study (N=325)] were conducted to examine the safety and effectiveness of the Angio-Seal* device in achieving hemostasis compared to standard manual pressure in both diagnostic angiography and PTCA patients. Safety and effectiveness were assessed with regard to time to hemostasis and frequency of complications.

Inclusion and exclusion criteria were chosen to avoid gender bias for both studies. The higher percentage of male patients enrolled in the studies reflects the gender referral pattern for cardiac disease.¹ All differences between the treatment groups with respect to hemostasis time and complication rates were consistent between the genders

A. U.S. Phase II Study

Conclusions: The use of the Angio-Seal* device (A-S) resulted in a statistically significant decrease in time to hemostasis (TTH) versus manual pressure (MP) in 481 patients undergoing procedures requiring 8F or smaller femoral artery punctures at 8 investigational sites (3.2 ± 10.5 vs. 16.0 ± 12.2 minutes; $p < 0.0001$). This was true despite a significantly higher activated clotting time (ACT) in the A-S group. The overall complication rates of A-S and MP were similar (33/218 [15%] vs. 22/217 [10%]; p-value not significant; relative risk [95% CI]=1.5 [0.9, 2.5]). When the data were analyzed by procedure subgroup (diagnostic

¹ Mark DB, Shaw LK, DeLong ER, Califf RM, Pryor DB. Absence of sex bias in the referral of patients for cardiac catheterization. N Engl J Med 1994; 330:1101-6.

angiography [DA] and PTCA), the results were consistent with the overall analysis. Safety and effectiveness results for TTH and complications are included in Table 2

Purpose: To study prospectively the TTH and incidence of complications for patients receiving either A-S or MP hemostasis following an invasive procedure requiring an 8F or smaller femoral artery puncture.

Design: A multi-center, randomized, controlled study of 481 patients receiving either A-S or MP. The study was conducted at eight U.S. investigational sites.

Methods: Patients were randomized when the decision to remove the sheath was made post-procedure. At sheath removal, either A-S was deployed or MP was applied. In the A-S group, the exact (observed) times to hemostasis upon device deployment and upon tamper/spring removal were summed for total TTH. In the MP group, the protocol specified for safety reasons that pressure be applied for 15 minutes initially, at which time the puncture site was first checked for hemostasis. Subsequent MP periods of 10 minutes were applied until hemostasis was observed. The mean of the last checkpoint at which bleeding was observed and the first checkpoint at which hemostasis was observed was used as an unbiased "total TTH" for the manual pressure group

Population Characteristics: Patients were initially enrolled from November 6, 1992 to March 11, 1994. Of the 481 patients enrolled, 2 patients were disqualified prior to randomization, 437 were randomized, and 42 patients were not randomized. Assignment of the 479 patients was as follows: 253 to A-S and 226 to MP; 334 were DA patients, 121 PTCA patients, and 24 "other" procedure patients, "other" defined as a procedure that was not diagnostic angiography or PTCA. Baseline and procedure characteristics were similar between treatment groups. Of the 437 randomized patients, 418 were analyzed for effectiveness; the device did not deploy in 7, no data were available for 10, and 2 patients were excluded prior to sheath removal

Results

Table 2: Principal Effectiveness and Safety Results †
(Time to Hemostasis (TTH) and Frequency of Complications)

Effectiveness (Mean ± SD)	Overall			DA			PTCA		
	A-S N=203	MP N=215	95% CI	A-S N=157	MP N=149	95% CI	A-S N=38	MP N=53	95% CI
TTH (minutes)	3.2±11	16.0±12	(11-15)**	2.5±9	14.2±12	(9-14)**	6.8±15	20.3±13	(8-19)**
Safety Number (%)†	A-S N=218	MP N=217	95% RR	A-S N=167	MP N=149	95% RR	A-S N=42	MP N=55	95% RR
Vascular Repair	1 (1%)	1 (1%)	(0.1-15.8)	1 (1%)	1 (1%)	(0.06-14.5)	0 (0%)	0 (0%)	—
Transfusion	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—
Infection + hospital stay	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—
Device malfunction	9 (4%)	—	—	5 (3%)	—	—	3 (8%)	—	—
Device failure	1 (1%)	—	—	0 (0%)	—	—	1 (0.03%)	—	—
Hema. ≥6 cm	2 (1%)	5 (2%)	(0.1-2.0)	2 (1%)	3 (2%)	(0.1-3.6)	0 (0%)	2 (4%)	—
Hema. <6 cm	5 (2%)	10 (5%)	(0.2-1.4)	5 (3%)	4 (3%)	(0.3-4.1)	0 (0%)	6 (11%)	*—
Late bleeding	8 (4%)	3 (1%)	(0.7-9.9)	5 (3%)	3 (2%)	(0.4-6.1)	3 (7%)	0 (0%)	—
Any comp.	33 (15%)	22 (10%)	(0.9-2.5)	23 (14%)	12 (8%)	(0.9-3.3)	8 (19%)	10 (18%)	(0.5-2.4)
No major comp.	217 (99.5%)	216 (99.5%)	(1-1)	166 (99.4%)	148 (99.3%)	—	42 (100%)	55 (100%)	—

‡ Details of "other" group omitted from table due to missing data, disqualified patients, or procedure other than DA or PTCA.

** TTH difference (A-S/control) statistically significant (p<0.0001) based on Wilcoxon test.

† RR=Relative risk (A-S/control) based on Mantel-Haenszel test.

* P-value < 0.05.

B. European Phase II Study

Conclusions: The use of the Angio-Seal* device (A-S) resulted in a statistically significant decrease in time to hemostasis (TTH) versus manual pressure (MP) in 435 patients undergoing procedures requiring 8F or smaller femoral artery punctures at 5 investigational sites (2.8±6 vs. 13.0±13 minutes; p < 0.0001). The overall A-S complication rate was similar to the rate observed in the U.S. Phase II Study (12% vs. 15%, respectively). However, rates were significantly different between A-S and MP within the European study, possibly due to under-reporting in the MP group (29/234 [12%] vs. 8/201 [4%]; p = 0.002; relative risk [95% CI]=3.1 [1.5-6.7]). When the data were analyzed by procedure subgroup, the results were similar to the overall analysis. Safety and effectiveness results for TTH and complications are included in Table 3.

Purpose: To study prospectively the TTH and incidence of complications for patients receiving either A-S or MP hemostasis following an invasive procedure requiring an 8F or smaller femoral artery puncture.

Design: A multi-center, randomized, controlled study of 435 patients receiving either A-S or MP. The study was conducted at five European investigational sites.

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Methods: Patients were randomized when the decision to remove the sheath was made post-procedure. At sheath removal, either A-S was deployed or MP was applied. In the A-S group, the exact (observed) times to hemostasis upon device deployment and upon tamper/spring removal were summed for total TTH. In the MP group, the protocol specified for safety reasons that pressure be applied for 15 minutes initially, at which time the puncture site was checked for hemostasis. Subsequent MP periods of 10 minutes were applied until hemostasis was observed. The mean of the last checkpoint at which bleeding was observed and the first checkpoint at which hemostasis was observed was used as an unbiased "total TTH" for the manual pressure group.

Population Characteristics: Patients were initially enrolled from January, 1993 to July, 1994. Assignment was as follows: 234 to A-S and 201 to MP; 170 were diagnostic angiography (DA) patients, 109 PTCA patients, 56 stent patients, 96 PTA patients, and 4 "other" procedure patients. Baseline and procedure characteristics were similar between treatment groups. Of the 435 randomized patients, 388 were analyzed for effectiveness; the device was not successfully placed in 8 patients, no data were available for 35, and 4 patients were excluded prior to sheath removal.

Results:

Table 3: Principal Effectiveness and Safety Results [‡]
(Time to Hemostasis (TTH) and Frequency of Complications)

	Overall			DA			PTCA		
	A-S N=188	MP N=200	95% CI	A-S N=78	MP N=81	95% CI	A-S N=49	MP N=47	95% CI
Effectiveness									
Mean ± SD									
TTH (minutes)	2.8±6	13.0±13	(8-12)**	1.3±3	14.7±14	(10-17)**	3.5±6	12.9±15	(5-14)**
Safety									
Number (%)†	N=234	N=201	95% RR	N=89	N=81	95% RR	N=61	N=48	95% RR
Vascular repair	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—
Transfusion	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—
Infection+hosp.	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—
Device malfunc.	8 (3%)	—	—	0 (0%)	—	—	2 (3%)	—	—
Device failure	1 (0.4%)	—	—	0 (0%)	—	—	0 (0%)	—	—
Hema. ≥6 cm	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	—
Hema. <6 cm	7 (3%)	4 (2%)	(0.5-5.1)	3 (4%)	3 (4%)	(0.2-4.4)	1 (2%)	0 (0%)	—
Late bleeding	6 (3%)	3 (2%)	(0.4-6.8)	3 (4%)	2 (3%)	(0.2-8.0)	2 (3%)	1 (2%)	(0.2-17)
Any comp.	29 (12%)	8 (4%)	(1.5-6.7)*	9 (10%)	6 (7%)	(0.5-3.7)	5 (8%)	1 (2%)	(0.5-33)
No major comp.	234 (100%)	201 (100%)	—	89 (100%)	81 (100%)	—	61 (100%)	48 (100%)	—

‡ Details of PTA, stent, and "other" procedure categories excluded from this table.
 ** TTH difference (A-S/control) statistically significant (p<0.0001) based on Wilcoxon test.
 † RR=Relative risk (A-S/control) based on Mantel-Haenszel test
 * P-value < 0.05.

C. Collagen Comparison Study

Conclusions: Angio-Seal* (A-S) devices containing P1076 collagen (PA-S) were found to be equivalent in safety and effectiveness to A-S devices containing Helistat® collagen (HA-S). Time to hemostasis (TTH) was similar between the

HA-S and PA-S devices (6.7 ± 16 vs. 1.9 ± 5 minutes, respectively; p-value not significant). TTH was also significantly lower in both device groups versus manual pressure (MP) (20.0 ± 9 minutes; $p < 0.0001$ vs. each device group) in a total of 325 patients undergoing diagnostic angiography (DA) or PTCA procedures requiring 8F or smaller femoral artery punctures. The overall complication rates between the two device groups were similar (HA-S 10/91 [11%] vs. PA-S 12/95 [13%], excluding device malfunction; p-value not significant; relative risk [95% CI]=1.1 [0.5-2.5]) and were consistent with rates observed in the U.S. Phase II study. The complication rates were also similar between the PA-S and MP groups (PA-S 13% vs. MP 4/92 [4%]; p-value not significant). When the data were analyzed by procedure subgroup (DA and PTCA), the results were consistent with the overall analysis. Safety and effectiveness results for TTH and complications are included in Tables 4A and 4B.

Purpose: To study prospectively the TTH and incidence of complications for patients receiving devices containing either Helistat® collagen or P1076 collagen following a DA or PTCA procedure requiring an 8F or smaller femoral artery puncture. A MP control group was also enrolled. This study was conducted to qualify P1076 collagen as an alternate collagen material for the Angio-Seal* device

Design: A multi-center, randomized, controlled study of 325 patients receiving either HA-S, PA-S, or MP. The study was conducted at five U.S. investigational sites.

Methods: Patients were randomized when the decision to remove the sheath was made post-procedure. At sheath removal, either an A-S was deployed or MP was applied. In both A-S groups, the exact (observed) times to hemostasis upon device deployment and upon tamper/spring removal were summed for total TTH. In the MP group, the protocol specified that pressure be applied according to the institution's standard procedure. Total TTH was defined as the elapsed time between sheath removal and the point hemostasis was first observed.

Population Characteristics: Three hundred twenty-five patients were initially enrolled from July 6, 1994 to September 20, 1995. Of the 325, 20 were disqualified prior to randomization, and 25 additional high risk and training patients were not randomized. Thus, 280 patients were randomized (93 HA-S, 95 PA-S, and 92 MP). Two hundred sixty-one of these 280 patients were analyzed for effectiveness; the device was not placed in 17 (due to device nondeployment or other device malfunction) and 2 were disqualified after randomization due to loss of intra-arterial procedure sheath position. Baseline and procedure characteristics were similar between treatment groups

Results:

Table 4A: Principal Effectiveness and Safety Results [§]
(Time to Hemostasis (TTH) and Complications)

Effectiveness <i>Mean ± SD</i>	Overall			Overall		
	HA-S N=85	PA-S N=84	MP N=92	PA-S/HA-S 95% CI	HA-S/MP 95% CI	PA-S/MP 95% CI
TTH (minutes)	6.7±16	1.9±5	20.0±9	(1.3-8.3)	(9.5-17.1)**	(16.0-20.2)**
Safety <i>Number (%)†</i>	HA-S N=91	PA-S N=95	MP N=92	PA-S/HA-S 95% RR	HA-S/MP 95% RR	PA-S/MP 95% RR
Vascular Repair	0 (0%)	1 (1%)	1 (1%)	—	—	(0.1-15.3)
Transfusion	0 (0%)	0 (0%)	0 (0%)	—	—	—
Infection plus hospital	0 (0%)	0 (0%)	0 (0%)	—	—	—
Device malfunction	9 (10%)	13 (14%)	N/A	(0.6-3.1)	—	—
Hema. ≥6 cm	2 (2%)	4 (4%)	0 (0%)	(0.4-10.2)	—	—
Hema. <6 cm	1 (1%)	2 (2%)	2 (2%)	(0.2-20.8)	(0.1-5.5)	(0.1-6.7)
Late bleeding	5 (5%)	2 (2%)	1 (1%)	(0.1-1.9)	(0.6-42.4)	(0.2-21)
Any comp. §§	10 (11%)	12 (13%)	4 (4%)	(0.5-2.5)	(0.8-7.8)	(1.0-8.7)
No major comp.	91 (100%)	94 (99%)	91 (99%)	—	—	(0.1-15.3)

Table 4B: Principal Effectiveness and Safety Results ^{§†}
(Time to Hemostasis (TTH) and Complications)

Effectiveness <i>Mean ± SD</i>	DA				PTCA			
	HA-S N=70	PA-S N=72	MP N=72	PA-S/HA-S 95% CI	HA-S N=15	PA-S N=10	MP N=18	PA-S/HA-S 95% CI
TTH (minutes)	5.0±14	1.3±4	18.9±7	(0.4-6.9)	14.6±23	4.3±8	24.4±11	(-2.4-23)
Safety <i>Number (%)†</i>	HA-S N=74	PA-S N=80	MP N=72	PA-S/HA-S 95% RR	HA-S N=17	PA-S N=12	MP N=18	PA-S/HA-S 95% RR
Vascular Repair	0 (0%)	1 (1%)	0 (0%)	—	0 (0%)	0 (0%)	1 (6%)	—
Transfusion	0 (0%)	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	0 (0%)	—
Infection + hospital stay	0 (0%)	0 (0%)	0 (0%)	—	0 (0%)	0 (0%)	0 (0%)	—
Device malfunction	7 (9%)	10 (13%)	N/A	(0.5-3.3)	2 (12%)	2 (17%)	N/A	(0.2-8.7)
Hema. ≥6 cm	2 (3%)	3 (4%)	0 (0%)	(0.2-8.1)	0 (0%)	1 (8%)	0 (0%)	—
Hema. <6 cm	1 (1%)	2 (3%)	1 (1%)	(0.2-20)	0 (0%)	0 (0%)	1 (6%)	—
Late bleeding	5 (7%)	2 (3%)	1 (1%)	(0.1-1.8)	0 (0%)	0 (0%)	0 (0%)	—
Any comp. §§	9 (12%)	11 (14%)	2 (3%)	(0.5-2.6)	1 (6%)	1 (8%)	2 (11%)	(0.1-21)
No major comp.	74 (100%)	79 (99%)	72 (100%)	—	17 (100%)	12 (100%)	17 (94%)	—

§ Randomized patients only.

** P-value < 0.0001

† RR=Relative risk (treatment/control) based on Mantel-Haenszel test.

§§ Excluding device malfunction and including any "other" complication.

‡ Details of "other" procedure group omitted from this table due to small sample size.

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XII. Conclusions Drawn from Studies

The results of the *in vivo* and *in vitro* non-clinical laboratory studies together with the clinical studies provide valid scientific evidence and reasonable assurance that the Angio-Seal* device is safe and effective when used in accordance with its labeling.

The safety of the device has been demonstrated through the low incidence of peripheral vascular complications in patients treated with the Angio-Seal* device compared to patients receiving standard manual pressure. The effectiveness of the device has been demonstrated through the reduction of time to hemostasis in angiography and PTCA patients compared to standard manual pressure.

XIII. Panel Recommendations

The Circulatory System Devices Panel met on May 8, 1995, and unanimously recommended approval of the Angio-Seal* Hemostatic Puncture Closure Device with the following conditions:

1. Certain changes to the Indications, Contraindications, Warnings, and Precautions sections of the labeling be made.
2. A postapproval study be conducted to examine the incidence of infection and vascular compromise associated with Angio-Seal* device use. Follow-up ultrasound information should be analyzed by a blinded core laboratory for objective interpretation of the data.

XIV. FDA Decision

The FDA concurred with the recommendations of the Circulatory System Devices Panel and issued an approvable letter on July 7, 1995. Subsequent to issuance of the approvable letter, the applicant submitted amendments proposing: device design and manufacturing changes (July 13, 1995); a change in the manufacturing facility (September 19, 1995); a change in the sterilization facility (September 22, 1995); and a second source of supply for the collagen component (November 1, 1995). Following the review of these amendments and the submission of additional information, a second approvable letter was issued on June 28, 1996. After issuance of the second approvable letter, an amendment was received which proposed: manufacturing changes in response to a voluntary recall of the device which was being distributed in Europe, other minor device design and manufacturing changes, and information responding to the second approvable letter. FDA found the information in this amendment to be adequate. In addition, an inspection was conducted and on July 25, 1996, FDA found the manufacturing facility to be in compliance with the Good Manufacturing Practices regulation (21 CFR Part 820)

XV. Approval Specifications

Instructions for Use: See the labeling

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events sections of the labeling.

Postapproval Requirements and Restrictions: See approval order.



SAFETY INFORMATION

STERILE R

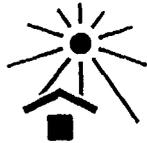
The Angio-Seal® Device Kit has been sterilized by gamma radiation.



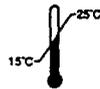
The Angio-Seal® Device Kit is for single use only.



The Angio-Seal® Device Kit should be kept dry.



The Angio-Seal® Device Kit should be kept away from heat sources.



The Angio-Seal® Device Kit should be stored only at temperatures between 15° C and 25° C.

Front Inside Panel

Manufactured by Quinton Instrument Company (Bothell, WA) for Sherwood Medical Company

ANGIO-SEAL and the Ribbon Design are trademarks of Sherwood Medical Company (St. Louis, MO). Covered by one or more of the following patents: US 4744364, 4852568, 4890612, Re 34866, 5021059, 5222974, 5282827, 5306254, 5312435, 5392918, 5411520, 5441517; AU 651595, CA 1322922, JP 1854475, EP 0422046, EP 0474752, EP 0527923. Other US and foreign patents pending.

Label Code No. 172-0396

P/N 033461-002A

ANGIO-SEAL®

Hemostatic Puncture Closure Device

INSTRUCTIONS FOR USE

TO ENSURE PROPER DEPLOYMENT AND USE OF THIS DEVICE AND TO PREVENT INJURY TO PATIENTS, READ ALL INFORMATION CONTAINED IN THESE INSTRUCTIONS FOR USE.

Back Panel

Front Panel

Sherwood Medical Company
1915 Olive Street
St. Louis, MO 63103

Sherwood
MEDICAL
ST. LOUIS, MO 63103

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

DEVICE DESCRIPTION

The Angio-Seal® Hemostatic Puncture Closure Device consists of the Angio-Seal® device, an 8F insertion sheath, an arteriotomy locator (modified dilator), a 0.038" guidewire, and a post-placement tension spring. The Angio-Seal® device is composed of a collagen sponge and a specially designed absorbable polymer anchor that are connected by an absorbable positioning suture. The device seals and sandwiches the arteriotomy between its two primary members, the anchor and the collagen sponge. Hemostasis is achieved primarily by the mechanical means of the anchor-arteriotomy-collagen sandwich, which is supplemented by the coagulation-inducing properties of the collagen. The device is contained in a delivery system that stores and then delivers the absorbable components to the arterial puncture.

INDICATIONS

The Angio-Seal® device is indicated for use in closing and in reducing time to hemostasis at the femoral arterial puncture site in patients who have undergone diagnostic angiography or percutaneous transluminal coronary angioplasty (PTCA) procedures using an 8F or smaller procedural sheath.

CONTRAINDICATIONS

The Angio-Seal® device is contraindicated in patients with arteriotomies in which sheaths or devices larger than 8F have been used.

WARNINGS

Do not use if temperature indicator dot on package has changed from light grey to dark grey or black.

Use of this device where bacterial contamination of the procedure sheath or surrounding tissues may have occurred may cause infection.

Do not use the Angio-Seal® device if there is suspicion that the introducer has been placed through the superficial femoral artery and into the profunda femoris. Collagen deposition into the superficial femoral artery could result.

If the puncture site is at the bifurcation of the superficial femoral and profunda femoris arteries, the Angio-Seal® device should not be used due to the risk of the anchor catching on the bifurcation and collagen being deposited into the vessel.

PRECAUTIONS

Special Patient Populations

The safety and effectiveness of the Angio-Seal® device has not been established in the following patient populations.

- Patients who have known allergies to beef products, collagen and/or collagen products, or polyglycolic or polylactic acid polymers
- Patients with pre-existing autoimmune disease.
- Patients undergoing therapeutic thrombolysis.
- Patients punctured through a vascular graft.
- Patients with clinically significant peripheral vascular disease.
- Patients with uncontrolled hypertension (>180 mm Hg systolic).
- Patients with a bleeding disorder, including thrombocytopenia (<100,000 platelet count), thrombasthenia, von Willebrand's disease, or anemia (Hgb<10 mg/dl, Hct<30).
- Pediatric patients or others with small femoral artery size (< 4 mm in diameter). Small femoral artery size may prevent the Angio-Seal® anchor from deploying properly in these patients.
- Patients who are pregnant or lactating.

The safety of early ambulation (<6 hours) after Angio-Seal® device use has not been studied in a controlled clinical trial.

The Angio-Seal® device should only be used by physicians possessing adequate instruction in the use of the device, e.g., participation in an Angio-Seal® physician instruction program or equivalent.

Use a single wall puncture technique. Do not puncture the posterior wall of the artery.

If a patient has had a procedure sheath left in place for longer than 8 hours, consideration should be given to the use of prophylactic antibiotics before insertion of the Angio-Seal® device.

The Angio-Seal® device should be used within one hour of opening the foil pouch. The biodegradable components will begin to deteriorate upon exposure to ambient conditions.

Observe sterile technique at all times when using the Angio-Seal® device.

The Angio-Seal® device contains materials that are degraded by heat and moisture; therefore, the device must not be resterilized.

The Angio-Seal® device is for single use only and should not be reused in any manner.

When a venous sheath has been placed in the same leg as the arterial sheath, the venous sheath should be removed and hemostasis obtained prior to use of the Angio-Seal® device.

The Angio-Seal® device must be inserted through the insertion sheath provided in the kit. Do not substitute any other sheath.

If the Angio-Seal® device does not anchor in the artery due to improper orientation of the anchor or patient vascular anatomy, the entire absorbable plug and delivery system should be withdrawn from the patient. Hemostasis can then be achieved by applying manual pressure.

Leave the tension spring in place for at least 20 minutes, but not more than 45 minutes, following placement of the Angio-Seal® device. Anchor deformation could occur if the tension spring is allowed to remain in place for longer than 45 minutes.

Repuncture at the same location of previous Angio-Seal® device use has not been studied in humans and is not recommended for 90 days.

ADVERSE EVENTS

The Angio-Seal® device was evaluated in three independent, randomized, controlled clinical trials involving 1,241 patients (N=481, N=439, and N=321). The studies compared the Angio-Seal® device (A-S) to manual pressure. In the third study also compared two versions of the device each containing a different type of collagen. Of the 699 patients treated with the Angio-Seal® device, 442 (63%) were post diagnostic angiography, 158 (23%) were post PTCA, and 99 (14%) had undergone another procedure.

Of all patients enrolled in the three trials, eight patients (5 A-S and 3 MP) died within one month of the procedure. No deaths, however, were considered to be related to use of the device.

Table 1 reports the adverse events as a percentage of patients exposed to the Angio-Seal® device in the three clinical investigations. Patients receiving the different collagen types in the third trial are combined into a single A-S group. Patients who underwent a procedure other than diagnostic angiography or PTCA are not included.

Based on experience in the clinical trials, the following describes possible treatments for several risks or situations which are associated with use of the Angio-Seal® device or vascular access procedures:

- Bleeding or hematoma - Apply digital or manual pressure to puncture site. If necessary, pressure devices, such as a clamp or pressure bandage, may be used to provide supplemental compression.
- AV fistula or pseudoaneurysm - If suspected, the condition may be evaluated with duplex ultrasound. When indicated, ultrasound guided compression of a pseudoaneurysm may be used after the Angio-Seal® device has been placed.

Table 1: Percentage of Patients Experiencing Adverse Events
(All diagnostic angiography and PTCA patients enrolled in Angio-Seal® clinical studies; N=1029)[^]

Procedure	Diagnostic Angiography				PTCA	
	A-S (N=441)		MP (N=304)		A-S (N=157)	MP (N=127)
	N	%	N	%	N	%
Device malfunction	25	5.7%	N/A		11	7.0%
Device failure (anchor/suture failure)	0	0.0%	N/A		1	0.6%
vascular repair	2	0.5%	1	0.3%	1	0.6%
transfusion	0	0.0%	0	0.0%	0	0.0%
infection extending hospitalization	0	0.0%	0	0.0%	1	0.6%
Deep vein thrombosis	0	0.0%	0	0.0%	0	0.0%
Hematoma ≥6 cm	7	1.6%	3	1.0%	2	1.3%
Hematoma <6 cm	12	2.7%	8	2.6%	5	3.2%
Late bleeding	16	3.6%	6	2.0%	7	4.5%
Pseudoaneurysm	8	1.8%	2	0.7%	1	0.6%
Late pain	4	0.9%	0	0.0%	1	0.6%
Vagal response	1	0.2%	1	0.3%	3	1.9%
AV fistula	0	0.0%	2	0.7%	1	0.6%
Retro-peritoneal bleeding	1	0.2%	0	0.0%	0	0.0%
Thrombus formation	1	0.2%	0	0.0%	0	0.0%
Irritation/swelling	1	0.2%	0	0.0%	0	0.0%
Low grade fever	1	0.2%	0	0.0%	0	0.0%
Cerebral embolus	0	0.0%	1	0.3%	0	0.0%
Any complication [†]	50	11.3%	20	6.6%	22	14.0%
No major complication	439	99.5%	303	99.7%	156	99.4%

[^] Excludes patients who were disqualified from the study following randomization but prior to sheath removal. Some patients may have experienced more than one complication.
[†] In all but one case, the "vascular repair" consisted of ultrasound guided compression of a pseudoaneurysm.
[‡] Not including device malfunction or failure.

- Device non-deployment - Follow instructions for use if anchor does not catch at tip of sheath during deployment procedure. If device pulls out with sheath upon withdrawal, apply manual or mechanical pressure per standard procedure. Examine device to ensure all absorbable components have been withdrawn.
- Anchor fracture or embolism - Examine device to determine if anchor has been withdrawn. If bleeding occurs, apply manual or mechanical pressure to the puncture site per standard procedures. If anchor is not attached to the device, monitor patient (for at least 24 hours) for signs of vascular occlusion. Clinical experience to date indicates that tissue ischemia from an embolized anchor is unlikely. Should ischemic symptoms appear, treatment options include thrombolysis, percutaneous extraction of the anchor or fragments, or surgical intervention.
- Infection - Any sign of infection at the puncture site should be taken seriously and the patient monitored carefully. Surgical removal of the device should be given careful consideration whenever an access site infection is suspected.
- Collagen deposition into the artery or thrombosis at puncture site - If this condition is suspected, the diagnosis can be confirmed by duplex ultrasound. Treatment of this event may include thrombolysis, percutaneous thrombectomy, or surgical intervention.
- very thin patients - Collagen may protrude from the skin after tamping has been completed. Attempt to push the collagen under the skin using the tamper or a sterile hemostat. DO NOT cut off the excess collagen, as the suture woven through the collagen may be cut and the integrity of the anchor/collagen sandwich could be compromised.
- Obese patients - The tamper tube may not be long enough to be exposed or grasped at the skin. Place fingers on either side of the suture, compress the surrounding tissue, and attempt to expose the tamper tube. If necessary, a sterile hemostat may be used to grasp the tamper tube so the collagen can be tamped adequately.

The following potential adverse reactions or conditions may also be associated with one or more Angio-Seal® device components (i.e., collagen, synthetic absorbable suture, and/or synthetic absorbable polymer):

- allergic reaction
- foreign body reaction
- potentiation of infection
- inflammation
- edema

CLINICAL TRIALS

Three randomized, controlled clinical trials (N=481, N=435, and N=325) compared the Angio-Seal® device (A-S) to manual pressure (MP) regarding time to hemostasis and frequency of complications in both diagnostic angiography and PTCA patients. The trials, conducted at eleven institutions in the U.S. and five in Europe, involved a total of 1241 patients. Patients had primarily undergone diagnostic angiography or PTCA procedures; a small number of patients underwent another invasive intravascular procedure. Exclusion criteria included patients who had clinically significant peripheral vascular disease, bleeding disorders, uncontrolled hypertension (> 180 mm Hg systolic), were pregnant or lactating, underwent therapeutic thrombolysis, or experienced a hematoma prior to sheath removal. Results are presented below only for diagnostic angiography and PTCA patients.

Of the 1241 patients enrolled in the three studies, 1031 patients underwent either diagnostic angiography or PTCA and were analyzed for this summary. Patients' ages ranged between 26 and 86 years (mean age of diagnostic angiography = 59.3 and PTCA = 58.7 years). Seventy-five percent were male. For diagnostic angiography, 442 patients were assigned to A-S and 304 patients to MP. For PTCA, 158 patients were assigned to A-S and 127 patients to MP. Thirty-five percent of patients had 8F procedural sheaths, 26% had 7F sheaths, 37% had 6F sheaths, and 2% had other size sheaths. There were no clinically significant differences in baseline or procedure characteristics between the A-S and MP groups within any of the three studies, except for activated clotting time at the time of sheath removal, as discussed below.

In both diagnostic angiography and PTCA patients, use of the Angio-Seal® device resulted in a statistically significantly shorter time to hemostasis (TTH) compared to manual pressure (see Table 2). Time to hemostasis was significantly reduced in the A-S PTCA patients despite a statistically significantly longer activated clotting time (ACT) at the time of sheath removal in the A-S patients.

Mean (min.); all diagnostic angiography and PTCA patients enrolled; N=1031 ^{1,2}		
Type of Procedure	Diagnostic Angiography	PTCA
Treatment Group	Mean ± SD (Number)	Mean ± SD (Number)
Angio-Seal (A-S)	2.2 ± 8 (N=405)	6.5 ± 12 (N=131)
Manual Pressure (MP)	15.2 ± 12 (N=304)	17.6 ± 14 (N=124)
(A-S) - (MP) Difference [95% Conf. Interval]	-13.0* [-13.5, -12.5]	-11.0* [-13.0, -10.0]

¹ N's vary due to missing data for some patients. Patients who were disqualified from the studies or who underwent a procedure other than diagnostic angiography or PTCA are also excluded.
² Difference [(A-S) - (MP)] statistically significant (p<0.0001) by Wilcoxon test.

The only statistically significant difference in complication rates within any of the three studies was in the diagnostic angiography group of the third study which compared two types of collagen (A-S 13% vs. MP 3%).² There were no other statistically significant differences in complication rates between the A-S and MP groups in either procedure subgroup (diagnostic angiography or PTCA) of the other two studies or in the PTCA subgroup of the collagen study.

Follow-up in all three studies consisted of duplex ultrasound (color Doppler) scanning of the femoral artery at 24 hours and at 2 months post-sheath removal. Follow-up also included physical examination of the puncture site, evaluation of the pedal pulses, presence or absence of femoral bruit, and measurement of the ankle/brachial systolic pressure index. In all three studies, these follow-up evaluations demonstrated that the Angio-Seal® device does not have any significant effect on vascular flow. The device was not visualized on duplex ultrasound at 60-90 days. (Animal data indicate that device absorption is essentially complete by 60-90 days.)

¹ Of the remaining 210 patients, 26 were disqualified from the study prior to randomization and 184 underwent a procedure other than diagnostic angiography or PTCA. In comparison, the complication rates for diagnostic angiography patients in the U.S. Phase II study were 10% and 8% for A-S and MP, respectively (p-value = NS).

PROCEDURE

The medical techniques and procedures described in these instructions do not represent ALL medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgment in treating any specific patient.

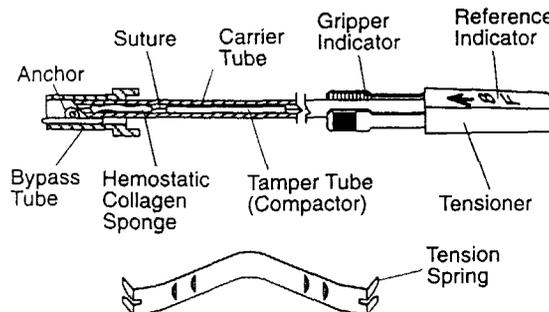
The procedure entails three parts: (1) locating the arteriotomy, (2) deploying the anchor in the artery, and (3) positioning the collagen.

SUPPLIES

The Angio-Seal® Device Kit contains the following:

- (1) 8F insertion sheath
- (1) Arteriotomy locator
- (1) Guidewire, 0.038 in., with J-straightener
- (1) Angio-Seal® device
- (1) Tension spring

COMPONENTS



LOCATING THE ARTERIOTOMY

1. Under strict sterile conditions and using a sterile field, remove the Angio-Seal® device contents from the foil package, taking care to keep the pieces apart completely before removing the Angio-Seal® device.

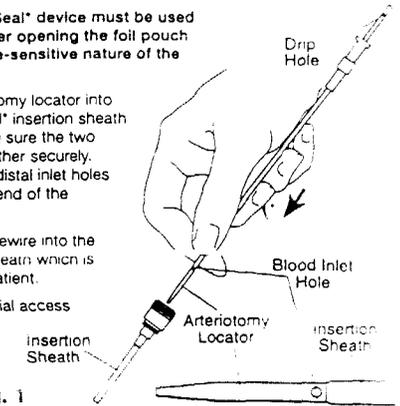
NOTE: The Angio-Seal® device must be used within one hour after opening the foil pouch due to the moisture-sensitive nature of the product.

2. Insert the arteriotomy locator into the 8F Angio-Seal® insertion sheath (Figure 1), making sure the two pieces snap together securely. Confirm that the distal inlet holes are visible at the end of the insertion sheath.

3. Insert the kit guidewire into the arterial access sheath which is currently in the patient.

4. Remove the arterial access sheath.

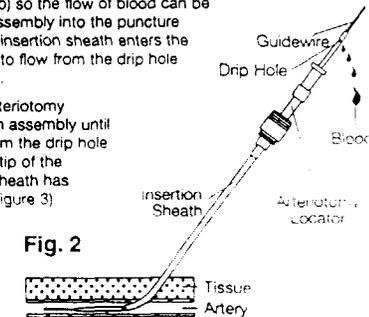
Fig. 1



5. Thread the 8F Angio-Seal® arteriotomy locator/insertion sheath assembly over the guidewire; be certain to orient the drip hole (above the locator's hub) so the flow of blood can be observed. Insert the assembly into the puncture tract. As the tip of the insertion sheath enters the artery, blood will begin to flow from the drip hole in the locator (Figure 2).

6. Slowly withdraw the arteriotomy locator/insertion sheath assembly until blood stops flowing from the drip hole. This indicates that the tip of the Angio-Seal® insertion sheath has just exited the artery (Figure 3).

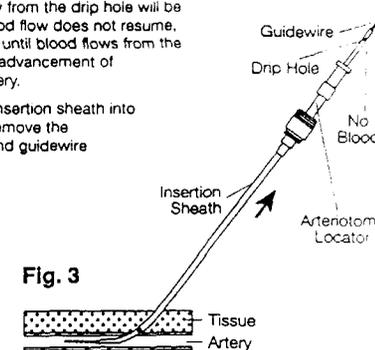
Fig. 2



7. Advance the assembly 1 cm or less into the artery. Blood flow from the drip hole will be re-established. If blood flow does not resume, repeat Steps 6 and 7 until blood flows from the drip hole again upon advancement of assembly into the artery.

8. Without moving the insertion sheath into or out of the artery, remove the arteriotomy locator and guidewire from the sheath.

Fig. 3



WARNING
 The Angio-Seal® insertion sheath should not move into or out of the artery for the remainder of the Angio-Seal® device deployment procedure.

DEPLOYING THE ANCHOR IN THE ARTERY

1. Hold the **Angio-Seal[®]** bypass tube and, with the **8F** reference indicator facing up, feed the bypass tube and carrier tube into the hemostasis valve of the insertion sheath (Figure 4).

2. Keeping the insertion sheath in place, advance the carrier tube completely into the insertion sheath to deploy the anchor.

3. Hold the insertion sheath steady to prevent movement into or out of the artery. Carefully pull the carrier tube out of the sheath until it meets resistance from the anchor catching on the distal tip of the insertion sheath. Note the position of the colored bands on the gripper indicator. In a correct deployment (Figure 5a), the colored bands of the gripper indicator will line up with the colored band on the insertion sheath hub.

NOTE: Do not use excessive force when testing the anchor for resistance. If excessive upward force is applied when premature anchor deployment has occurred, the tensioner mechanism may be activated and collagen could deploy into the sheath. If this occurs, do not reinsert the device. Reinsertion of the device could deploy the collagen into the artery.

4. When resistance is felt and the colored bands are properly lined up, correct anchor deployment should be reconfirmed. Reinsert the carrier tube into the sheath and rotate it 1/4 turn. Withdraw the carrier and again confirm resistance of the anchor at the sheath tip and the correct position of the colored bands.

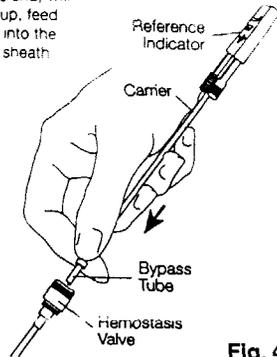
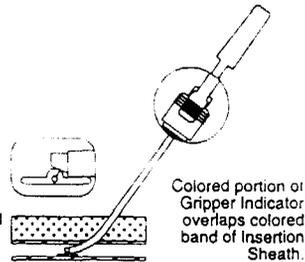


Fig. 4

Fig. 5a

(Correct)
The anchor will catch the artery wall as the carrier tube is withdrawn.



Do not proceed until you are certain that the anchor has been properly deployed (Figure 5a). If the anchor is improperly deployed, the device will not function.

INCORRECT ANCHOR DEPLOYMENT

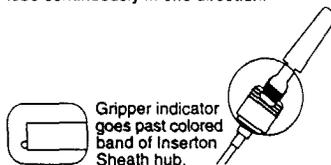
No Resistance

If at any time while testing anchor resistance at the sheath tip, you do not feel resistance or if the anchor is placed incorrectly as in Figure 5b, advance the carrier tube, rotate it 1/4 turn and repeat Step 3. If you still do not feel resistance, insert the carrier tube again, and then rotate it 1/2 turn in the opposite direction. Repeat Step 3.

Do not rotate the carrier tube continuously in one direction.

FIG. 5b

(Incorrect)
Anchor has re-entered the sheath and no resistance is detected.



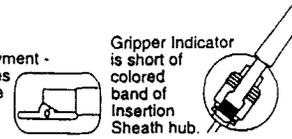
Premature Deployment

If the anchor catches prematurely as in Figure 5c, advance the carrier tube into the sheath again, rotate it 1/4 turn, then withdraw the tube until the anchor catches correctly.

Again, do not proceed until you are certain that the anchor has been properly deployed (Figure 5a). If the anchor is improperly deployed, the device will not function.

Fig. 5c

(Incorrect)
Premature deployment - anchor leg catches sheath for oblique deployment



POSITIONING THE COLLAGEN

1. Once the anchor has been deployed correctly (Figure 5a), pinch the gripper indicators against the insertion sheath hub so the serrations on the two parts are locked together. Withdraw the carrier assembly and insertion sheath together vertically from the skin (Figures 6 and 7).

2. When the insertion sheath clears the skin, a tamper tube appears (Figure 8).

3. Continue to pull the insertion sheath and carrier up the suture until the crimp stop on the suture appears (Figure 9). Immediately tamp the collagen firmly three or four times while maintaining tension on the carrier tube and insertion sheath. Do not remove the carrier assembly at this time.

Fig. 6



Hold Gripper Indicator and Insertion Sheath together

WARNING

Failure to maintain tension on the suture while compacting the collagen could cause the collagen to enter the artery.

4. While maintaining tension on the suture, attach the tension spring to the suture between the tamper tube and the crimp stop.

NOTE: The distance between the two ends of the spring should be 2 to 3 cm. A shorter distance indicates that the collagen has not compacted completely. If the space is less than 2 cm, apply upward tension to the suture, remove the spring, tamp further, then re-apply the spring.

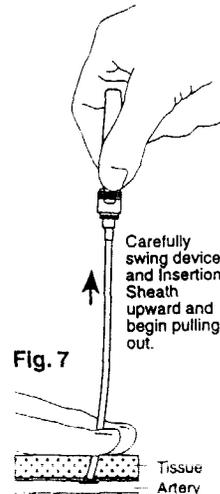


Fig. 7

Carefully swing device and Insertion Sheath upward and begin pulling out.

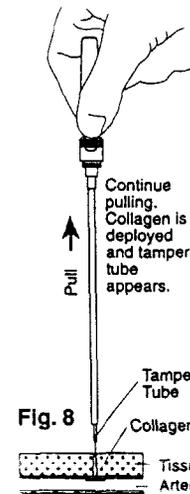


Fig. 8

Continue pulling. Collagen is deployed and tamper tube appears.

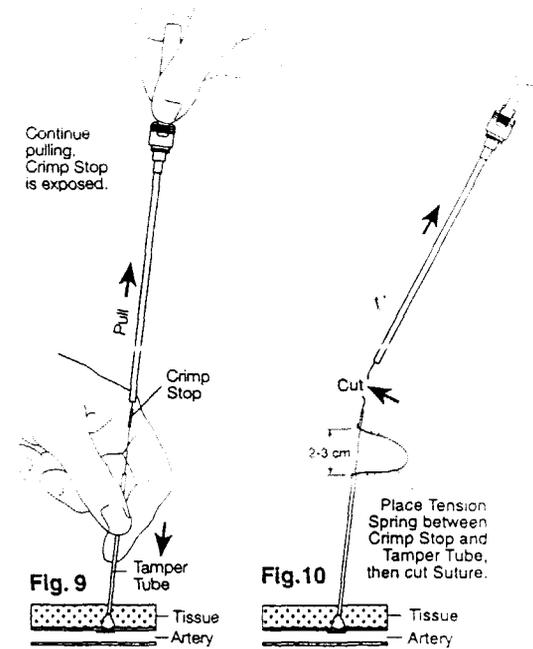


Fig. 9

Fig. 10

5. Once the tension spring is in place, cut the suture above the crimp stop and remove the carrier tube and insertion sheath completely (Figure 10).

6. Leave the tension spring in place at least 20 minutes to assure hemostasis. Do not leave the spring in place for more than 45 minutes.

7. Remove the tension spring and cut the suture below the crimp stop (Figure 11). Remove the tamper tube.

NOTE: If seeping of blood occurs after placing the **Angio-Seal[®]** device, after removing the tamper and spring, gentle digital pressure (one or two fingers) at the puncture site is usually sufficient to produce hemostasis. However, heavier manual pressure or pressure devices may be applied if necessary.

8. Provided sufficient hemostasis has been achieved, cut the suture below the skin level (Figure 12), and apply a sterile dressing.

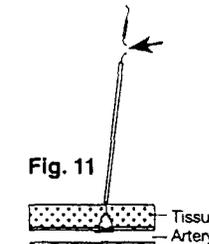


Fig. 11

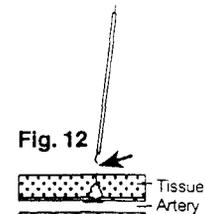


Fig. 12

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5 *Angio-Seal*TM

QUANTITY

Hemostatic Puncture Closure Device

Système hémostatique de fermeture des points de ponction

Hämostatisches Punktionsverschlußsystem

Hemostatic Puncture Closure Device

Dispositivo per l'amosiasi di punture arteriose

Dispositivo haemostático para cierre de punción

Haemostatisk punkturförlutning



DOT NO. 124111-0011

MFG DATE
08/1996



02/1997



Manufactured by Quinton Instrument Company for
Sherwood Medical Company

8F

Ref. 8888-610089

LOT 879905

Developed by Kensey Nash Corporation

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QUANTITY

Angio-Seal™

Hemostatic Puncture Closure Device

- F** **Système hémostatique de fermeture des points de ponction**
- D** **Hämostatisches Punktionsverschlußsystem**
- NL** **Hemostatic Puncture Closure Device**
- I** **Dispositivo per l'emostasi di puntura arteriale**
- E** **Dispositivo haemostático para cierre de punción**
- S** **Haemostatisk punkturförslutning**



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5
QUANTITY

Angio-Seal™

Hemostatic Puncture Closure Device

For single use. Sterility guaranteed if package unopened or undamaged.
DO NOT USE IF TEMPERATURE INDICATOR DOT IS BLACK.
SEE INSTRUCTIONS FOR USE.

- F** **Système hémostatique de fermeture des points de ponction.** Destiné à l'usage unique. Stérilité garantie si l'emballage individuel de stérilité n'est pas endommagé. NE PAS UTILISER SI LE THERMOPHORE DE TEMPERATURE EST DEVENU NOIR. VOIR LES INSTRUCTIONS D'UTILISATION.
- D** **Hämostatische Punktionsverschlussystem.** Zum Einmalgebrauch. Sterilität gewährleistet, unbeschädigte und unbeschädigte Einzelverpackung. NICHT VERWENDEN, WENN DER TEMPERATUR-INDIKATORPUNKT SCHWARZ IST. SIEHE GEBRAUCHSANLEITUNG.
- NL** **Hemostatische punctuurfsluiting.** Voor éénmalig gebruik. Steriliteit gegarandeerd als de verpakking onbeschadigd en ongeopend is. ALS DE TEMPERATUUR-INDICATORPUNT ZWART IS, MAG DIT PRODUCT NIET WORDEN GEBRUIKT. ZIE GEBRUIKSAANWIJZING.



Temperature Indicator
Thermophore - Temperature
Indikator - Temperatur
Indikator - Temperatur
Indikator - Temperatur



- I** **Dispositivo per l'emostasi di punture arteriosae.** Monouso. Sterilità garantita a confezione integra. NON UTILIZZARE IL PRODOTTO SE L'INDICATORE SULLA CONFEZIONE È DI COLORE NERO. VEDERE ISTRUZIONI PER L'USO.
- E** **Dispositivo hemostático para cierre de punción.** Para un solo uso. Esterilidad asegurada excepto cuando el envase está roto o abierto. NO UTILIZAR SI EL INDICADOR DE TEMPERATURA ESTA EN NEGRO. VER LAS INSTRUCCIONES DE USO.
- S** **Hämostatisk punktuurfslutning.** För engångsbruk. Sterilitet garanterad om förpackningen är oöppnad och oskadad. ANVÄND EJ IFALL TEMPERATURINDIKATORN VISAR SVART MARKERING. SE ANVÄNDARINSTRUKTIONERNA.



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5 *Angio-Seal*TM

QUANTITY

Hemostatic Puncture Closure Device

- [F]** Système hemostatique de fermeture des points de ponction
- [D]** Hämostatisches Punktionsverschlußsystem
- [NL]** Hemostatic Puncture Closure Device

- [I]** Dispositivo per l'emostasi di puncture arteriose
- [E]** Dispositivo haemostático para cierre de punción
- [S]** Haemostatisk punkturförslutningw



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QUANTITY

*Angio-Seal*TM

Hemostatic Puncture Closure Device

- F** Système hémostatique de fermeture des points de ponction
- D** Hämostatisches Punktionsverschlußsystem
- NL** Hemostatic Puncture Closure Device
- I** Dispositivo per l' emostasi di punture arteriose
- E** Dispositivo haemostático para cierre de punción
- S** Haemostatisk punkturförslutning



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10
QUANTITY

Angio-Seal™

Hemostatic Puncture Closure Device Developed by the Kensey Nash Corporation

For single use. Sterility guaranteed if package unopened or undamaged.

E **Système hémostatique de fermeture des points de ponction**
Destiné à l'usage unique. Vérifier l'intégrité de l'emballage individuel de stérilité avant usage. Ne pas réutiliser.

D **Hämostatisches Punktionsverschlußsystem**
Zum Einmalgebrauch. Sterilität gewährleistet bei ungeöffneter und unbeschädigter Einzelverpackung.

L **Hemostatic Puncture Closure Device**
Voor éénmalig gebruik. Steriliteit gegarandeerd indien de verpakking onbeschadigd en ongeopend is.

I **Dispositivo per l'emostasi di punture arteriose**
Memorevole. Sterilità garantita a confezione integra.

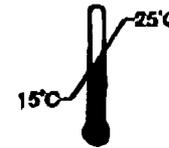
E **Dispositivo haemostático para cierre de punción**
Para un solo uso. Esterilidad asegurada excepto cuando el envase este roto o abierto.

S **Haemostatisk punkturförslutning**
För engångsbruk. Sterilitet garanterad om förpackningen är oöppnad och oskadad.

® Trademark of Quinton Instrument Company (Bellevue, Washington) within the United States and Sherwood Medical Company (St. Louis, Missouri) in all other countries. Manufactured under one or more of the following patents: US, 4,744,884, 4,852,568, 4,852,569, 5,021,059, 5,061,274, 5,222,874, 5,282,827 Canada 1,322,822. Other US and foreign patents pending.



STERILE R



Orswell, Sussex RH11 1 7YD, UK
BP 1138, F-91011 Evry Cedex 8, France
D-65843 Sulzbach, Deutschland
Postbus 477, 6201 AL 's-Hertogenbosch, Nederland
Via della Nocetta, 109, 40184 Parma, Italia
Markham, Ontario L3R 9Y1, Canada
Perrennita, N.S.W., 2150 Australia
Happy Valley, Hong Kong

Cimas S.A., Almagueres 180, 06018 Barcelona, Spain

Sherwood
MEDICAL

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QUANTITY

Angio-Seal™

Hemostatic Puncture Closure Device
Developed by the Kensey Nash Corporation

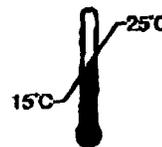
For single use. Sterility guaranteed if package unopened or undamaged.

- F** **Système hémostatique de fermeture des points de ponction**
Devient l'objet après usage. Vérifier l'intégrité du protecteur individuel de stérilité avant usage. Ne pas réutiliser.
- D** **Hämostatisches Punktionsverschlußsystem**
Zum Einmalgebrauch. Sterilität gewährleistet bei ungeöffneter und unbeschädigter Einzelverpackung.
- ML** **Hemostatic Puncture Closure Device**
Voor éénmalig gebruik. Steriliteit gegarandeerd indien de verpakking onbeschadigd en ongeopend is.
- I** **Dispositivo per l'emostasi di punture arteriose**
Monouso. Sterilità garantita a confezione integra.
- E** **Dispositivo haemostático para cierre de punción**
Para un solo uso. Esterilidad asegurada excepto cuando se abra esta rotación.
- S** **Haemostatisk punkturöslutning**
För engångsbruk. Sterilitet garanterad om förpackningen är oöppnad och oöskadad.

®Trademark of Quinton Instrument Company (Bethell, Washington) within the United States and Sherwood Medical Company (St. Louis, Missouri) in all other countries. Manufactured under one or more of the following patents: US, 4,744,384, 4,652,568, 4,682,612, 6,021,059, 5,061,274, 6,222,974, 5,262,827 Canada 1,322,822. Other US and foreign patents pending.



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Via della Nocetta, 106, 00184 Roma, Italia
Markham, Ontario L3R 9T1, Canada
Parramatta, N.S.W., 2150 Australia
Happy Valley, Hong Kong

Clerise S.A., Almaguera 160, 08016 Barcelona, Spain

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QUANTITY

Angio-Seal™

Hemostatic Puncture Closure Device

- F** Système hémostatique de fermeture des points de ponction
- D** Hämostatisches Punktionsverschlußsystem
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- I** Dispositivo per l'emostasi di punture arteriose
- E** Dispositivo haemostático para cierre de punción
- S** Haemostatisk punkturförslutning



ART. NO. 04344-011

STERILE | R

Temperature Indicator



Do not use if temperature indicator dot on package has changed from light grey to dark grey or black.

ART. NO. 02253-042

MFG DATE
04/7/95



(02) (04) (00) (00) (00) (00)



(02) (04) (00) (00) (00) (00)



Use by

02/1997



8F

Manufactured by DeLia's Customart Company for
Sherwood Medical Company

Ref. 8888-610889

LOT 079905

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DRAFT

1 AngioSeal

Hemostatic Puncture Closure Device Developed by Kensey Nash Corporation

Contents: One Angio-Seal Device, Introducer, Guidewire, Arteriotomy Locator and Tension Spring. For single use. Sterility guaranteed if package unopened or undamaged. DO NOT USE IF TEMPERATURE INDICATOR DOT IS BLACK. SEE INSTRUCTIONS FOR USE.

F Système hémostatique de fermeture des points de ponction

Contenu: Un Angio-Seal, un introducteur, un guide, un localisateur artériel et une patte de tension. Destiné à l'usage unique. Stérilité garantie si l'emballage individuel de stérilité n'est pas ouvert. Ne pas réutiliser. NE PAS UTILISER SI LE Témoin DE TEMPERATURE EST DEVENU NOIR. LIRE LES INSTRUCTIONS D'UTILISATION.

D Hämostatisches Punktionsverschlußsystem

Inhalt: 1 Angio-Seal, Einführrohr, Führungsdraht, Arterienlokalisator und Metallfeder. Zum Einmalgebrauch. Sterilität gewährleistet bei ungeöffneter und unbeschädigter Einzelverpackung. Sherwood Medical GmbH, D-65843 Sulzbach, Deutschland. NICHT VERWENDEN, WENN DER TEMPERATUR-INDIKATORPUNKT SCHWARZ IST. SIEHE GEBRAUCHSINFORMATION.

NL Hemostatic Puncture Closure Device

Inhoud: Een Angio-Seal, inbrengcanule, guldraad, Arteriotomielocater en metalen drukveer. Voor éénmalig gebruik. Steriliteit gegarandeerd indien de verpakking onbeschadigd en ongeopend is. ALS DE TEMPERATUUR-INDICATOR ZWART IS, MAG DIT PRODUCT NIET WORDEN GEBRUIKT. ZIE GEBRUIKSAANWIJZING.

I Dispositivo per l'emostasi di punture arteriose

Contenuto: Un Angio-Seal, un introduttore, un filo guida, una molla in metallo, un localizzatore per arteriosomia. Monouso. Sterilità garantita a confezione integra. Rappresentante per le vendite in Italia: Sherwood Medical Italia S.r.l., Via delle Nocce, 109, 00184 Roma Italia. NON UTILIZZARE IL PRODOTTO SE L'INDICATORE SULLA CONFEZIONE È DI COLORE NERO. VEDERE ISTRUZIONI PER L'USO.

E Dispositivo haemostático para cierre de punción

Contenido: Un Angio-Seal, un introductor, una guía, un localizador de arteria y un muelle metálico. Para un solo uso. Esterilidad asegurada siempre cuando el envase está roto o abierto. Distribuido por: Ciermas S.A., Almaguera 180, 08016, Barcelona, Spain. NO UTILIZAR SI EL INDICADOR DE TEMPERATURA ESTA EN NEGRO. VER LAS INSTRUCCIONES DE USO.

S Haemostatisk punkurförlutning

Innehåll: En Angio-Seal, introduktionsrör, guide-tråd, artär lokator och spårtrådar. För engångsbruk. Sterilitet garanterad om förpackningen är obryten och oöppnad. ANVÄND EJ I FALL TEMPERATURINDIKATORN VISAR SVART MARKERING. SE ANVÄNDARINSTRUKTIONERNA.

Temperature Indicator
Témoin de Température
Temperatur - Indikatorpunkt
Temperatur - Indikator
Indicador de temperatura
Temperaturindikator



STERILE R



41 20 00014-001

MFG DATE
02/1996



Use Before

02/1997



Sherwood
MEDICAL
St. Louis, MO 63103

8F

Manufactured by Solutra Instrument Company for
Sherwood Medical Company

Ref. 8888-610089

LOT 879805

In A trademark of Solutra Instrument Company, Solutra, Solutra with No United States and Sherwood Medical Company St. Louis, Missouri is a registered trademark. Manufactured under and in name of the following countries: USA, Canada, Mexico, Argentina, Australia, Austria, Belgium, Brazil, Canada, Denmark, France, Germany, Italy, Japan, Korea, Spain, Sweden, Switzerland, Taiwan, Thailand, United Kingdom, USA, West Germany.



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DRAFT

Foil Pouch BF 11/8/95 7:26 PM Page 1



ANGIO-SEAL
8F HEMOSTATIC PUNCTURE CLOSURE DEVICE
 Peel foil pouch completely before removing device. Device must be used within one hour of opening foil pouch.



~~Quadrant~~
Black

- F** Ouvrir complètement le sachet avant de retirer le système qui doit être utilisé dans l'heure qui suit l'ouverture de l'emballage.
- D** Vor Entnahme des Produktes die Blisterverpackung vollständig auseinanderpacken. Nach Öffnen der Blisterverpackung das Produkt innerhalb einer Stunde verwenden.
- NL** Trek de aluminium/kunststof verpakking volledig los voordat u de Angio-Seal uit de verpakking neemt. Na opening moet het implantaat binnen 1 uur worden gebruikt.

- I** Aprire completamente la confezione per rimuovere il presidio il presidio deve essere utilizzato entro un'ora dall'apertura della confezione.
- E** Antes de extraer el dispositivo retire totalmente la cubierta del envoltorio. El dispositivo debe utilizarse durante la hora siguiente a la apertura del envoltorio.
- S** Öppna förpackningen fullständigt innan produkten tas ut. Produkten måste användas inom 1 timme från öppnandet.



Poly Foil Pouch
 034084-001
 Rev. New
 1 of 2