510(k) Summary

AUG 17 2010

Submitter:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Contact Person:
Tricia Miller
Director of Regulatory
Telephone: 319-294-3745
Facsimile: 319-393-3494
Email: tmiller@lildrugstore.com

Date:
August 13, 2010

Proprietary Name:
Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Common name:
Personal Lubricant

Classification name:
21 C.F.R. 884.5300 Lubricant, Patient, Vaginal, Latex Compatible
Product Code: NUC
Class: 2
Review Panel: Obstetrics/Gynecology

Predicate Devices:

Device Name: CVS Personal Lubricant & Moisturizer
510(k) Number: K062682
Product Code: NUC, MMS

Intended Use:

Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible

with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.

Description of Device

Replens Vaginal Moisturizer is a non-sterile, water-based, white to off-white, non-irritating, non-greasy, non-staining vaginal gel delivered in a tube with a reusable applicator as a long-lasting moisturizer for vaginal dryness. The use of the reusable applicator provides less mess in application. Replens Vaginal Moisturizer is intended for ongoing use, not exclusively for use during intimate sexual activity.

Replens Vaginal Moisturizer contains ingredients commonly used in other products for vaginal use sold as medical devices and cosmetics. All ingredients are either NF, USP, or are considered "generally recognized as safe for their intended use". The quantitative formulation is considered confidential commercial information.

Technological Characteristics of the Device

Replens Vaginal Moisturizer is substantially equivalent to the identified previously cleared vaginal lubricant predicate with respect to its design and materials, principle of operation, function, formulation, and intended use. It is also substantially equivalent to other water-based vaginal lubricants and personal lubricants being commercially marketed in the U.S.

Summary of Performance Data

Biocompatibility Testing: The following biocompatibility testing has been performed on Replens Long-Lasting Vaginal Moisturizer:

- Cytotoxicity
- Acute Vaginal Irritation
- Subacute Vaginal Irritation
- Subacute Vaginal Irritation with Histological Examination
- Acute Systemic Toxicity
- Hypersensitivity
- Acute Oral Toxicity
- Acute Dermal Toxicity
- Dermal Irritation
- Eye Irritation.

Clinical Studies: The following clinical studies have been performed on Replens Long-Lasting Vaginal Moisturizer:

- Bachmann GA, Notelovitz M, Gonzalez SJ, Thompson C, Morecraft BA. (1991) Vaginal Dryness in Menopausal Women: Clinical Characteristics and Nonhormonal Treatment. Clinical Practice in Sexuality, 7(9): 1-8.
- Bachmann GA, Notelovitz M, Kelly SJ, Owens A, Thompson C. (1992) Long Term Nonhormonal Treatment of Vaginal Dryness. Clinical Practice in Sexuality, 8(8/9): 3-8.
- Zinny MA, Lee S. (1991) Double-Blind Study of the Comparative Effects of Two Gels on Vaginal pH in Postmenopausal Women. Today's Therapeutic Trends, 8(4): 65-72.
- Young R, Goldzieher J, Kaufman R. (1991) A Study of the Effects of Col-1003 In Postmenopausal Women. Unpublished.
- Nakamura R. (1991) Evaluation of Col-1003 in the treatment of vaginal dryness in postmenopausal women. Unpublished.
- Whitehead M. (1991) A Randomised Double Blind Evaluation of Col-1003, a bioadhesive polymer system vaginal moisturizing gel and, KY Brand Lubricating Jelly in the treatment of vaginal dryness in postmenopausal women receiving concomitant oral hormone replacement therapy. Unpublished
- Nachtigall LE. (1994) Comparative study: Replens versus local estrogen in menopausal women. Fertility and Sterility, 61(1): 178-180.
- Gelfand MM, Wendman E. (1994) Treating Vaginal Dryness in Breast Cancer Patients: Results of Applying a Polycarbophil Moisturizing Gel. J. Women's Health, 3(6): 427-433.

The format of the studies listed above is summarized in the table below:

Citation	No. Patients Enrolled (Replens)	Study Design*	Dosage Regimen	Duration
Bachmann et al	89	D-B, X-over	2.5 g per day	5 days
Bachmann et al	54	Open	2.5 g, 3 x weekly	12 months
Zinny and Lee	26	D-B, parallel	2.5 g alternate nights	4 weeks
Young et al	30	Open	2.5 g, 3 x weekly, plus option of additional application prior to intercourse.	12 months
Nakamura	10	Open, X-over between treatment durations	2.5 g daily	1-5 days

Citation	No. Patients Enrolled (Replens)	Study Design*	Dosage Regimen	Duration
Whitehead	32	D-B, X-over	2.5 g, 3 x weekly plus option of additional application prior to intercourse.	8 weeks
Nachtigall	15	Open, parallel	2.5 g, 3 x weekly	3 months
Gelfand and Wendman	25	Open	2.5 g, 3 x weekly, plus option of additional application prior to intercourse.	3 months

* D-B = double-blind; X-over = cross-over design

The parameters employed in the studies included the influence of Replens on vaginal pH and the vaginal mucosa, the relief of the patient's symptoms, the vaginal dryness index, determination of vaginal pH at varying time intervals after single or multiple applications of the gel, PAP smears and the completion of diary cards by the patient. All of the studies concluded that Replens was safe and well-tolerated.

Stability Data: Real-time stability data confirms a shelf life of three (3) years for Replens Long-Lasting Vaginal Moisturizer.
Preservative Effectiveness: Replens Long-Lasting Vaginal Moisturizer has successfully passed the requirements of the USP <51> Antimicrobial Effectiveness Test.
Condom Compatibility Testing: Condom compatibility testing confirms that Replens Long-Lasting Vaginal Moisturizer does not materially affect the strength or integrity of natural rubber latex or synthetic condoms (polyurethane and polyisoprene).

Conclusion

Based on the information presented in the 510(k) notice, it is concluded that Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) for OTC use is safe and effective for its proposed indications and is substantially equivalent in intended use, formulation, safety, and technological characteristics to the identified predicate device and other similar water-based personal lubricants.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-G609
Silver Spring, MD 20993-0002

Lil Drug Store Products, Inc.
c/o Mr. Mark A. Job
Responsible Third Party
Regulatory Technology Services, Inc
1394 25th Street, NW
BUFFALO MN 55313

AUG 17 2010

Re: K101098
Trade/Device Name: Replens Long-Lasting Vaginal Moisturizer
(in 35 Tube with Reusable Applicator)
Regulation Number: 21 CFR §884.5300
Regulation Name: Condom
Regulatory Class: II
Product Code: NUC
Dated: July 30, 2010
Received: August 2, 2010

Dear Mr. Job:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related

adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Herbert P. Lerner, M.D., Director (Acting)
Division of Reproductive, Gastro-Renal
and Urological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

K101098

STATEMENT OF INDICATIONS FOR USE

510(k) Number: K101098

Device Name: Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Indications for Use: Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.

Prescription Use _____ OR Over-the-Counter Use __X__
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K101098

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Document Mail Center - WO66-G609
Silver Spring, MD 20993-0002

Lil Drug Store Products, Inc.
c/o Mr. Mark A. Job
Responsible Third Party
Regulatory Technology Services, Inc
1394 25th Street, NW
BUFFALO MN 55313

AUG 17 2010

Re: K101098
Trade/Device Name: Replens Long-Lasting Vaginal Moisturizer
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Regulation Number: 21 CFR §884.5300
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Sincerely yours,

Herbert P. Lerner, M.D., Director (Acting)
Division of Reproductive, Gastro-Renal
and Urological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

K101098

STATEMENT OF INDICATIONS FOR USE

510(k) Number: K101098

Device Name: Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

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(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K101098

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

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

July 21, 2010

LIL DRUG STORE PRODUCTS, INC.
c/o REGULATORY TECHNOLOGY SERVICES, LLC
1394 25TH STREET, NW
BUFFALO, MINNESOTA 55313
UNITED STATES
ATTN: MARK JOB

510k Number: K101098
Product: REPLENS LONG-LASTING

Extended Until: 09/08/2010

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

Marjorie Shulman

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and Radiological Health

Date: July 16, 2010

U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Additional Information for **K101098**
Lil' Drug Store Products Inc..
Long-Lasting Vaginal Moisturizer Gel

To Whom It May Concern:

Enclosed in duplicate is the following information:

This letter is a request for a 60 day extension in order to complete the preparation of the response to the email received from Colin Pollard dated June 10, 2010.

If you should have any questions regarding this submission please contact me at 763 682 4139 or fax 763 682 4420. Please fax any correspondence regarding this submission to Regulatory Technology Services LLC.

Sincerely,

Mark Job
Responsible Third Party Official

K39

1 of 8

Date: July 16, 2010

U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Additional Information for **K101098**
Lil' Drug Store Products Inc..
Long-Lasting Vaginal Moisturizer Gel

To Whom It May Concern:

Enclosed in duplicate is the following information:

This letter is a request for a 60 day extension in order to complete the preparation of the response to the email received from Colin Pollard dated June 10, 2010.

If you should have any questions regarding this submission please contact me at 763 682 4139 or fax 763 682 4420. Please fax any correspondence regarding this submission to Regulatory Technology Services LLC.

Sincerely,

Mark Job
Responsible Third Party Official

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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

June 11, 2010

LIL DRUG STORE PRODUCTS, INC.
c/o REGULATORY TECHNOLOGY SERVICES, LLC
1394 25TH STREET, NW
BUFFALO, MINNESOTA 55313
UNITED STATES
ATTN: MARK JOB

510k Number: K101098
Product: REPLENS LONG-LASTING VAGINAL M

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm.

The deficiencies identified represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceProvisionsofFDAModernizationAct/ucm136685.htm.

If after 30 days the additional information (AI), or a request for an extension of time, is not received, we will discontinue review of your submission and proceed to delete your file from our review system (21 CFR 807.87(l)). Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission.

Please remember that the Safe Medical Devices Act of 1990 states that you may not place this device into commercial distribution until you receive a decision letter from FDA allowing you to do so.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

May 06, 2010

LIL DRUG STORE PRODUCTS, INC.
c/o REGULATORY TECHNOLOGY SERVICES, LLC
1394 25TH STREET, NW
BUFFALO, MINNESOTA 55313
UNITED STATES
ATTN: MARK JOB

510k Number: K101098
Product: REPLENS LONG-LASTING VAGINAL M

We are holding your above-referenced Premarket Notification (510(k)) for 30 days pending receipt of the additional information that was requested by the Office of Device Evaluation. Please remember that all correspondence concerning your submission MUST cite your 510(k) number and be sent in duplicate to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm.

The deficiencies identified represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceProvisionsofFDAModernizationAct/ucm136685.htm.

If after 30 days the additional information (AI), or a request for an extension of time, is not received, we will discontinue review of your submission and proceed to delete your file from our review system (21 CFR 807.87(l)). Please note our guidance document entitled, "Guidance for Industry and FDA Staff, FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request. The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm. Pursuant to 21 CFR 20.29, a copy of your 510(k) submission will remain in the Office of Device Evaluation. If you then wish to resubmit this 510(k) notification, a new number will be assigned and your submission will be considered a new premarket notification submission.

 729

 Please remember that the Safe Medical Devices Act of 1990 states that you may not place this device into commercial distribution until you receive a decision letter from FDA allowing you to do so.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

April 20, 2010

LIL DRUG STORE PRODUCTS, INC.
c/o REGULATORY TECHNOLOGY SERVICES, LLC
1394 25TH STREET, NW
BUFFALO, MINNESOTA 55313
UNITED STATES
ATTN: MARK JOB

510k Number: K101098

Received: 4/20/2010

Product: REPLENS LONG-LASTING VAGINAL M

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act(Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you when the processing of your 510(k) has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

On September 27, 2007, the President signed an act reauthorizing medical device user fees for fiscal years 2008 - 2012. The legislation - the Medical Device User Fee Amendments of 2007 is part of a larger bill, the Food and Drug Amendments Act of 2007. Please visit our website at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/default.htm
for more information regarding fees and FDA review goals. In addition, effective January 2, 2008, any firm that chooses to use a standard in the review of ANY new 510(k) needs to fill out the new standards form (Form 3654) and submit it with their 510(k). The form may be found at http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm.

We remind you that Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amended the PHS Act by adding new section 402(j) (42 U.S.C. § 282(j)), which expanded the current database known as ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices. Section 402(j) requires that a certification form http://www.fda.gov/AboutFDA/ReportsManualsForms/Forms/default.htm accompany 510(k)/HDE/PMA submissions. The agency has issued a draft guidance titled: "Certifications To Accompany Drug, Biological

Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007" http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissio ns/PremarketNotification510k/ucm134034.htm. According to the draft guidance, 510(k) submissions that do not contain clinical data do not need the certification form.

Please note the following documents as they relate to 510(k) review: 1) Guidance for Industry and FDA Staff entitled, "Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs and BLA Supplements". This guidance can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm. Please refer to this guidance for information on a formalized interactive review process. 2) Guidance for Industry and FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.html. In addition, the 510(k) Program Video is now available for viewing on line at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/ucm070201.htm .

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm. If you have questions on the status of your submission, please contact DSMICA at (301)796-7100 or the toll-free number (800)638-2041 , or at their internet address http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm. If you have procedural questions, please contact the 510(k) Staff at (301)796-5640.

Sincerely,

510(k) Staff

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STATEMENT OF INDICATIONS FOR USE

510(k) Number: _____

Device Name: Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Indications for Use: A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Prescription Use _____ OR Over-the-Counter Use __X__
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) Summary

Submitter:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Contact Person:
Tricia Miller
Director of Regulatory
Telephone: 319-294-3745
Facsimile: 319-393-3494
Email: tmiller@lildrugstore.com

Date:
February 25, 2010

Proprietary Name:
Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Common name:
Personal Lubricant

Classification name:
21 C.F.R. 880.6375 Lubricant, Patient, Vaginal
Product Code: MMS
Class: 1
Review Panel: General Hospital

Predicate Devices:

Device Name: CVS Personal Lubricant & Moisturizer
510(k) Number: K062682
Product Code: NUC, MMS

Intended Use:

A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease

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and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Description of Device

Replens Vaginal Moisturizer is a non-sterile, water-based, white to off-white, non-irritating, non-greasy, non-staining vaginal gel delivered in a tube with a reusable applicator as a long-lasting moisturizer for vaginal dryness. The use of the reusable applicator provides less mess in application. Replens Vaginal Moisturizer is intended for ongoing use, not exclusively for use during intimate sexual activity.

Replens Vaginal Moisturizer contains ingredients commonly used in other products for vaginal use sold as medical devices and cosmetics. All ingredients are either NF, USP, or are considered "generally recognized as safe for their intended use". The quantitative formulation is considered confidential commercial information.

Technological Characteristics of the Device

Replens Vaginal Moisturizer is substantially equivalent to the identified previously cleared vaginal lubricant predicate with respect to its design and materials, principle of operation, function, formulation, and intended use. It is also substantially equivalent to other water-based vaginal lubricants and personal lubricants being commercially marketed in the U.S.

Summary of Performance Data

Biocompatibility Testing: The following biocompatibility testing has been performed on Replens Long-Lasting Vaginal Moisturizer:

- Cytotoxicity
- Acute Vaginal Irritation
- Subacute Vaginal Irritation
- Subacute Vaginal Irritation with Histological Examination
- Acute Systemic Toxicity
- Hypersensitivity
- Acute Oral Toxicity
- Acute Dermal Toxicity
- Dermal Irritation
- Eye Irritation.

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Stability Data: Real-time stability data confirms a shelf life of three (3) years for Replens Long-Lasting Vaginal Moisturizer.

Preservative Effectiveness: Replens Long-Lasting Vaginal Moisturizer has successfully passed the requirements of the USP <51> Antimicrobial Effectiveness Test.

Condom Compatibility Testing: Condom compatibility testing confirms that Replens Long-Lasting Vaginal Moisturizer does not materially affect the strength or integrity of latex or synthetic condoms.

Conclusion

Based on the information presented in the 510(k) notice, it is concluded that Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) for OTC use is safe and effective for its proposed indications and is substantially equivalent in intended use, formulation, safety, and technological characteristics to the identified predicate device and other similar water-based personal lubricants.

Date: April 18, 2010

FDA CDRH DMC

APR 20 2010

Received

U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Premarket Notification

To Whom It May Concern:

Enclosed in duplicate is the following information:

A. Purpose of Submission: New Device

B. Name and Address of the Third Party:

Regulatory Technology Services LLC
1394 25th Street NW
Buffalo, MN 55313

C. Name and Address of the Manufacturer:

Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

K20

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D. Device Name

Trade or Proprietary Name: Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reuseable Applicator)

Classification Name: Patient Lubricant

Regulation Number: 21 CFR 880.6375

Recommendation: Substantially Equivalent

Date Submission was received by Regulatory Technology Services LLC: February 26, 2010

We have enclosed the following materials:

E. Authorization Letter from the applicant (MAL-F-0006).
F. Complete 510(k) application submitted by the applicant.
G. Documented review of the 510(k) application (RPP-F-0012, RPP-F-14 and all correspondence and documents related to the review).
H. Conflict of Interest Certification (COI-F-0018)
I. Certification (RPP-F-0020)

If you should have any questions regarding this submission please contact me at 763 682 4139 or fax 763 682 4420 or email at mark@markjob.com. Please fax any correspondence regarding this submission to Regulatory Technology Services LLC.

Sincerely,

Mark Job
Responsible Third Party Official

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Submission Certification

1. I certify that Regulatory Technology Services LLC continues to meet the personnel qualifications and prevention of conflict of interest criteria reviewed by the FDA;

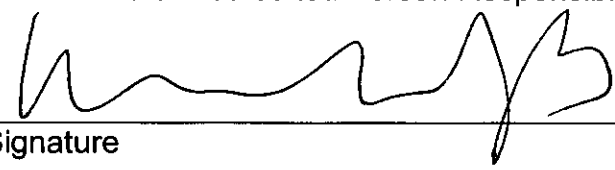
2. In addition, I state that Regulatory Technology Services LLC believes that statements made in the review are true and accurate to the best knowledge of Regulatory Technology Services LLC;

3. Regulatory Technology Services LLC's review is based on the 510(k) that is attached with the review; and

4. Regulatory Technology Services LLC understands that the submission of false information to the government is prohibited by 18 U.S.C. 1001 and 21 U.S.C. 33(q).

Mark Job

Print Name of Accredited Person Responsible Official



Signature

Date: April 18, 2010

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Conflict of Interest Declaration and Certification For the review of the 510(k) submission from

Applicant: **Lil' Drug Store Products, Inc.**

Device Name or Model Name: **Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reuseable Applicator)**

Initials

- I have read and understand Regulatory Technology Services LLC's Conflict of interest and Confidentiality Procedure (COI-S-0023), regarding conflict of interests and the attachments accompanying the procedure and am aware of my responsibilities under them.
- I have not been employed within the last two years by the firm who submitted the 510(k) for evaluation.
- I did not charge fees contingent or based upon the recommendation for initial classification (SE decision).
- I have not performed testing in connection with this specific device 510(k).
- I understand that the Accredited Persons (AP) Program requires that the Accredited Person or any of its personnel involved in 510(k) reviews, which includes those who have authority over the review process, have no ownership or other financial interest in a device manufacturer or distributor that presents the appearance of a conflict of interest.
- I do not participate in the design, manufacture or distribution of any medical device.
- I do not provide consultative services to any device manufacturer or distributor regarding specific devices.

Signed: _____

Printed Name: Mark Job

Date: February 26, 2010

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Conflict of Interest
Declaration and Certification
For the review of the 510(k) submission from

Applicant: Lil' Drug Store Products, Inc.

Device Name or Model Name: Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reuseable Applicator)

Initials

CS I have read and understand Regulatory Technology Services LLC's Conflict of interest and Confidentiality Procedure (COI-S-0023), regarding conflict of interests and the attachments accompanying the procedure and am aware of my responsibilities under them.

CS I have not been employed within the last two years by the firm who submitted the 510(k) for evaluation.

CS I did not charge fees contingent or based upon the recommendation for initial classification (SE decision).

CS I have not performed testing in connection with this specific device 510(k).

CS I understand that the Accredited Persons (AP) Program requires that the Accredited Person or any of its personnel involved in 510(k) reviews, which includes those who have authority over the review process, have no ownership or other financial interest in a device manufacturer or distributor that presents the appearance of a conflict of interest.

CS I do not participate in the design, manufacture or distribution of any medical device.

CS I do not provide consultative services to any device manufacturer or distributor regarding specific devices.

Signed: Carole Stamp

Printed Name: Carole Stamp

Date: February 26, 2010

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RTS
Regulatory Technology Services LLC

Third Party Review
Reviewer Memorandum

Third Party Organization: Regulatory Technology Services LLC

Reviewer: Carole Stamp

Signature: Carole Stamp Date: April 18, 2010

Print Name: Carole Stamp Title: Reviewer

Primary Reviewer: Mark Job

Signature: Date: April 18, 2010

Print Name: Mark Job Title: Reviewer

Responsible Third Party Official

Signature: Date: April 18, 2010

Print Name: Todd J Shopp Title: Program Supervisor

510(k) Applicant's Name: **Lil' Drug Store Products, Inc.**

Device Name: **Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reusable Applicator)**

Contact Person: **Patricia L. Miller**

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I. Purpose and Submission Summary:

The 510(k) holder **Lil' Drug Store Products, Inc.** would like to introduce the **Replens Long-Lasting Vaginal Moisturizer** into interstate commerce as a vaginal patient lubricant device. This product, **Replens**, has been sold as a cosmetic in the U.S. since 1989 based on its intended use as a moisturizer. The sponsor has been marketing **Replens** with the understanding that it did not fall under the definition of a medical device under Section 201(h) of the Federal Food, Drug, and Cosmetic Act ("the Act") and was therefore not subject to the requirements for premarket clearance or approval under the Act. Based on recent discussions with CDRH, the sponsor understands that the Center's current position is that claims for relief of vaginal dryness may render a product a medical device under 21 C.F.R. § 880.6375 (Class I, Product Code MMS). **Lil' Drug Store Products, Inc.** has submitted a 510(k) premarket notification to support the marketing of Replens as a medical device for over-the-counter (OTC) use. During the review of the original submission dated February 25, 2010 one round of deficiencies was issued (March 16, 2010). Additional information was provided April 9, 2010 to respond to the deficiencies. All deficiencies have been adequately addressed.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use = **Over-the-Counter** Page Number: **Section 1.0**	X		
Truthful and Accuracy Statement Page Number: **Section 3.0**	X		
510(k) Summary Page Number: **Section 2.0**	X		
Standards Form (FDA Form 3654) Page Number: **Section 0.5**	X		

III. Device Description

	Yes	No	N/A
Is the device life-supporting or life sustaining?		X	
Is the device an implant (implanted longer than 30 days)?		X	
Does the device design use software?		X	
Is the device sterile?		X	
Is the device reusable (not reprocessed single use)?		X	
Are "cleaning" instructions included for the end user?		X	

The submission describes the **Replens Long-Lasting Vaginal Moisturizer Gel** as a non-sterile, water-based, vaginal moisturizing gel for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. It is not a contraceptive or spermicide and it does not contain any such component. Replens is a

(b)(4)

[redacted]

List of Materials

The list of materials for the **Replens Long-Lasting Vaginal Moisturizer Gel** is provided in the table below.

(b)(4) Proprietary Information

[redacted]

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(b)(4) Proprietary Information

[redacted]

IV. Indications for Use

The Replens Long-Lasting Vaginal Moisturizer is a non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

The indications for use of the new device are very similar to the indications for use of the predicate device without the claims for condom use and latex condom compatibility.

V. Predicate Device Comparison

Section 7.1 of the submission provides a comparison between the new device **Replens Long-Lasting Vaginal Moisturizer** submitted in this 510(k) and the CVS Personal Lubricant & Moisturizer by Lake Consumer Products, Inc. cleared under K062682. The following comparison information has been extracted from the submission and the 510(k) Summary for K062682 which includes a comparison of the device technological characteristics and the indications for use.

Characteristic / Feature	Replens Long-Lasting Vaginal Moisturizer (new device)	CVS Personal Lubricant & Moisturizer (K062682)
Labeled Condom Compatible	No	Yes
Personal lubricant	Yes	Yes
pH appropriate for vaginal use	Yes	Yes
Highly Viscous Gel	Yes	Yes
Color	White to Off-white	Clear
Density	1.01-1.04	Unknown
Safe for Long-term Use	Yes	Yes
Fragrance Free	Yes	Yes
Contains Water	Yes	Yes
Contains Glycerin	Yes	Yes
Contains Propylene Glycol	No	Yes
Contains Polyquaternium 15	No	Yes
Contains Methylparaben	Yes	Yes
Contains Polyparaben	No	Yes
Contains Mineral Oil NF	Yes	No
Contains Polycarbophil USP	Yes	No
Contains Carbomer Homopolymer Type	Yes	No

B NF		
Contains Hydrogenated Palm Oil Glyceride (GRAS per 21 CFR 184.1505)	Yes	No
Contains Sodium Hydroxide NF	Yes	No
Contains Sorbic Acid	Yes	No
Container	Aluminum Tube with Plastic (Polyethylene Applicator)	Plastic Bottle
Delivery	Applicator	Manually
Sterile	No	No

Both products are composed of similar ingredients and the technological characteristics are very similar. Replens is delivered in a reusable polyethylene applicator designed for vaginal use. The safety of the applicator has been demonstrated through its commercial use in the Replens Vaginal Moisturizer cosmetic product. Additionally, a vaginal applicator is used with RepHresh Vaginal Gel (K021737).

The formulation of Replens is similar to that of the CVS Personal Lubricant & Moisturizer. Water and glycerin represent approximately 92% of the Replens formulation and provide the primary lubrication and moisturizer characteristics of both Replens and the predicate device. While certain of the other ingredients differ between the two formulations, these other ingredients perform equivalent functions that can be safely accomplished via a variety of ingredients. Each product has ingredients that perform the following functions: vehicle, humectant, gel former and preservative. All ingredients included in Replens are either NF, USP, or are considered "generally recognized as safe for their intended use". In addition, these other Replens ingredients are commonly used in other devices and cosmetics for vaginal use.

Although they perform the same functions as analogous ingredients included in the CVS Personal Lubricant & Moisturizer, Replens contains the following ingredients that are not utilized in the predicate: polycarbophil, Carbomer Homopolymer Type B, mineral oil, hydrogenated palm oil glyceride, sorbic acid, and sodium hydroxide. All of these ingredients are well characterized and are used in other vaginal lubricants. Each ingredient and its characteristics are discussed in detail in section 7.1 of the submission.

Intended Use:

The Replens Long-Lasting Vaginal Moisturizer is intended for the same use as the over-the-counter predicate device, CVS Lubricant & Moisturizer. Both devices are non-sterile, aqueous gels intended for use as a vaginal lubricant and moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity.

The comparison of the indications for use statements is provided in the following table. The portions of the CVS Personal Lubricant & Moisturizer statement that do not match the proposed Replens Long-Lasting Vaginal Moisturizer statement are in bolded text.

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Replens Vaginal Moisturizer (35g Tube) New Device	CVS® Personal Lubricant & Moisturizer (K062682)
A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.	A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area **to enhance condom use and** to facilitate ease and comfort during intimate sexual activity. **CVS Personal Lubricant & Moisturizer is compatible with latex condoms.** This device is not a contraceptive or spermicide nor does it contain any such component.

The only differences between the Replens Long-Lasting Vaginal Moisturizer indications for use statement and the predicate device are that Replens does not claim to enhance condom use or to be compatible with latex condoms.

Conclusion

The differences in formulations between the predicate device and the new device have been adequately addressed by the biocompatibility testing, condom compatibility testing, and preservative effectiveness testing of the new device. Performance testing demonstrates that Replens is as safe as the predicate and other vaginal moisturizers. Therefore, based on the comparison of the device technological characteristics, the indications for use, and the safety and performance testing results, the Replens Long-Lasting Vaginal Moisturizer is substantially equivalent to the predicate device and does not raise new questions of safety or effectiveness.

VI. Labeling

The labeling is provided in section 5.4 and in the additional information that was provided April 9, 2010. The labeling includes all the appropriate instructions for use of this over-the-counter device and the applicable warnings to the user. Based on biocompatibility testing results that indicated the device was an eye irritant, a warning stating, "Keep out of eyes and ears" was added to the instructions for use. There are detailed instructions and diagrams to assist the user in understanding the proper use of the device, cleaning of the reusable applicator, along with a description of how the device works and a list of commonly asked questions with answers. No other specific claims are made which would raise questions of safety and effectiveness.

VII. Sterilization/Shelf Life/Reuse

(b)(4) Proprietary Information

[redacted]

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(b)(4) Proprietary Information

[redacted]

(b)(4) Proprietary Information

[redacted]

(b)(4) Proprietary Information

[redacted]

VIII. Biocompatibility

(b)(4) Proprietary Information

[redacted]

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(b)(4) Proprietary Information

[redacted]

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(b)(4) Proprietary Information

[redacted]

(b)(4) Proprietary Information

[redacted]

IX. Software

Version:		
Level of Concern:		
	Yes	No
Software description:		
Device Hazard Analysis:		
Software Requirements Specifications:		
Architecture Design Chart:		
Design Specifications:		
Traceability Analysis/Matrix:		
Development:		
Verification & Validation Testing:		
Revision level history:		
Unresolved anomalies:		

The device does not employ software.

X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

The device is not electrically powered.

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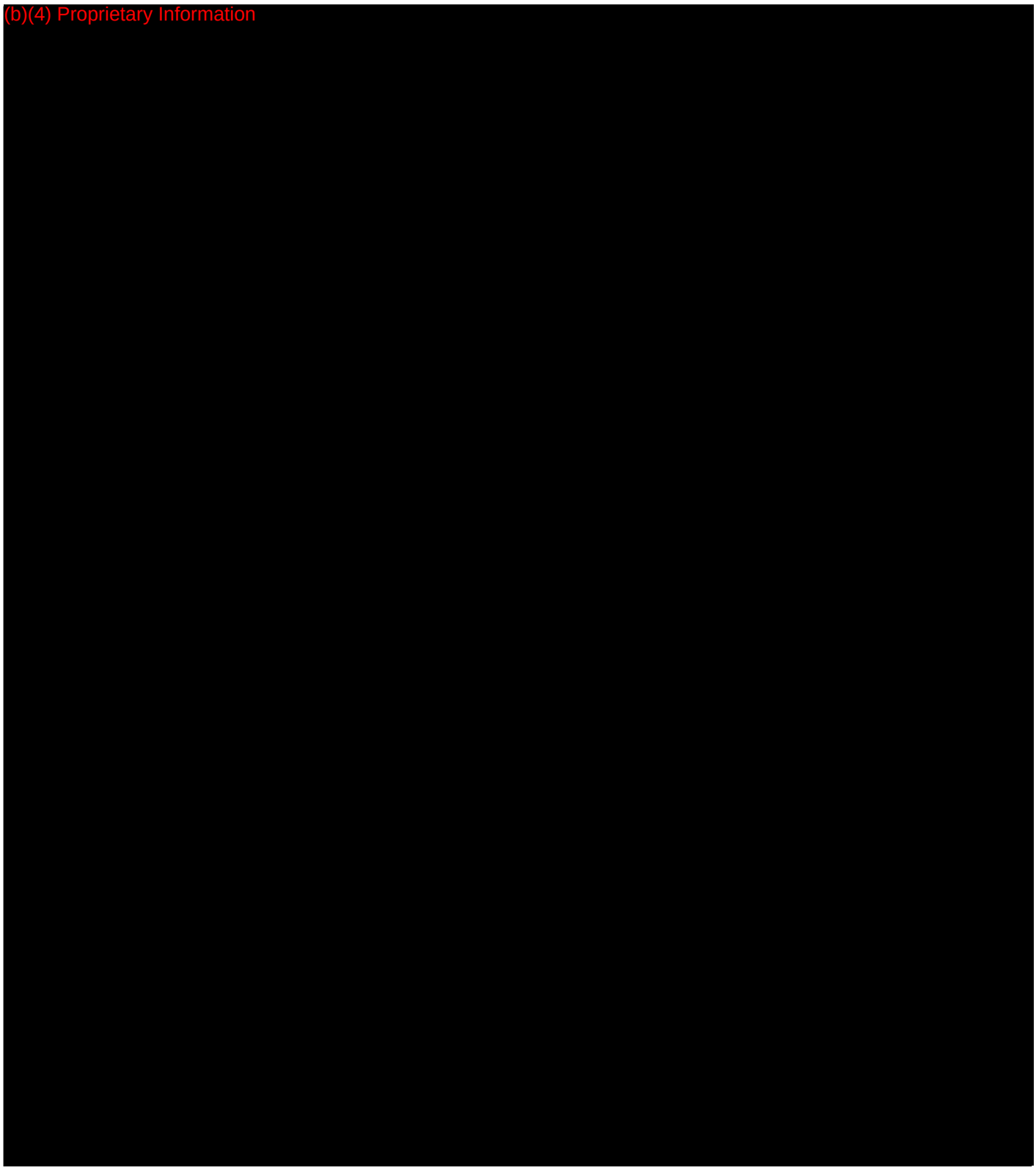
XI. Performance Testing – Bench

(b)(4) Proprietary Information

[redacted]

(b)(4) Proprietary Information



Conclusion

These biocompatibility and performance tests, along with the 20 year history of safe use of Replens in the U.S. when sold as a cosmetic (which, based on sales volume, translates to over 100 million doses), support the safety and effectiveness of the device for its intended use and its substantial equivalence to the predicate device. No new questions of safety and effectiveness are raised.

XII. Performance Testing – Animal

This submission does not include animal clinical testing or data.

XIII. Performance Testing – Clinical

This submission does not include human clinical testing or data

XIV. Substantial Equivalence Discussion

	Yes	No	
1. Same Indication Statement?	X		If **YES** = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If **YES** = Stop **NSE**
3. Same Technological Characteristics?	X		If **YES** = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If **YES** = Go To 6
5. Descriptive Characteristics Precise Enough?		X	If **NO** = Go To 8 If **YES** = Stop **SE**
6. New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NSE**
7. Accepted Scientific Methods Exist?			If **NO** = Stop **NSE**
8. Performance Data Available?	X		If **NO** = Request Data
9. Data Demonstrate Equivalence?	X		Final Decision: **SE**

Note: Document the decision path by marking the arrows followed on the FDA flowchart.

Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

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1. Explain how the new indication differs from the predicate device's indication:

2. Explain why there is or is not a new effect or safety or effectiveness issue:

3. Describe the new technological characteristics:

4. Explain how new characteristics could or could not affect safety or effectiveness:

5. Explain how descriptive characteristics are not precise enough:

   The submission includes the descriptive characteristics but the performance testing is needed to support substantial equivalence and demonstrate the similarities between the new device and the predicate device.

6. Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:

7. Explain why existing scientific methods cannot be used:

8. Explain what performance data is needed:

9. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

   As the reviewer of this submission I have reviewed the instructions for use, the sponsor's description of the device and compared this information against the information for the predicate device that was provided by the sponsor. The specifications for the predicate device and the new device have been compared. They are very similar. The comparison table demonstrates the similarities and differences between the new device and predicate device. The submission includes biocompatibility and performance testing which demonstrates the new device and the predicate device have similar performance characteristics. The labeling included in the submission was reviewed and found to be similar to the predicate labeling. There are no new questions of safety and effectiveness raised during this review.

   Based upon the above summary, a substantially equivalent decision is recommended.

XV. Deficiencies

During the review of the original submission dated February 25, 2010 one round of deficiencies was issued (March 16, 2010). Additional information was provided April 9, 2010 to respond to the deficiencies. All deficiencies have been adequately addressed.

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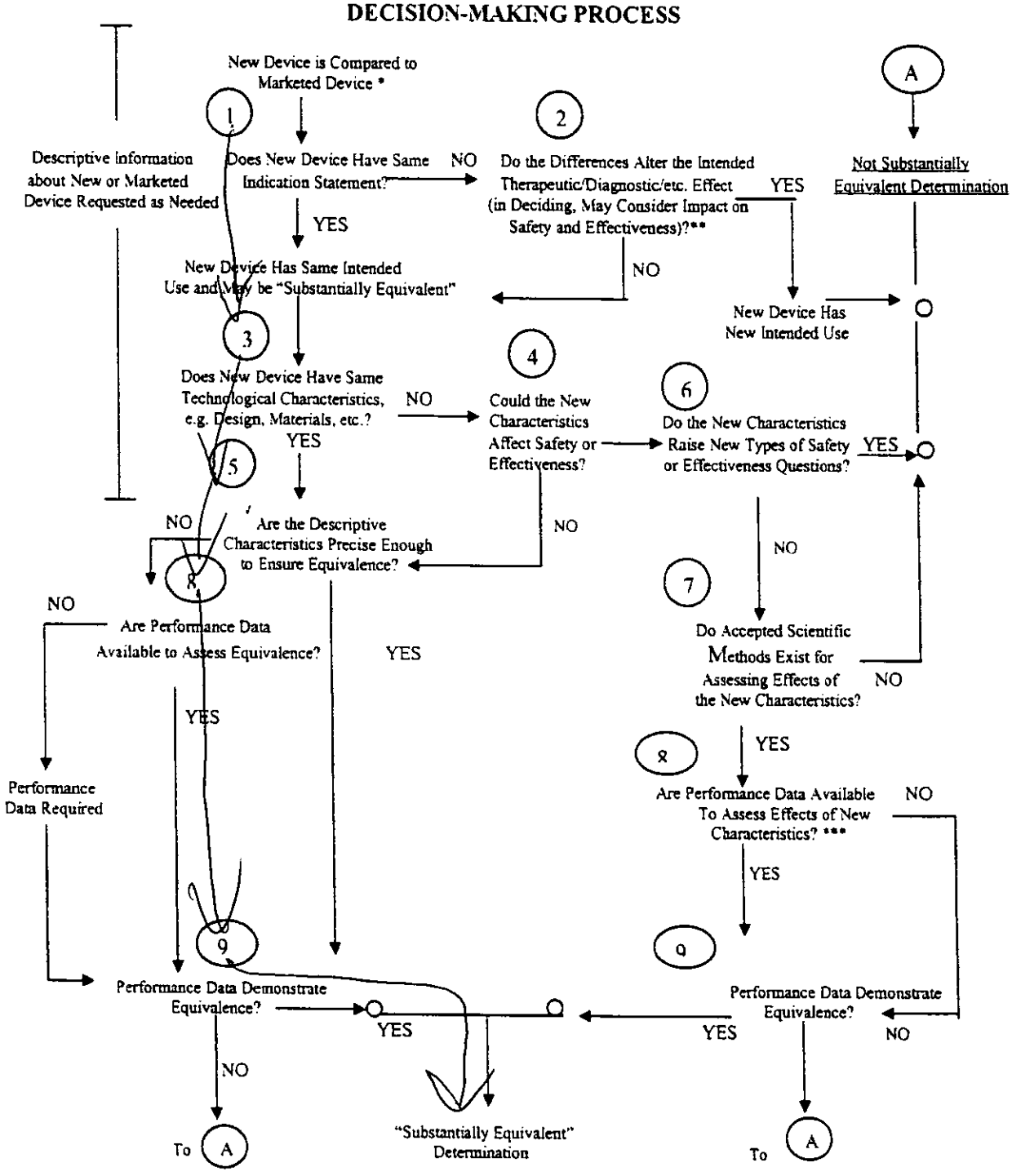
XVI. Contact History

All correspondence is included in the submission.

XVII. Recommendation

Classification Name:	**Lubricant, Vaginal, Patient**
Regulatory Class:	**I**
Product Code:	**MMS**
Classification Number:	**21 CFR 880.6375**

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



* 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

** This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

*** Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

Carole Stamp

From: Miller, Tricia [TMiller@lildrugstore.com]
Sent: Sunday, April 18, 2010 3:32 PM
To: Carole Stamp
Cc: MARK JOB
Subject: RE: Responses to Replens Deficiencies
Attachments: Stability (3159) 40C 75RH Lot RP01089T Feasibility batch 2 Mos Replens w paraben 23-Nov-09.pdf; Stability (3159) 25C 60RH Lot RP01089T Feasibility batch 3 Mos Replens w paraben 11-Nov-09.pdf; Stability (IGF) 25C 60RH Lot RP01123C Pilot batch 36 Mos Replens w paraben Dec-06.pdf

Carole--

Here's the information I have (available today) related to the 35g tube material changes and the new stability study data.

The validation batch that is part of the stability protocol that we provided in Appendix E.1 of the Replens 35g Tube 510(k) has not passed the three months yet so I don't have stability data to give you for that batch. However, we manufactured a feasibility batch at Pharmetics using exactly the same raw materials, aluminum tube, etc. and we do have data for that lot (RP01089T). I have attached the 3 month 25C/60RH and 2 month 40C/75RH stability data for that lot. We have data through 6 months for both of those temperatures, but I won't have access to those reports until tomorrow. I am also sending 36 month stability data at 25C/60RH for lot RP01123C. This lot made at Pharmetics is the same Replens formula as is used today (the suppliers for some of the raw materials have changed, but it was made with USP grade materials) and it is in the same aluminum tube as we currently use and it was packaged with the same reusable applicator as we currently use. I'm hopeful that these sets of stability data will be sufficient. If not, please let me know and I'll get the additional information tomorrow.

As far as what changed in the aluminum tube used at Fleet and Pharmetics, I'd have to consult with some others on a specific list of differences. They're from different suppliers, but the Pharmetics one was intended to match the Fleet one. I do have specifications for the Fleet aluminum tube if you'd like to see those. However, as I've now provided three year real time data from Pharmetics in the same gel formulation and aluminum tube as we submitted in the 510(k), it seems to me that it's not necessary to know the exact differences. Please let me know if you agree.

Thanks,
Tricia

-----Original Message-----
From: Carole Stamp [mailto:stamp.carole@gmail.com]
Sent: Sunday, April 18, 2010 2:28 PM
To: Miller, Tricia
Cc: 'MARK JOB'
Subject: RE: Responses to Replens Deficiencies

Hi Tricia,

Okay, I understand that the materials are different for the reusable and single use applicators.

So, you will still be updating me whether there were any reusable applicator material changes.

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And providing the information requested in the original email for the 35g tube material changes and the new stability study data.

hanks,
Carole

-----Original Message-----
From: Miller, Tricia [mailto:TMiller@lildrugstore.com]
Sent: Sunday, April 18, 2010 1:47 PM
To: Carole Stamp
Cc: MARK JOB
Subject: RE: Responses to Replens Deficiencies

Hi Carole,

I just saw your emails. I'm going to run into the office to try to grab the stability data for the 35g tube from the current supplier and information on the minor changes, but I can answer your questions from the email below at this point.

The reusable applicator material is different than the single-use applicator. I'd have to check at the office if it's the same as was used at the prior supplier. The biocompatibility tests we provided were performed on the current versions of both the reusable applicator and the pre-filled applicator. And for the 35g Tube version, the gel isn't stored in the reusable applicator. It only comes in contact with it when it's loaded with gel and then immediately dispensed. So there's no impact on stability. So t shouldn't matter if it's the same as was used at the prior supplier. Let e know if this isn't clear or you have a further question on it.

Regarding the Acute Exposure Dermal Toxicity test, that's one of the tests we inherited when purchased the rights to the product. So I can't give you an explanation of why it was only conducted on the Replens without methylparaben formulation. But as submitted in the response, it's not a required test (which is why we didn't run it at this time) and we included it more for informational purposes and because the other tests did not vary significantly between the two formulations so it should be representative of the results that would be obtained from the Replens with methylparaben formulation.

I'll check email when I get in the office to see if you have any follow-up questions on this.

Tricia

From: Carole Stamp [mailto:stamp.carole@gmail.com]
Sent: Sun 4/18/2010 12:09 PM
To: Miller, Tricia
Cc: 'MARK JOB'
Subject: RE: Responses to Replens Deficiencies

Hi Tricia,

Was the 35g Tube reusable applicator material changed the same as the single use applicator material? This was not clear in the 35g Tube response.

Also, there is no explanation in the 35g Tube response why the Acute Exposure Dermal Toxicity test was conducted only with the Replens without methylparaben formulation. Please explain.

Thanks,

Carole

From: Carole Stamp [mailto:stamp.carole@gmail.com]
Sent: Saturday, April 17, 2010 9:45 PM
To: 'Miller, Tricia'
Cc: 'MARK JOB'
Subject: RE: Responses to Replens Deficiencies

Hi Tricia,

As I was reading through your response to deficiency #8 on page 11 regarding the stability testing, I see there also was a material change to the 35g tube material. It says, "The tube material does vary between the two manufacturers." But you didn't identify what the change in material was. Can you clarify this for me? What are the two materials and what data do you have to demonstrate they perform the same and the change won't impact the stability data? Again, as this tube material is the container that is used to store the product while you determine the stability of the product, we will need the current stability study summary for the 35g Tube as well.

Thank you,

Carole

From: Miller, Tricia [mailto:TMiller@lildrugstore.com]
Sent: Friday, April 09, 2010 3:32 PM
To: MARK JOB; Carole Stamp
Subject: Responses to Replens Deficiencies

Hi Mark & Carole,

As soon as I hit send on this email, I will be running to UPS to drop off the hardcopies of the responses to the Replens 510(k) deficiency letters. I also included CDs in the package with all the files and I have attached them to this email in zip files as well in case you'd like to get started reviewing them. Within the zip files, you will find the main deficiency response letters along with related attachments. The main letters are titled:

- Replens (Apps) Response Letter v1.0.doc
- Replens (35g Tube) Response Letter v1.0.doc

As always, please let me know if you have any questions.

Best Regards,

Tricia Miller

Lil' Drug Store Products, Inc.

319-294-3745

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Lil' Drug Store Products

Response to 510(k) Deficiency Letter

April 9, 2010

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

Reference: **Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) 510(k) Deficiency Letter dated March 16, 2010**
Applicant: **Lil' Drug Store Products, Inc.**

Dear Sir or Madam:

Further to your deficiency letter dated March 16, 2010 for the Traditional 510(k) Premarket Notification for Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) ("Replens"), a vaginal moisturizer for treatment of vaginal dryness, please see below the response from the applicant. Your comments are restated in bold followed by the response.

1. **Please provide an updated 510(k) Summary with the word "Confidential" removed from the footer.**

   Please find attached an updated 510(k) Summary with the entire footer, including the word "Confidential" removed.

2. **Please provide an updated Indications for Use Form with the OTC line checked (to match with the OTC indications listed on the form).**

   Please find attached an updated Indications for Use Form with the OTC line checked and with the entire footer, including the word "Confidential" removed.

3. **The proposed draft labeling for the Replens device includes information and numerous statements that are not in the predicate device labeling provided. Similar statements can be found in the cosmetic labeling provided, however, these statements could be considered claims for a medical device requiring supporting data. We have contacted FDA for their recommendations. Based on their feedback any statements that are not in the labeling for other similar products currently**

on the market with a cleared 510(k) will have to be evaluated carefully on a case-by-case basis. Here is a general statement, indications for use, that FDA finds acceptable for this type of device:

[product name] is a [personal lubricant or vaginal moisturizer] for penile and/or vaginal application, intended to moisturize or lubricate, to enhance the ease or comfort of intimate sexual activity and supplement the body's natural lubrication.

This product is [or is not] compatible with latex [and/or synthetic] condoms.

Please provide updated labeling more similar to the predicate device labeling.

Please find attached carton, insert, and tube labeling for Replens to replace sections 5.1, 5.2, and 5.3 in the original 510(k) that have been updated based on the deficiency letter and a conference call between Tricia Miller (Lil' Drug Store Products), Mark Job (Regulatory Technology Services) and Carole Stamp (Regulatory Technology Services) on March 15, 2010. Additionally, a similar statement in the "Description of Device" section of the 510(k) Summary (section 2.0), also attached, has been updated. Table 1 below shows the labeling statements that have been revised.

Table 1: Labeling Revisions

Old Labeling Statement	New Labeling Statement(s)
Replenishes Vaginal Moisture	Helps Replenish Vaginal Moisture Supplements the body's natural lubrication
Long Lasting Formula lasts and lasts	Long Lasting Formula
Soothing, immediate relief	n/a
Natural Feeling	n/a

Old Labeling Statement	New Labeling Statement(s)
Provide vaginal dryness relief at the source of discomfort	Provide vaginal moisture at the source of discomfort
Relieves vaginal dryness	Helps replenish vaginal moisture
...there is no need to apply it just prior to intercourse in order to replenish vaginal moisture.	...there is no need to apply it just prior to intercourse.
Replenishes your natural vaginal moisture	Helps replenish your natural vaginal moisture

4. **Section 8.1 of the 510(k) states that Replens exhibited mild reactivity and was considered to be non-toxic based on the combined results of two Cytotoxicity (Agar Overlay) tests performed using the same protocol and lot. However, the report in Appendix B.1 states that "The sample meets USP and ISO requirements if none of the cell culture exposed to the sample shows greater than a mild reactivity (grade 2)." The results for Test 1 for the three test wells include two cell culture test wells with a score of 3. Please explain why two tests were run (Test 1 on 8 Jan 2010 and Test 2 on 29 Jan 2010). Please explain your conclusion considering there were 2 wells with a score of 3.**

   As noted in Deficiencies #4 and #7, Lil' Drug Store (through Nelson Laboratories) performed a series of tests to assess the biocompatibility of the Replens (35g Tube) formulation. All of these tests (as summarized fully in the attachment provided in response to Deficiency #7), with the exception of the cytotoxicity tests (and the IV Acute Systemic Toxicity test, which the company maintains is not an appropriate measure of the toxicity of Replens), supported the biocompatibility of the product. Of special note, both the vaginal irritation tests and local histology assessments following exposure of vaginal mucosa to Replens demonstrated that the product does not produce localized irritation.

   To address this apparent discrepancy between the cytotoxicity tests and the remaining panel of biocompatibility tests, the company

conducted a thorough investigation with the assistance of expert toxicologists and the testing facility. Specifically, while initial cytotoxicity tests showed variable reactivity, the company determined through its investigations and subsequent testing that the cause of the test result was the low pH of the sample being tested. The investigation and additional product testing to assess the impact of product pH is described below, and a table detailing the test methodologies used and results obtained is provided in Table 2, below.

As noted in this question, an initial cytotoxicity test was conducted for Replens (35g Tube) in which variable reactivity (*i.e.,* cytotoxicity scores of 2 or 3) were observed. As part of the preclinical test facility's investigation, the test was repeated using the same methodology and the results were non-cytotoxic for Replens (35g Tube) (*i.e.,* all three replicates produced a score of 2). The company concluded that the product was non-toxic based upon an average score of 2 for the six wells tested in these two tests. This data was presented in the 510(k) notice.

Upon further review of the cytotoxicity testing standards, Lil' Drug Store recognizes that the initial and retest results demonstrate a potential ambiguity. To further evaluate the potential for "borderline cytotoxic" results and to respond to the Third Party Reviewer's questions, the company consulted with the test laboratory to investigate the theory that the observed borderline cytotoxic test result observed in the initial test may have been due to an excess of the Replens gel applied to the filter paper that could have spread beyond the paper's surface area during the incubation period and caused a result classified as cytotoxic. The company performed a third cytotoxicity test utilizing a highly controlled amount of product. This experimental test, as summarized in Table 2, below, also demonstrated a potential cytotoxic response that differs from the remaining, applicable biocompatibility tests for the Replens (35g Tube) samples.

Lil' Drug Store then consulted with a toxicologist to understand possible root causes for the observed discrepancy between cytotoxicity tests and, more importantly, between the cytotoxicity tests and the completed vaginal mucosal contact tests. During this review, the company and its consultants noted that the Replens product specification for pH ranges between 2.5-3.5, while the approximate pH of the cell culture media used in the cytotoxicity test is 7.5. Therefore, the low pH of Replens would be expected to contribute to the observed reactivity. ISO 10993-5 §8.5.2 recommends that care is taken in the

choice of evaluation methods, as the test results can be invalid if the test sample releases substances (e.g., low pH) that interfere with the test system or measurement. The difference between product pH and the cytotoxicity media pH also may explain the discrepancy between the cytotoxicity test and the vaginal irritation tests, as the vaginal mucosa routinely maintains a pH ≤ 4.5[1].

Therefore, to assess whether sample pH could be the cause of the discrepant results, the company repeated the cytotoxicity after adjusting the pH of the Replens gel sample to a range of 7.0-7.5 by titrating the sample with sodium hydroxide, which is already part of the Replens formulation. This method was expected to accurately characterize the cytotoxicity of the Replens (35g Tube) formulation, as the toxic effect of low pH on the L929 cell line will have been accounted for. As summarized in Table 2, this test showed non-cytotoxic results for the Replens (35g Tube) samples.

Lil' Drug Store concludes that the results of the additional testing demonstrate that the pH of Replens played a significant role in the previously observed, variable cytotoxicity results. Therefore, the company believes that the results of the first three tests are not valid because the test methodology was not appropriate to the product, given the product's low pH. As confirmed by both the *in vivo* vaginal irritation tests and the repeated cytotoxicity tests (with pH adjustment), Lil' Drug Store concludes that the product is not cytotoxic. It is important to note that, while the low pH of Replens may be harmful to the cells used in this test (L929 mouse fibroblast cell line), it is appropriate to the product's intended use as a vaginal moisturizer and lubricant, as the healthy vaginal pH is also low (<4.5). In support of this conclusion, Replens was found to be a non-irritant in acute and subacute vaginal irritation studies. These studies were presented in the original 510(k) notice.

[1] Boskey ER, Telsch KM, Whaley KJ, et al. Acid production by vaginal flora in vitro is consistent with the rate and extent of vaginal acidification. *Infect Immun.* 1999;67:5170-5175.

(b)(4) Test Data

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5. **Several reports in Appendix B were for different sponsors than Lil' Drug Store (such as, Guidelines, Inc. of Miami, FL and Columbia Research Labs, Inc. of New York, NY). Please explain how all the various sponsors are related to Lil' Drug Store.**

   Columbia Laboratories developed Replens and first launched it in May 1989. Warner Lambert marketed the product under license from 1991 to April 1998. From May 1998 to approximately May 2000, Columbia again marketed the product. Lil' Drug Store Products has marketed Replens in the U.S. under license from Columbia Laboratories from May 2000 to present. Lil' Drug Store Products has marketed Replens worldwide under license from Columbia Laboratories from June 2004 to present.

   Lil' Drug Store Products has no relationship with Guidelines, Inc. of Miami, FL. Lil' Drug Store Products received the reports for the tests sponsored by both Columbia Laboratories and Guidelines, Inc. from Columbia.

6. **Several test reports in Appendix B were completed in 1989 and 1991 using test samples called "vaginal moisturizer, Lot 324CB2" or "Polycarbophil gel, Lot DGBE" or "PKPS 001, Lot 324CB2." Please explain what formulations were tested and whether they are identical to the current formulation of Replens with methylparaben described in this submission.**

   The Replens gel formulation used in the biocompatibility tests completed in 1989 and 1991 is identical to the formulation of Replens with methylparaben described in this application with the exception of the Acute Exposure Dermal Toxicity test in Appendix B.9. This test was performed on the Replens gel formulation that does not include methylparaben, but is otherwise identical. The ingredients and grade of the formulation used in the biocompatibility tests are identical; however, the suppliers are different for some of the materials.

   As further clarification, Table 3 below lists each Appendix in the 510(k) that contains a Biocompatibility Test Report for Replens gel with methylparaben and then identifies the lot number used in that test (as identified in the report) and the Replens formulation that corresponds with the lot number.

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

Table 3: Replens Formulation Used in Testing

Appendix	Lot Number	Formulation
B.1	RP01079T	Identical formulation
B.2	324CB2	Identical formulation
B.3	324CB2	Identical formulation
B.4	324CB2	Identical formulation
B.5	RP01079T	Identical formulation
B.6	324CB2	Identical formulation
B.7	DLBD	Identical formulation
B.8	DLBD	Identical formulation
B.9	DGBE	Replens without methylparaben
B.10	DLBD	Identical formulation
B.11	DLBD	Identical formulation

7. **Please update the Biocompatibility summary tables in section 8.1 to include the test method or standard that was followed.**

   Please find attached a Detailed Summary of Biocompatibility Testing for Replens.

8. **Please explain what formulations manufactured by Fleet were tested in the 4 lots of product stability testing (Appendix E.2) and whether they are identical to the current formulation of Replens manufactured by Pharmetics Incorporated.**

   The gel formulation manufactured by Fleet, tested in the 4 lots of product stability testing (Appendix E.2), is identical to the current formulation of Replens manufactured by Pharmetics Incorporated. The ingredients and grade are identical; however, the suppliers are different for some of the materials. The tube material does vary between the two manufacturers.

   As outlined in Appendix E.1, Pharmetics is in the process of conducting stability testing on the current configuration of Replens. The Pharmetics stability data for Replens completed to date, trends to be within specification for three years and also trends consistently with the Fleet stability data. Therefore, Lil' Drug Store does not consider the difference in gel material suppliers or tube materials to be significant in terms of the shelf life of the product and believes that a shelf life of three years is supported.

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

Lil' Drug Store Products

Please do not hesitate to contact me at (319) 294-3745 or by email at tmiller@lildrugstore.com should you require any clarification regarding this response.

Sincerely,

Patricia L. Miller
Lil' Drug Store Products, Inc.
Director of Regulatory

Lil' Drug Store Products

Attachments:

2.0 510k Summary (35g Tube) v2.0 (Revised)

1.0 Indications for Use Statement v2.0 (Revised)

5.1 Tube Carton (87100C-US-03-10) v3.0 (Revised)

5.2 Tube Insert (87100I-US-03-10) v3.0 (Revised)

5.3 Tube (87100T-US-03-10) v3.0 (Revised)

Replens (Tube) Cytotoxicity Test Report (518870) 3 (New)

Replens (Tube) Cytotoxicity Test Report (521126) pH adj (New)

Detailed Summary of Biocompatibility Testing (35g Tube) v1.0 (New)

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

510(k) Summary

Submitter:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Contact Person:
Tricia Miller
Director of Regulatory
Telephone: 319-294-3745
Facsimile: 319-393-3494
Email: tmiller@lildrugstore.com

Date:
February 25, 2010

Proprietary Name:
Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Common name:
Personal Lubricant

Classification name:
21 C.F.R. 880.6375 Lubricant, Patient, Vaginal
Product Code: MMS
Class: 1
Review Panel: General Hospital

Predicate Devices:

Device Name: CVS Personal Lubricant & Moisturizer
510(k) Number: K062682
Product Code: NUC, MMS

Intended Use:

A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease

and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Description of Device

Replens Vaginal Moisturizer is a non-sterile, water-based, white to off-white, non-irritating, non-greasy, non-staining vaginal gel delivered in a tube with a reusable applicator as a long-lasting moisturizer for vaginal dryness. The use of the reusable applicator provides less mess in application. Replens Vaginal Moisturizer is intended for ongoing use, not exclusively for use during intimate sexual activity.

Replens Vaginal Moisturizer contains ingredients commonly used in other products for vaginal use sold as medical devices and cosmetics. All ingredients are either NF, USP, or are considered "generally recognized as safe for their intended use". The quantitative formulation is considered confidential commercial information.

Technological Characteristics of the Device

Replens Vaginal Moisturizer is substantially equivalent to the identified previously cleared vaginal lubricant predicate with respect to its design and materials, principle of operation, function, formulation, and intended use. It is also substantially equivalent to other water-based vaginal lubricants and personal lubricants being commercially marketed in the U.S.

Summary of Performance Data

Biocompatibility Testing: The following biocompatibility testing has been performed on Replens Long-Lasting Vaginal Moisturizer:

- Cytotoxicity
- Acute Vaginal Irritation
- Subacute Vaginal Irritation
- Subacute Vaginal Irritation with Histological Examination
- Acute Systemic Toxicity
- Hypersensitivity
- Acute Oral Toxicity
- Acute Dermal Toxicity
- Dermal Irritation
- Eye Irritation.

Stability Data: Real-time stability data confirms a shelf life of three (3) years for Replens Long-Lasting Vaginal Moisturizer.
Preservative Effectiveness: Replens Long-Lasting Vaginal Moisturizer has successfully passed the requirements of the USP <51> Antimicrobial Effectiveness Test.
Condom Compatibility Testing: Condom compatibility testing confirms that Replens Long-Lasting Vaginal Moisturizer does not materially affect the strength or integrity of latex or synthetic condoms.

Conclusion

Based on the information presented in the 510(k) notice, it is concluded that Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) for OTC use is safe and effective for its proposed indications and is substantially equivalent in intended use, formulation, safety, and technological characteristics to the identified predicate device and other similar water-based personal lubricants.

STATEMENT OF INDICATIONS FOR USE

510(k) Number: _____

Device Name: Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Indications for Use: A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Prescription Use _____ OR Over-the-Counter Use __X___
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Replens Vaginal Moisturizer (35g Tube) 510k

Front & Back Panel

Estrogen Free
Replens Logo
Long-Lasting Vaginal Moisturizer

- Helps Replenish Vaginal Moisture
- Supplements the body's natural lubrication
- Long Lasting Formula

14 Applications
One reusable applicator

NET WT 1.23 OZ (35 G) EACH

Side Panels

- Estrogen Free
- Fragrance Free

Vaginal dryness can be a serious problem for women of menopausal age and beyond, new mothers, cancer/chemotherapy patients and women with dryness due to medications, stress or tampon use. Replens helps replenish vaginal moisture and provides long-lasting results.

Comfortable applicator delivers just the right amount of Replens Long-Lasting Vaginal Moisturizer to provide vaginal moisture at the source of discomfort. The patented formula keeps Replens in place to deliver moisture for long-lasting hydration with less mess.

(Applicator diagram)

Usage: Use one application every three days or as needed for day-to-day comfort and moisture.

Warnings:

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE:
For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened.

Ingredients:
PURIFIED WATER, GLYCERIN, MINERAL OIL, POLYCARBOPHIL, CARBOMER HOMOPOLYMER TYPE B, HYDROGENATED PALM OIL GLYCERIDE, METHYLPARABEN, SORBIC ACID, SODIUM HYDROXIDE

Questions? 1-877-507-6516 (M-F 8AM-4:30PM CST) or www.replens.com
Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Top Panel
Replens Logo
Long-Lasting vaginal moisturizer

Bottom Panel
Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.
UPC code
LOT #
EXP
Made in Canada

Right Bottom Tab
87100C-US-03-10

Replens LONG-LASTING vaginal moisturizer

Please read the following carefully before use.

Warnings

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of the reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE: For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened. Return entire contents with receipt to place of purchase.

Directions for Reusable Applicator

Note: Do not roll the tube up like a toothpaste tube. This may cause the tube to crack.

1. Remove cap from Replens tube. Break seal on tube opening by puncturing it with the opposite end of the cap. Screw the open end of the applicator onto the tube. (Figure 1).
2. Gently squeeze the tube, pushing Replens into the open barrel of the applicator. DO NOT roll up the tube. The applicator contains the recommended amount when the plunger stops (approx. 1 inch). (Figure 2)
3. Unscrew the applicator from the tube. Replace cap.
4. While sitting, standing or lying on your back with knees bent, gently insert open end of applicator into the vagina as deeply as it will go comfortably. Holding the applicator in place with thumb and middle finger, press the plunger until it stops. (Figure 3) Withdraw the applicator.
5. After use, pull the plunger all the way out of the barrel. (Figure 4) Wash both parts of the applicator in warm, soapy water. Rinse thoroughly and dry. To reassemble, gently push the plunger back into the barrel as far as it will go.

How Does Replens Work?

Replens Long-Lasting Vaginal Moisturizer contains a patented ingredient for soothing and long-lasting moisture. When you apply Replens, it immediately goes to work to provide long lasting moisture. As the cells of the vaginal wall are regenerated, dry cells are cleared and Replens is eliminated naturally. As with dry skin that you experience on your face and hands, regular moisturizing treatment may be necessary to prevent dryness from recurring.

Commonly Asked Questions...

How often should Replens Long-Lasting Vaginal Moisturizer be used?
For most women, Replens Long-Lasting Vaginal Moisturizer should be used every three days for best results. However, depending on the severity of your dryness, Replens can be used more or less frequently, as necessary. Replens is safe to use daily.

When should Replens Long-Lasting Vaginal Moisturizer be used?
Replens can be used any time of day or night. Replens works best when used on a regular schedule and not just prior to intercourse. Because Replens delivers long lasting moisture, there is no need to apply it just prior to intercourse. We recommend using Replens at least 2 hours prior to intercourse to allow proper moisturization.

Will Replens Long Lasting Moisturizer make intimacy more enjoyable? One of the most common ways that women discover vaginal dryness is during intimacy. When used regularly, Replens helps replenish your natural vaginal moisture, making intimacy more enjoyable. Replens' formula delivers long lasting moisture so sexual intercourse can be more spontaneous. Since Replens does not need to be applied immediately before intercourse, it does not interrupt the moment by being runny, messy or slippery. Instead, Replens provides long-lasting lubrication whenever the moment is right.

What causes vaginal dryness? Nearly every woman will experience vaginal dryness sometime in her life. It is most often associated with the normal decline or fluctuation of the female hormone estrogen. This fluctuation can be triggered by childbirth, breastfeeding or menopause. Dryness can also be caused by taking certain medications, exercising intensively or being under stress. It is also common to experience vaginal dryness when douching, using tampons or at the end of the menstrual cycle.

Can Replens be used as birth control? No. Replens does not contain spermicide. It is not a contraceptive.

Should I use Replens during my period? No. It is best to resume use after your flow completely stops.

Are there any side effects after using Replens? Some women notice a residue or discharge after initial use of Replens. This is caused by the elimination of dead skin cells. Your body naturally sheds dry vaginal tissue that has built up over time. When used on a regular basis, Replens will help prevent the buildup of dead skin cells and the discharge should dissipate. If the discharge does not dissipate, you may wish to wait an extra day or two between applications. While use is recommended every three days, every woman is unique and you may wish to increase or decrease the amount of time between Replens applications to maximize moisture and minimize discharge.

For additional information, visit our website at: www.replens.com or call toll-free 1-877-507-6516 (M-F 8AM – 4:30PM CST).

Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.

Replens Logo
Long-Lasting Vaginal Moisturizer

- Helps Replenish Vaginal Moisture
- Supplements the body's natural lubrication
- Long Lasting Formula

14 Applications NET WT 1.23 OZ (35 G) TUBE

The Replens applicator delivers just the right amount of Replens Long-Lasting Vaginal Moisturizer to provide vaginal moisture at the source of discomfort.

Usage: Use one application every three days or as needed for day-to-day comfort and moisture.
Directions: See enclosed pamphlet.

TAMPER EVIDENT FEATURE: For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened.

Ingredients: PURIFIED WATER, GLYCERIN, MINERAL OIL, POLYCARBOPHIL, CARBOMER HOMOPOLYMER TYPE B, HYDROGENATED PALM OIL GLYCERIDE, METHYLPARABEN, SORBIC ACID, SODIUM HYDROXIDE

Questions? 1-877-507-6516 (M-F 8AM-4:30PM CST) or www.replens.com

Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

87100T-US-03-10

(Near end of tube) Do not roll the tube as this may cause the tube to crack.

LOT
EXP

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

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(b)(4) Proprietary Information, Test Data

Carole Stamp

From: Carole Stamp [stamp.carole@gmail.com]
ent: Tuesday, March 16, 2010 8:49 PM
To: 'Miller, Tricia'
Cc: 'Mark Job'
Subject: Deficiency Record for Replens 35g Tube
Attachments: Replens 35g Tube Deficiencies 16 Mar 2010.doc

Hello Tricia,

Attached is the deficiency record for the substantive review of the Replens 35g Tube. This is very similar to the one you have already except I added something that I missed on the first one (see #7). Please also provide updated biocompatibility tables for the Applicator 510(k) as well.

Any questions, let me know.

Thanks!
Carole

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Record of Deficiencies From Substantive Review

Device Name or Model Name: **Replens Long-Lasting Vaginal Moisturizer (35g Tube)**

Date: **March 16, 2010**

Please provide the following information.

1. Please provide an updated 510(k) Summary with the word "Confidential" removed from the footer.
2. Please provide an updated Indications for Use Form with the OTC line checked (to match with the OTC indications listed on the form).
3. The proposed draft labeling for the Replens device includes information and numerous statements that are not in the predicate device labeling provided. Similar statements can be found in the cosmetic labeling provided, however, these statements could be considered claims for a medical device requiring supporting data. We have contacted FDA for their recommendations. Based on their feedback any statements that are not in the labeling for other similar products currently on the market with a cleared 510(k) will have to be evaluated carefully on a case-by-case basis. Here is a general statement, indications for use, that FDA finds acceptable for this type of device:

   [product name] is a [personal lubricant or vaginal moisturizer] for penile and/or vaginal application, intended to moisturize or lubricate, to enhance the ease or comfort of intimate sexual activity and supplement the body's natural lubrication.

   This product is [or is not] compatible with latex [and/or synthetic] condoms.

   Please provide updated labeling more similar to the predicate device labeling.
4. Section 8.1 of the 510(k) states that Replens exhibited mild reactivity and was considered to be non-toxic based on the combined results of two Cytotoxicity (Agar Overlay) tests performed using the same protocol and lot. However, the report in Appendix B.1 states that "The sample meets USP and ISO requirements if none of the cell culture exposed to the sample shows greater than a mild reactivity (grade 2)." The results for Test 1 for the three test wells include two cell culture test wells with a score of 3. Please explain why two tests were run (Test 1 on 8 Jan 2010 and Test 2 on 29 Jan 2010). Please explain your conclusion considering there were 2 wells with a score of 3.
5. Several reports in Appendix B were for different sponsors than Lil' Drug Store (such as, Guidelines, Inc. of Miami, FL and Columbia Research Labs, Inc. of New York, NY). Please explain how all the various sponsors are related to Lil' Drug Store.
6. Several test reports in Appendix B were completed in 1989 and 1991 using test samples called "vaginal moisturizer, Lot 324CB2" or "Polycarbophil gel, Lot DGBE" or "PKPS 001, Lot 324CB2." Please explain what formulations were tested and whether

they are identical to the current formulation of Replens with methylparaben described in this submission.

7. Please update the Biocompatibility summary tables in section 8.1 to include the test method or standard that was followed.
8. Please explain what formulations manufactured by Fleet were tested in the 4 lots of product stability testing (Appendix E.2) and whether they are identical to the current formulation of Replens manufactured by Pharmetics Incorporated.

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Date: February 26, 2010

Patricia Miller
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Re: Replens Long-Lasting Vaginal Moisturizer
(35g Tube with Reuseable Applicator)

Dear Ms. Miller,

This letter is to acknowledge on February 26, 2010, Regulatory Technology Services LLC received the 510(k) dated February 25, 2010 for the Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reuseable Applicator).

We have completed the administrative review according to the 510(k) checklist, the FDA guidance documents titled ***"Format for Traditional and Abbreviated 510(k)s"*** **Dated: August 12, 2005** for preparing a 510(k) **and contact with the General Hospital Branch Chief** for device under third party review. We have found all required items present and have begun the substantive review. We will keep you informed as the review continues.

If you have any questions, please do not hesitate to contact me. You may reach me at 763 682 4139.

Sincerely,

Mark Job
Reviewer

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Part Acceptance / Non-acceptance

1. Accredited Person:

Name: Regulatory Technology Services LLC

Address 1394 25th Street NW

Buffalo, MN 55313

Contact: Mark Job

Telephone: 763 682 4139 Fax: 763 682 4420

2. Foreign Accredited Person, Specify a Domestic Correspondent:

Name: N/A

Address

Contact:

Telephone: Fax:

3. 510(k) Owner (Applicant, Manufacturer, other persons preparing 510(k))

Name: Lil' Drug Store Products, Inc.

Address 1201 Continental Place NE

Cedar Rapids, IA 52402

Contact: Patricia (Tricia) L. Miller

Telephone: 319-294-3745 Fax: 319-393-3494

STOP!

Before completing items 4 to 9 below, complete pages 3 – 6 of this document.

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4. Device Name:

Trade or Proprietary Name: Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reusable Applicator)

Classification Name: Lubricant, Vaginal, Patient

5. CFR Classification Citation: 21 CFR 880.6375 (see 21 CFR 862 through 892)

6. Classification Panel: General Hospital

7. Based on my completion of this document, I recommend that this 510(k):

☒ Be accepted for substantive review and I have notified the 510(k) owner using RPP-F-0016.

☐ Not be accepted for substantive review and I have listed the deficiencies on RPP-F-0016.

8. Primary Reviewer

Carole Stamp
Signature

3/4/2010
Date

CAROLE STAMP
Print Name

9. Supervisor

Todd J. Shopp
Signature

4/18/10
Date

TODD J. SHOPP
Print Name

Checklist Questions:	YES	NO	Instructions
1. a). Is the device one that FDA has determined as being acceptable for third party review?	☒	☐	If NO, telephone DSMA for instructions. --STOP REVIEW--
1 b). Have you confirmed that the manufacturer has not engaged in forum shopping?	☒	☐	If NO, telephone DSMA for instructions. --STOP REVIEW--
2. Is the device trade or proprietary name included?	☒	☐	If NO, note deficiency on RPP-F-0013.
3. Is the device common or usual name included?	☒	☐	If NO, note deficiency on RPP-F-0013.
4. Is the device classification name, class of the device, and regulation number (21 CFR 880.6375) included?	☒	☐	If NO, note deficiency on RPP-F-0013.
5. Is the classification panel included?	☒	☐	If NO, note deficiency on RPP-F-0013.
6. Has the applicant complied with Section 514 of the Act? (Section 514 relates to performance standards for class II devices. At this time, there are no 514 standards. Therefore, your answer should be yes.)	☒	☐	If NO, note deficiency on RPP-F-0013.
7. Does the submission include proposed labels, labeling, and advertisements (if available) that describe the device, its intended use, and directions for use (ODE Guidance Memorandum #G91-1)?	☒	☐	If NO, note deficiency on RPP-F-0013.
8. Does the submission contain the "Indications for Use" form?	☒	☐	If YES, indicate page number Section 1.0. If NO, note deficiency on RPP-F-0013.

Checklist Questions:	YES	NO	Instructions
9. Does the submission contain an acceptable 510(k) Summary of Safety and Effectiveness (per 21 CFR 807.92) OR an acceptable 510(k) Statement (per 21 CFR 807.93) that safety and effectiveness information will be made available to any person upon request?	☒	☐	If YES, indicate page number Section 2.0. If NO, note deficiency on RPP-F-0013.
10. Does the submission contain photographs of the device if applicable?	☒	☐	If NO, note deficiency on RPP-F-0013.
11. Does the submission contain drawings for the device with dimensions and tolerances if applicable?	☒	☐	If NO, note deficiency on RPP-F-0013.
12. Does the submission identify the device to which equivalence is claimed?	☒	☐	
13. If the answer to question 12 is YES, did the applicant identify:			
a. Predicate device (referred to as marketed device)?	☐	☒	
b. Legally marketed device (referred to as marketed device)?	☒	☐	Note deficiency on RPP-F-0013.
Note: A predicate device is a device that was legally in commercial distribution in the U.S. on or before May 28, 1976 (referred to as a pre-amendments device) or a device that was marketed after May 28, 1976 (referred to as a post amendments device) that was reclassified from class III to class I or II. A marketed device can be a predicate device but is most often a device that FDA has determined is SE to another marketed device (21 CFR 807.92(a)3). IT IS YOUR RESPONSIBILITY TO MAKE SURE THAT THE PREDICATE DEVICE OR LEGALLY MARKETED DEVICE IDENTIFIED IS LEGITIMATE. If it is not, the review must STOP. Telephone DSMA for assistance.			List all 510(k) control numbers: K062682

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Checklist Questions:	YES	NO	Instructions
14. Does the submission contain information about the marketed device(s) identified in questions 12 and 13 above to which equivalence is claimed, including labeling and a description of the device?	☒	☐	If NO, note deficiency on RPP-F-0013.
15. Does the submission contain a statement/comparison of similarities and/or differences between the new device and the marketed device? (The new device that is the subject of this 510(k) can be either a new device or a modification to the existing device.)	☒	☐	If NO, note deficiency on RPP-F-0013.
16. Does the submission contain the Truthful and Accurate Statement (per 21 CFR 807.87(j))?	☒	☐	If YES, indicate page number Section 3.0. If NO, note deficiency on RPP-F-0013.
17. Does the submission contain the submitter's name, address, contact person, telephone number, and fax number?	☒	☐	If NO, note deficiency on RPP-F-0013.
18. If there is a representative or consultant, does the submission contain their name, address, contact person, telephone number, and fax number?	☒	☐	If NO, note deficiency on RPP-F-0013.
19. Does the submission contain a table of contents with pagination?	☒	☐	If NO, note deficiency on RPP-F-0013.
20. If the submitter has a manufacturing facility (contract or owned), and/or a sterilization facility (contract or owned), is the address(es) contained in the submission?	☒	☐	If NO, note deficiency on RPP-F-0013.
21. Does the submission contain a comparison table of the new device to the marketed device?	☒	☐	If NO, note deficiency on RPP-F-0013.
22. Does the submission contain information about the action taken to comply with voluntary standards?	☒	☐	If NO, note deficiency on RPP-F-0013.

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Checklist Questions:	YES	NO	Instructions
23. Does the submission contain performance data (can be bench or animal but not clinical), i.e.: Is there performance data for the marketed device? a. Bench testing? b. Animal testing? Is there performance data for the new device? a. Bench testing? b. Animal testing?	☐ ☐ ☒ ☒	☒ ☒ ☐ ☐	If NO, note deficiency on RPP-F-0013. Predicate testing not needed, tested per standards. If NO, note deficiency on RPP-F-0013.
24. If the device is labeled as sterile, does the submission contain sterilization data?	☒	☐	If NO, note deficiency on RPP-F-0013.
25. Does the device incorporate a computer or computer software? a. If YES, is there information about the hardware? b. If YES, is there information about the software?	☐ ☐ ☐	☒ ☐ ☐	If NO, note deficiency on RPP-F-0013.
26. a) Is there a specific guidance document for this type of device? Title: _____	☐	☒	If YES, continue review with checklist from the specific guidance document and return to question 27. If NO, proceed to question 26 b).
26 b) Contact the appropriate ODE Branch Chief to obtain information for reviewing this type of device. Has a summary of this discussion been documented?	☒	☐	If YES, answer question 27. If NO, do not proceed to question 27; stop review until summary completed.
27 Is this 510(k) sufficiently complete to allow substantive review?	☒	☐	If YES, continue review using specific guidance document or if no specific guidance document, continue the review using documentation forms. If NO, note deficiency on RPP-F-0013.

Authorization Form

Regulatory Technology Services LLC

Date: February 25, 2010

Regulatory Technology Services LLC
1394 25th Street NW
Buffalo, MN 55313

Re: Authorization for Accredited Person Review of 510(k)

To Whom It May Concern:

Enclosed is the Premarket Notification 510(k) for the following product Replens Long-Lasting Vaginal Moisturizer (in 35g Tube) manufactured by Lil' Drug Store Products Inc.

We at Lil' Drug Store Products (*name of manufacturer*) hereby authorize Regulatory Technology Services LLC to submit the enclosed 510(k) to the Food and Drug Administration (FDA) on our behalf, discuss its contents with the FDA, and function as the Accredited Person to perform the third party review.

We certify that we have not contacted another Accredited Person to perform the review of this 510(k) submission.

We accept the quote for 510(k) review services including the Regulatory Technology Services LLC Terms and Conditions.

Sincerely,

Patricia L. Miller
Lil' Drug Store Products, Inc.

Signature and
Name of Manufacturer Representative
Director of Regulatory

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: August 31, 2010.
See OMB Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
February 25, 2010	n/a, using 3rd Party Review	

SECTION A TYPE OF SUBMISSION

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

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

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

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Lil' Drug Store Products, Inc.	3003491851		
Division Name *(if applicable)*	**Phone Number** *(including area code)*		
	319-294-3745		
Street Address	**FAX Number** *(including area code)*		
1201 Continental Place NE	319-393-3494		
City	**State / Province**	**ZIP/Postal Code**	**Country**
Cedar Rapids	IA	52402	USA
Contact Name			
Patricia (Tricia) L. Miller			
Contact Title	**Contact E-mail Address**		
Director of Regulatory	TMiller@lildrugstore.com		

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

Company / Institution Name			
Division Name *(if applicable)*	**Phone Number** *(including area code)*		
Street Address	**FAX Number** *(including area code)*		
City	**State / Province**	**ZIP Code**	**Country**
Contact Name			
Contact Title	**Contact E-mail Address**		

PSC Graphics (301) 443-1090 EF

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

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

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

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

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

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

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

- ☐ Response to FDA correspondence:

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

- ☐ Other Reason *(specify):*

SECTION D2 REASON FOR APPLICATION - IDE

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

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

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

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

- ☐ Other Reason *(specify):*

SECTION D3 REASON FOR SUBMISSION - 510(k)

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

- ☐ Other Reason *(specify):*

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	MMS	2	NUC	3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☒ 510 (k) summary attached
☐ 510 (k) statement

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

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K062682	1	CVS® Personal Lubricant &Moisturizer	1	Lake Consumer Products, Inc.
2		2		2	
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Lubricant, Patient, Vaginal

	Trade or Proprietary or Model Name for This Device		Model Number
1	Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reusable Applicator)	1	83035
2		2	
3		3	
4		4	
5		5	

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

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

☒ Laboratory Testing ☐ Animal Trials ☐ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
MMS	21 C.F.R. 880.6375	☒ Class I ☐ Class II ☐ Class III ☐ Unclassified

Classification Panel

General Hospital

Indications *(from labeling)*

A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.

FDA Document Number *(if known)*

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

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Sterilizer ☒ Contract Manufacturer ☐ Repackager / Relabeler	
Company / Institution Name: Pharmetics Incorporated		Establishment Registration Number: 3007743889	
Division Name *(if applicable)*		Phone Number *(including area code)*: 1-905-871-1870 x294	
Street Address: 333 Jarvis Street		FAX Number *(including area code)*: 1-905-871-7758	
City: Fort Eric		State / Province: Ontario	ZIP Code: L2A-2S9 / Country: Canada
Contact Name: Bill Mitchell	Contact Title: GMP Trainer / Quality Assurance	Contact E-mail Address: bmitchell@pharmetics.com	

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Sterilizer ☒ Contract Manufacturer ☐ Repackager / Relabeler	
Company / Institution Name: Heinke Technology, Inc. (HTI Plastics)		Establishment Registration Number: 1925276	
Division Name *(if applicable)*		Phone Number *(including area code)*: 402-470-2600	
Street Address: 5120 N.W. 38th St		FAX Number *(including area code)*: 402-470-2929	
City: Lincoln		State / Province: NE	ZIP Code: 68524 / Country: USA
Contact Name: Rick Thomas	Contact Title: Regulatory Manager	Contact E-mail Address: rthomas@htiplastic.com	

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☒ Repackager / Relabeler	
Company / Institution Name: PEACOCK ENGINEERING COMPANY, LLC		Establishment Registration Number: 2000014306	
Division Name *(if applicable)*		Phone Number *(including area code)*: 630-845-3766	
Street Address: 720 Center Avenue		FAX Number *(including area code)*	
City: Carol Stream		State / Province: IL	ZIP Code: 60188 / Country: USA
Contact Name: Michael Altman	Contact Title: VP Engineering & Quality	Contact E-mail Address: maltman@peacockeng.com	

SECTION I — UTILIZATION OF STANDARDS

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

	Standards No.	Standards Organization	Standards Title	Version	Date
1	10993	ISO	Biological evaluation of medical devices	current	
2	32 <51>	USP	Antimicrobial Effectiveness Testing	2009	
3	32 <61>	USP	Microbial Examination of Nonsterile Products: Microbial Enumeration Tests	2009	
4	32 <62>	USP	Microbial Examination of Nonsterile Products: Tests for Specified Microorganisms	2009	
5	D3492	ASTM	Standard Specification for Rubber Contraceptives (Male Condoms)	1993	
6	4074	ISO	Natural latex rubber condoms —Requirements and test methods	2002	
7					

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

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Lil' Drug Store Products

510(k) Pre-Market Notification

February 25, 2010

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

Reference: **Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)**
Applicant: **Lil' Drug Store Products, Inc.**

Dear Sir or Madam:

We hereby submit in triplicate this Traditional 510(k) Premarket Notification for Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) ("Replens"), a vaginal moisturizer for treatment of vaginal dryness.

This product, Replens, has been sold as a cosmetic in the U.S. since 1989 based on its intended use as a moisturizer. The company has been marketing Replens with the understanding that it did not fall under the definition of a medical device under Section 201(h) of the Federal Food, Drug, and Cosmetic Act ("the Act") and was therefore not subject to the requirements for premarket clearance or approval under the Act.[1]

Based on recent discussions with CDRH, we understand that the Center's current position is that claims for relief of vaginal dryness may render a product a medical device under 21 C.F.R. § 880.6375 (Class I, Product Code MMS). Accordingly, although the company continues to believe that the product, if properly labeled, may be appropriately marketed as a cosmetic, at the Center's request we herewith submit a 510(k) premarket notification to support the marketing of Replens as a medical device for over-the-counter (OTC) use.

[1] We have been advised by regulatory counsel that claims to moisturize, lubricate, and relieve dryness are traditionally considered to be "cosmetic" claims and have been used for decades by skin care products. In fact, there is a long history of marketing feminine moisturizers as cosmetics. See comments to Docket 2003N-0539. Additionally, prior inquiries directed to agency staff appeared to support the conclusion that vaginal moisturizers are regulated as cosmetics. While in 2003 FDA indicated that it was considering categorizing feminine moisturizing products making vaginal dryness claims and discomfort relief claims as OTC drug products (see 68 Fed. Reg. 75,585, 75,580 (Dec. 31, 2003)), no further action has been taken on the subject.

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

Lil' Drug Store Products

The review division should be aware that, on January 25, 2010, CDRH's Office of Compliance advised Lil' Drug Store Products that the agency would exercise enforcement discretion to allow the company to continue to market the Replens product until June 1, 2010, subject to the following conditions: (1) submission of a 510(k) notice by February 26, 2010 (either to FDA or to an accredited, third party review organization); and (2) monthly reports to the Office of Compliance by the first of each month (the first of which was submitted on January 29, 2010). This 510(k) notice is intended to satisfy the first condition (and its submission will be included in our next monthly report).

The agency should be aware that Lil' Drug Store has concurrently filed a 510(k) notice for another version of this product, Replens Long-Lasting Vaginal Moisturizer (in Pre-filled Applicators). The subject device differs from this product both in the method of delivery and the absence of one of the preservatives (methylparaben).

We consider our intent to market this device as confidential commercial information and request that it be treated as such by FDA. We have taken precautions to protect the confidentiality of the intent to market this device. We understand that the submission to the government of false information is prohibited by 18 U.S.C. 1001 and 21 U.S.C. 331(q).

Thank you in advance for your consideration of our submission. If there are any questions, please feel free to contact me as below.

Sincerely,

Patricia L. Miller

Patricia L. Miller
Lil' Drug Store Products, Inc.
Director of Regulatory
Tel: 319-294-3745

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7. Predicate Device & Substantial Equivalence Comparison

8. Testing Overview

Appendices

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Screening Checklist for Traditional/Abbreviated Premarket Notification [510(k)] Submissions

based on
Guidance for Industry and FDA Staff
Format for Traditional and Abbreviated 510(k)s

Title	Related Information	Present	Inadequate	N/A
MDUFMA Cover Sheet	Medical Device User Fee Cover Sheet			X
CDRH Premarket Review Submission Cover Sheet	CDRH Premarket Review Submission Cover Sheet	0.1		
510(k) Cover Letter	Appendix A of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	0.2		
Indications for Use Statement	Device Advice "Content of a 510(k)" Section D	1.0		
510(k) Summary or 510(k) Statement	Device Advice "Content of a 510(k)" Section E	2.0		
Truthful and Accuracy Statement	Device Advice "Content of a 510(k)" Section G	3.0		
Class III Summary and Certification	Class III Summary and Certification Form			X
Financial Certification or Disclosure Statement	FORM FDA 3454, Certification: Financial Interests and Arrangements of Clinical Investigators FORM FDA 3455, Disclosure: Financial Interests and Arrangements of Clinical Investigators Financial Disclosure by Clinical Investigators			X
Declarations of Conformity and Summary Reports (Abbreviated 510(k)s)	Use of Standards in Substantial Equivalence Determinations FDA Standards program Declaration of conformity Required Elements for Declaration of Conformity to Recognized Standard	0.5		

Title	Related Information	Present	Inadequate	N/A
Executive Summary	See section 10 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	4.0		
Device Description	See section 11 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	6.0		
Substantial Equivalence Discussion	Guidance on the CDRH Premarket Notification Review Program 6/30/86 (K86-3)	7.1		
Proposed Labeling	Device Advice " Content of a 510(k)" Section H	5.0		
Sterilization/Shelf Life	Updated 510(k) Sterility Review Guidance (K90-1) For reuse of single use devices, see Guidance for Industry and FDA Staff – Medical Device User Fee and Modernization Act of 2002 Validation Data in Premarket Notification Submissions (510(k)s) for Reprocessed Single-Use Medical Devices	2.0		
Biocompatibility	FDA Blue Book Memo, G95-1, Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing"	8.1		
Software	Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices			X
Electromagnetic Compatibility/Electrical Safety	CDRH Medical Device Electromagnetic Compatibility Program See also IEC 60601-1- 2 Medical Electrical Equipment -- Part 1: General Requirements for Safety; Electromagnetic Compatibility -- Requirements and Tests (Second Edition, 2001)			X

Title	Related Information	Present	Inadequate	N/A
Performance Testing – Bench	See section 18 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005	8.1 8.2		
Performance Testing – Animal	See section 19 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005			X
Performance Testing – Clinical	See section 20 in Chapter II of "Guidance for Industry and FDA Staff Format for Traditional and Abbreviated 510(k)s" updated November 17, 2005 FORM FDA 3454, Certification: Financial Interests and Arrangements of Clinical Investigators FORM FDA 3455, Disclosure: Financial Interests and Arrangements of Clinical Investigators			X
Kit Certification	Device Advice: Special Considerations			X

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Department of Health and Human Services
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STANDARDS DATA REPORT FOR 510(k)s

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 10993-1:2003, Biological evaluation of medical devices -- Part 1: Evaluation and testing. (Biocompatibility)

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 2-98	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☑	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☑
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☑	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☑	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☑	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☑
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☑
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☑
Is there an FDA guidance [6] that is associated with this standard?	☑	☐
If yes, was the guidance document followed in preparation of this 510k?	☑	☐

Title of guidance: FDA Bluebook Memo G95-1 "Use of International Standard ISO 10993, 'Biological Eval of Med Dvc..."

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE

ISO 10993-1:2003, Biological evaluation of medical devices -- Part 1: Evaluation and testing. (Biocompatibility)

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
1	Evaluation and testing. (Biocompatibility)	☑ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED*

Cytotoxicity; Sensitization; and Irritation or Intracutaneous reactivity are required tests

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED*

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED*

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

* Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

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Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

USP 32:2009, <51> Antimicrobial Effectiveness Testing

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☐	☑
FDA Recognition number [3] #		
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☑	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☑
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☑	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☑	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☑
Were there any deviations or adaptations made in the use of the standard?	☐	☑
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☑
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☑
Is there an FDA guidance [6] that is associated with this standard?	☐	☑
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority (21 U.S.C. 360d), www.fda.gov/cdrh/stdsprog.html

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[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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[6] The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
USP 32:2009, <51> Antimicrobial Effectiveness Testing

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
51	Antimicrobial Effectiveness Testing	☑ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

USP 32:2009, <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3] # 14-265		
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☑	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☑
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☑	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☑	☐
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Is there an FDA guidance [6] that is associated with this standard?	☐	☑
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE

USP 32:2009, <61> Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
61	Microbiological Exam of Nonsterile Products: Microbial Enumeration Tests	☑ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

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DESCRIPTION

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

USP 32:2009, <62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 14-278	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☑	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☑
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☑	☐
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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE

USP 32:2009, <62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
62	Micro Exam of Nonsterile Products: Tests for Specified Microorganisms	☑ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

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TYPE OF 510(K) SUBMISSION

☑ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ASTM D3492:1993 Standard Specification for Rubber Contraceptives (Male Condoms)

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 9-56 for v.2008	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☑	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☑
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If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☑
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☑
Is there an FDA guidance [6] that is associated with this standard?	☐	☑
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
ASTM D3492:1993 Standard Specification for Rubber Contraceptives (Male Condoms)

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
Apdx X.1	Tensile Testing	☑ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *
used for tensile testing standards only, test procedure pulled from current ISO 4074 standard

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

* Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to:

Center for Devices and Radiological Health
1350 Piccard Drive
Rockville, MD 20850

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

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Form Approved: OMB No. 0910-0120; Expiration Date: 8/31/10

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

[✓] Traditional [ ] Special [ ] Abbreviated

STANDARD TITLE [1]

ISO 4074:2002/Cor.1:2003(E), Natural latex rubber condoms - Requirements and test methods, Tech Corr 1, 09/08/2009

Please answer the following questions	*Yes*	*No*
Is this standard recognized by FDA [2]?	☑	☐
FDA Recognition number [3]	# 9-34	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☑	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☑
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☑	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☑	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☑	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☑
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☑
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☑
Is there an FDA guidance [6] that is associated with this standard?	☐	☑
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], www.fda.gov/cdrh/stdsprog.html

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[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at www.fda.gov/cdrh/guidance.html

EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE

ISO 4074:2002/Cor.1:2003(E), Natural latex rubber condoms - Requirements and test methods, Tech Corr 1, 09/08/2009

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
	Tensile & Air Burst Testing	☑ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

Tensile and Air Burst Testing, not leak testing

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED *

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

* Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

Paperwork Reduction Act Statement

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to:

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See OMB Statement on Reverse. Form Approved: OMB No. 0910-0616, Expiration Date: 10-31-2011

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

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

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

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. NAME OF SPONSOR/APPLICANT/SUBMITTER
Lil' Drug Store Products, Inc.

2. DATE OF THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
February 19, 2010

3. ADDRESS *(Number, Street, State, and ZIP Code)*
1201 Continental Place NE
Cedar Rapids, IA 52402, USA

4. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 319-294-3745
(Fax) 319-393-3494

PRODUCT INFORMATION

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

Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reusable Applicator) (83035)

APPLICATION / SUBMISSION INFORMATION

6. TYPE OF APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES

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

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

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

CERTIFICATION STATEMENT / INFORMATION

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

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

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

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

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

NCT Number(s):

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

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

12. NAME AND TITLE OF THE PERSON WHO SIGNED IN NO. 11
(Name) Patricia L. Miller
(Title) Director of Regulatory

13. ADDRESS *(Number, Street, State, and ZIP Code) (of person identified in Nos. 11 and 12)*
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402, USA

14. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 319-294-3745
(Fax) 319-393-3494

15. DATE OF CERTIFICATION
2/9/10

Form FDA 3674 (11/08) (FRONT)

PSC Graphics (301) 443-6090 EF

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STATEMENT OF INDICATIONS FOR USE

510(k) Number: _____

Device Name: Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Indications for Use: A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Prescription Use _____ OR Over-the-Counter Use _____
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) Summary

Submitter:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Contact Person:
Tricia Miller
Director of Regulatory
Telephone: 319-294-3745
Facsimile: 319-393-3494
Email: tmiller@lildrugstore.com

Date:
February 25, 2010

Proprietary Name:
Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Common name:
Personal Lubricant

Classification name:
21 C.F.R. 880.6375 Lubricant, Patient, Vaginal
Product Code: MMS
Class: 1
Review Panel: General Hospital

Predicate Devices:

Device Name: CVS Personal Lubricant & Moisturizer
510(k) Number: K062682
Product Code: NUC, MMS

Intended Use:

A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease

and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.

Description of Device

Replens Vaginal Moisturizer is a non-sterile, water-based, white to off-white, non-irritating, non-greasy, non-staining vaginal gel delivered in a tube with a reusable applicator as a moisturizer for long-lasting relief of vaginal dryness. The use of the reusable applicator provides less mess in application. Replens Vaginal Moisturizer is intended for ongoing use, not exclusively for use during intimate sexual activity.

Replens Vaginal Moisturizer contains ingredients commonly used in other products for vaginal use sold as medical devices and cosmetics. All ingredients are either NF, USP, or are considered "generally recognized as safe for their intended use". The quantitative formulation is considered confidential commercial information.

Technological Characteristics of the Device

Replens Vaginal Moisturizer is substantially equivalent to the identified previously cleared vaginal lubricant predicate with respect to its design and materials, principle of operation, function, formulation, and intended use. It is also substantially equivalent to other water-based vaginal lubricants and personal lubricants being commercially marketed in the U.S.

Summary of Performance Data

Biocompatibility Testing: The following biocompatibility testing has been performed on Replens Long-Lasting Vaginal Moisturizer:

- Cytotoxicity
- Acute Vaginal Irritation
- Subacute Vaginal Irritation
- Subacute Vaginal Irritation with Histological Examination
- Acute Systemic Toxicity
- Hypersensitivity
- Acute Oral Toxicity
- Acute Dermal Toxicity
- Dermal Irritation
- Eye Irritation.

Stability Data: Real-time stability data confirms a shelf life of three (3) years for Replens Long-Lasting Vaginal Moisturizer.
Preservative Effectiveness: Replens Long-Lasting Vaginal Moisturizer has successfully passed the requirements of the USP <51> Antimicrobial Effectiveness Test.
Condom Compatibility Testing: Condom compatibility testing confirms that Replens Long-Lasting Vaginal Moisturizer does not materially affect the strength or integrity of latex or synthetic condoms.

Conclusion

Based on the information presented in the 510(k) notice, it is concluded that Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) for OTC use is safe and effective for its proposed indications and is substantially equivalent in intended use, formulation, safety, and technological characteristics to the identified predicate device and other similar water-based personal lubricants.

Premarket Notification [510(k)]
Truthful and Accurate Statement

(as required by 21 CFR 807.87(j))

I certify in my capacity as Director of Regulatory for Lil' Drug Store Products, Inc., that to the best of my knowledge, all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.

Patricia L Miller

Signature

Patricia L. Miller, Director of Regulatory, Lil' Drug Store Products, Inc.
Typed Name

1/25/10

Dated

Premarket Notification 510(k) Number

DEVICE INFORMATION

Proprietary name of the new device	Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)
Generic name of the device	Lubricant, Patient, Vaginal
Proposed regulatory class for the new device	1
Review Panel	General Hospital
Product Code	MMS
Regulation Number	880.6375
Previous/Concurrent Submissions	New, initial submission
Previously submitted to the FDA for identical or different indications	No
Currently being reviewed for different indications by the same or different branch within ODE	No
Previously cleared by the FDA for different indications	No

Replens Vaginal Moisturizer (35g Tube) 510k

Front & Back Panel

Estrogen Free
Replens Logo
Long-Lasting Vaginal Moisturizer

- Replenishes Vaginal Moisture
- Long Lasting Formula lasts and lasts
- Soothing, immediate relief

14 Applications
One reusable applicator

NET WT 1.23 OZ (35 G) EACH

Side Panels

- Estrogen Free
- Fragrance Free
- Natural Feeling

Vaginal dryness can be a serious problem for women of menopausal age and beyond, new mothers, cancer/chemotherapy patients and women with dryness due to medications, stress or tampon use. Replens relieves vaginal dryness and provides long-lasting results.

Comfortable applicator delivers just the right amount of Replens Long-Lasting Vaginal Moisturizer to provide vaginal dryness relief at the source of discomfort. The patented formula keeps Replens in place to deliver moisture for long-lasting hydration with less mess.

(Applicator diagram)

Usage: Use one application every three days or as needed for day-to-day comfort and moisture.

Warnings:

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE:
For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened.

Ingredients:
PURIFIED WATER, GLYCERIN, MINERAL OIL, POLYCARBOPHIL, CARBOMER HOMOPOLYMER TYPE B, HYDROGENATED PALM OIL GLYCERIDE, METHYLPARABEN, SORBIC ACID, SODIUM HYDROXIDE

Questions? 1-877-507-6516 (M-F 8AM-4:30PM CST) or www.replens.com
Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Top Panel
Replens Logo
Long-Lasting vaginal moisturizer

Bottom Panel
Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.
UPC code
LOT #
EXP
Made in Canada

Right Bottom Tab
87100C-US-02-10

427

Replens LONG-LASTING vaginal moisturizer

Please read the following carefully before use.

Warnings

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of the reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE: For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened. Return entire contents with receipt to place of purchase.

Directions for Reusable Applicator

Note: Do not roll the tube up like a toothpaste tube. This may cause the tube to crack.

1. Remove cap from Replens tube. Break seal on tube opening by puncturing it with the opposite end of the cap. Screw the open end of the applicator onto the tube. (Figure 1).
2. Gently squeeze the tube, pushing Replens into the open barrel of the applicator. DO NOT roll up the tube. The applicator contains the recommended amount when the plunger stops (approx. 1 inch). (Figure 2)
3. Unscrew the applicator from the tube. Replace cap.
4. While sitting, standing or lying on your back with knees bent, gently insert open end of applicator into the vagina as deeply as it will go comfortably. Holding the applicator in place with thumb and middle finger, press the plunger until it stops. (Figure 3) Withdraw the applicator.
5. After use, pull the plunger all the way out of the barrel. (Figure 4) Wash both parts of the applicator in warm, soapy water. Rinse thoroughly and dry. To reassemble, gently push the plunger back into the barrel as far as it will go.

How Does Replens Work?

Replens Long-Lasting Vaginal Moisturizer contains a patented ingredient for soothing and long-lasting moisture. When you apply Replens, it immediately goes to work to provide long lasting moisture. As the cells of the vaginal wall are regenerated, dry cells are cleared and Replens is eliminated naturally. As with dry skin that you experience on your face and hands, regular moisturizing treatment may be necessary to prevent dryness from recurring.

Commonly Asked Questions...

How often should Replens Long-Lasting Vaginal Moisturizer be used?
For most women, Replens Long-Lasting Vaginal Moisturizer should be used every three days for best results. However, depending on the severity of your dryness, Replens can be used more or less frequently, as necessary. Replens is safe to use daily.

When should Replens Long-Lasting Vaginal Moisturizer be used?
Replens can be used any time of day or night. Replens works best when used on a regular schedule and not just prior to intercourse. Because Replens delivers long lasting moisture, there is no need to apply it just prior to intercourse in order to replenish vaginal moisture. We recommend using Replens at least 2 hours prior to intercourse to allow proper moisturization.

Will Replens Long Lasting Moisturizer make intimacy more enjoyable? One of the most common ways that women discover vaginal dryness is during intimacy. When used regularly, Replens replenishes your natural vaginal moisture, making intimacy more enjoyable. Replens' formula delivers long lasting moisture so sexual intercourse can be more spontaneous. Since Replens does not need to be applied immediately before intercourse, it does not interrupt the moment by being runny, messy or slippery. Instead, Replens provides natural feeling long-lasting lubrication whenever the moment is right.

What causes vaginal dryness? Nearly every woman will experience vaginal dryness sometime in her life. It is most often associated with the normal decline or fluctuation of the female hormone estrogen. This fluctuation can be triggered by childbirth, breastfeeding or menopause. Dryness can also be caused by taking certain medications, exercising intensively or being under stress. It is also common to experience vaginal dryness when douching, using tampons or at the end of the menstrual cycle.

Can Replens be used as birth control? No. Replens does not contain spermicide. It is not a contraceptive.

Should I use Replens during my period? No. It is best to resume use after your flow completely stops.

Are there any side effects after using Replens? Some women notice a residue or discharge after initial use of Replens. This is caused by the elimination of dead skin cells. Your body naturally sheds dry vaginal tissue that has built up over time. When used on a regular basis, Replens will help prevent the buildup of dead skin cells and the discharge should dissipate. If the discharge does not dissipate, you may wish to wait an extra day or two between applications. While use is recommended every three days, every woman is unique and you may wish to increase or decrease the amount of time between Replens applications to maximize moisture and minimize discharge.

For additional information, visit our website at: www.replens.com or call toll-free 1-877-507-6516 (M-F 8AM – 4:30PM CST).

Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.

Replens Logo
Long-Lasting Vaginal Moisturizer

- Replenishes Vaginal Moisture
- Long Lasting Formula lasts and lasts
- Soothing, immediate relief

14 Applications NET WT 1.23 OZ (35 G) TUBE

The Replens applicator delivers just the right amount of Replens Long-Lasting Vaginal Moisturizer to provide vaginal dryness relief at the source of discomfort.

Usage: Use one application every three days or as needed for day-to-day comfort and moisture.
Directions: See enclosed pamphlet.

TAMPER EVIDENT FEATURE: For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened.

Ingredients: PURIFIED WATER, GLYCERIN, MINERAL OIL, POLYCARBOPHIL, CARBOMER HOMOPOLYMER TYPE B, HYDROGENATED PALM OIL GLYCERIDE, METHYLPARABEN, SORBIC ACID, SODIUM HYDROXIDE

Questions? 1-877-507-6516 (M-F 8AM-4:30PM CST) or www.replens.com

Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

87100T-US-02-10

(Near end of tube) Do not roll the tube as this may cause the tube to crack.

LOT
EXP

GENERAL DESCRIPTION OF DEVICE AND ITS CHARACTERISTICS

REPLENS LONG-LASTING VAGINAL MOISTURIZER GEL

Replens Long-Lasting Vaginal Moisturizer (Replens) is a non-sterile, water-based, vaginal moisturizing gel for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. It is not a contraceptive or spermicide and it does not contain any such component.

Replens is a smooth, homogenous gel with a white to off-white color, and has a pH of approximately 2.9 (within a range of 2.5-3.5), which is in the physiologic range of the normal vagina. Replens is a highly viscous gel with viscosity of approximately 70,000 (within a range of 30,000-110,000). Specific gravity of the gel is approximately 1.02 (within a range of 1.01-1.04).

The action of Replens is to hydrate the vaginal mucosa. This is achieved by the gel formulation, which holds the water in intimate contact with the mucosal epithelium and permits the water to be absorbed into the epithelial cells. This effect is related to the presence of polycarbophil in the gel base, which has the ability to hold 60 times its weight of water. The gel vehicle, which coats the vaginal epithelium and stays attached until the cells turn over 3 to 5 days later, is not absorbed.

Replens is not labeled for use with condoms, but testing has confirmed that the product does not materially affect condom strength or integrity (see section 8.2).

REUSABLE TUBE AND APPLICATOR

Replens Long-Lasting Vaginal Moisturizer is packaged in a 35g aluminum tube (for 14 applications) with a reusable, two-piece, clear, plastic (polyethylene) applicator that is designed to deliver 2.5 grams of gel. The applicator is over-wrapped in clear, biaxially oriented polypropylene film. The tube and applicator are packed in cartons with a consumer leaflet (i.e. instructions for use) for sale to consumers. Directions for application of the gel and appropriate cleaning of the applicator after each use are included in the consumer leaflet along with appropriate diagrams (see section 5.3).

Pictures of the tube, applicator, and gel can be found in section 6.2.

Specifications for Replens Vaginal Moisturizer in a 35g Tube can be found in section 6.3.1.

CONTRAINDICATIONS / PRECAUTIONS

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE

The opening of the aluminum tube is sealed and must be punctured before use. Additionally, each carton is sealed.

INGREDIENTS:

PURIFIED WATER, GLYCERIN, MINERAL OIL, POLYCARBOPHIL, CARBOMER HOMOPOLYMER TYPE B, HYDROGENATED PALM OIL GLYCERIDE, METHYLPARABEN, SORBIC ACID, SODIUM HYDROXIDE

Information about the formulation and raw materials can be found in sections 6.4 and 6.5 and Appendix A.

STORAGE AND SHELF LIFE

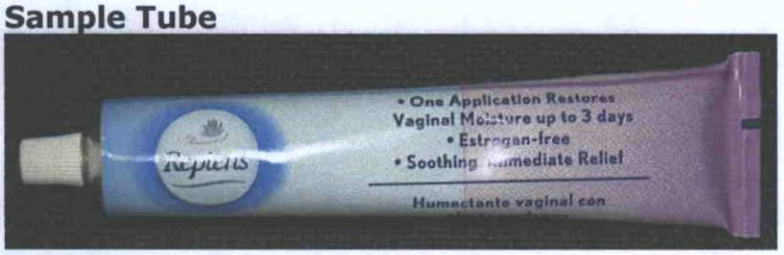
Replens should be stored at room temperature.

The shelf life is three (3) years based on stability data, which is provided in Appendix E.1 and E.2.

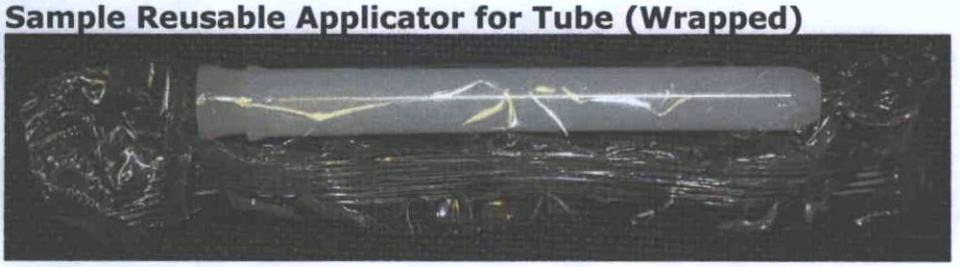
Replens Vaginal Moisturizer (35g Tube) 510k

Sample Tube Carton

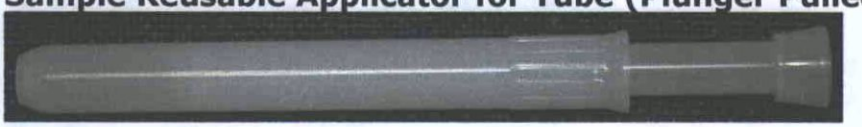
Sample Tube



Sample Reusable Applicator for Tube (Wrapped)



Sample Reusable Applicator for Tube (Plunger Pulled)



Sample Reusable Applicator for Tube with Gel

YRS

Replens Vaginal Moisturizer (35g Tube) 510k

The specification for Replens Long-Lasting Vaginal Moisturizer packaged in a 35g Tube can be found in section 6.3.1 and the product's MSDS can be found in section 6.3.2.

(b)(4) Proprietary Information

(b)(4) Proprietary Information

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

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(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

(b)(4) Proprietary Information, Test Data

The following is a discussion of the substantial equivalence of Replens Long-Lasting Vaginal Moisturizer (also referred to as "Replens" and "Replens Vaginal Moisturizer (35g Tube)") to a legally-marketed predicate device, CVS Personal Lubricant & Moisturizer (K062682). A detailed substantial equivalence comparison table is provided following this discussion.

Comparison of Intended Use and Indications to Predicate

Both Replens and the CVS Personal Lubricant & Moisturizer are intended to provide vaginal lubrication and moisturization for the relief of vaginal dryness. In other words, Replens has the same intended use as its predicate device. Therefore, Replens satisfies the first criteria of substantial equivalence.

In addition, the indications for use for Replens and the predicate device are substantially similar. The following table compares the Indications for Use statement of Replens to the predicate device. The portions of the CVS Personal Lubricant & Moisturizer statement that do not match the Replens statement are in bold.

Replens Vaginal Moisturizer (35g Tube)	CVS® Personal Lubricant & Moisturizer (K062682)
A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.	A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area **to enhance condom use and** to facilitate ease and comfort during intimate sexual activity. **CVS Personal Lubricant & Moisturizer is compatible with latex condoms.** This device is not a contraceptive or spermicide nor does it contain any such component.

The only difference between the Replens indications for use statement and the predicate device is that Replens does not claim to enhance condom use or be compatible with latex condoms. This difference does not alter the intended therapeutic effect of the product for the relief of vaginal dryness. In addition, in order to demonstrate that the Replens product does not materially affect condom strength or integrity, the company has conducted condom compatibility testing of Replens (Air Burst and Tensile Strength

testing) with both latex and synthetic condoms (provided in section 8.2). This testing demonstrates that there are no new questions of safety related to the use of Replens with condoms in comparison to the predicate device.

It should be noted that Replens is being submitted under only product code "MMS" (lubricant, vaginal, patient, class 1) instead of both product codes "MMS" and "NUC" (lubricant, patient, vaginal, latex compatible, class 2), under which the predicate device was approved, because it does not make a claim of condom compatibility.

Therefore, the intended use of both products is the same and the indications for use for the Replens Long Lasting Vaginal Moisturizer is substantially equivalent to the predicate device.

Comparison of Technological Characteristics to Predicate

The following table compares the technological characteristics of Replens to the predicate device.

Characteristic	Replens Vaginal Moisturizer (35g Tube)	CVS® Personal Lubricant & Moisturizer (K062682)
Physical Characteristics		
pH appropriate for vaginal use	Yes	Same
Highly Viscous Gel	Yes	Same
Color	White to Off-white	Clear
Density	1.01-1.04	Unknown
Sterile	No	Same
Safe for Long-term Use	Yes	Same
Fragrance Free	Yes	Same
Container	Aluminum Tube with Plastic (Polyethylene Applicator)	Plastic Bottle
Delivery	Applicator	Manually

Replens is substantially equivalent to the predicate device in all of its physical characteristics. The device and the predicate are both highly viscous gels with similar density, and a pH that is appropriate for vaginal use. The device and the predicate are non-sterile, fragrance free, and are safe for long term use. In terms of container material, Replens is equivalent to the predicate, and it has been shown to be stable in this material.

Replens is delivered in a reusable polyethylene applicator designed for vaginal use. The safety of the applicator has been demonstrated through its commercial use in the Replens Vaginal Moisturizer cosmetic product. Additionally, a vaginal applicator is used with RepHresh Vaginal Gel (K021737) and with all of the vaginal moisturizers sold as cosmetics identified in section 7.3. Although the appearance of the gel is white instead of clear (like the predicate), this does not affect the safety or effectiveness of the device for its intended purpose.

Similarly, the formulation of Replens is substantially equivalent to that of the CVS Personal Lubricant & Moisturizer. Water and glycerin represent approximately 92% of the Replens formulation and provide the primary lubrication and moisturizer characteristics of both Replens and the predicate device. While certain of the other ingredients differ between the two formulations, these other ingredients perform equivalent functions that can be safely accomplished via a variety of ingredients. Each product has ingredients that perform the following functions: vehicle, humectant, gel former and preservative. All ingredients included in Replens are either NF, USP, or are considered "generally recognized as safe for their intended use". In addition, these other Replens ingredients are commonly used in other devices and cosmetics for vaginal use, discussed in more detail below. Finally, the company has conducted biocompatibility testing and condom compatibility testing to demonstrate that Replens is as safe as the predicate and other vaginal moisturizers. Therefore, Lil' Drug Store Products does not believe that the differences in formulation between Replens and the predicate affect the safety or effectiveness of the device. In addition, these differences do not raise new questions of safety or effectiveness with regard to the Replens product.

Although they perform the same functions as analogous ingredients included in the CVS Personal Lubricant & Moisturizer, Replens contains the following ingredients that are not utilized in the predicate: polycarbophil, Carbomer Homopolymer Type B, mineral oil, hydrogenated palm oil glyceride, sorbic acid, and sodium hydroxide. All of these ingredients are well characterized and are used in other vaginal lubricants.[1] Each ingredient is discussed below.

[1] Replens' formulation is very similar to Crinone (NDA 20-701 and NDA 20-756), a gel with progesterone as the active ingredient, marketed in the U.S. since 1997 for vaginal use during the first trimester of pregnancy to support embryo implantation and maintain pregnancies as part of assisted reproductive technology treatment regimens. With the exception of water, methylparaben, and the active ingredient, the two gels have the same weight to weight ratio of all Replens ingredients, including the ones not in the identified

(b)(4) Proprietary Information

Thus, all of the ingredients in Replens are well characterized, and are well-accepted ingredients used in legally-marketed vaginal lubricants. The company believes that any differences in formulation between Replens and the predicate do not affect the safety or effectiveness of the device and do not raise new questions of safety or effectiveness with regard to the Replens product.

The company has included information and testing results in this 510(k) notice to support the equivalence of the Replens product to legally-marketed vaginal moisturizers, specifically CVS Personal Lubricant & Moisturizer (K062682). Biocompatibility testing is included in section 8.1, and condom compatibility testing is included in section 8.2 that demonstrate the safety of Replens. In addition, Replens Vaginal Moisturizer has been marketed in the U.S. since 1989 as a cosmetic with the same basic formulation provided above. Since its introduction, more than 100 million doses of Replens Vaginal Moisturizer have been used with no significant safety or health concerns. The long history of safe use of the product demonstrates that any differences from predicate devices do not affect the safety or effectiveness of the product, and supports its substantial equivalence to legally-marketed vaginal moisturizers.

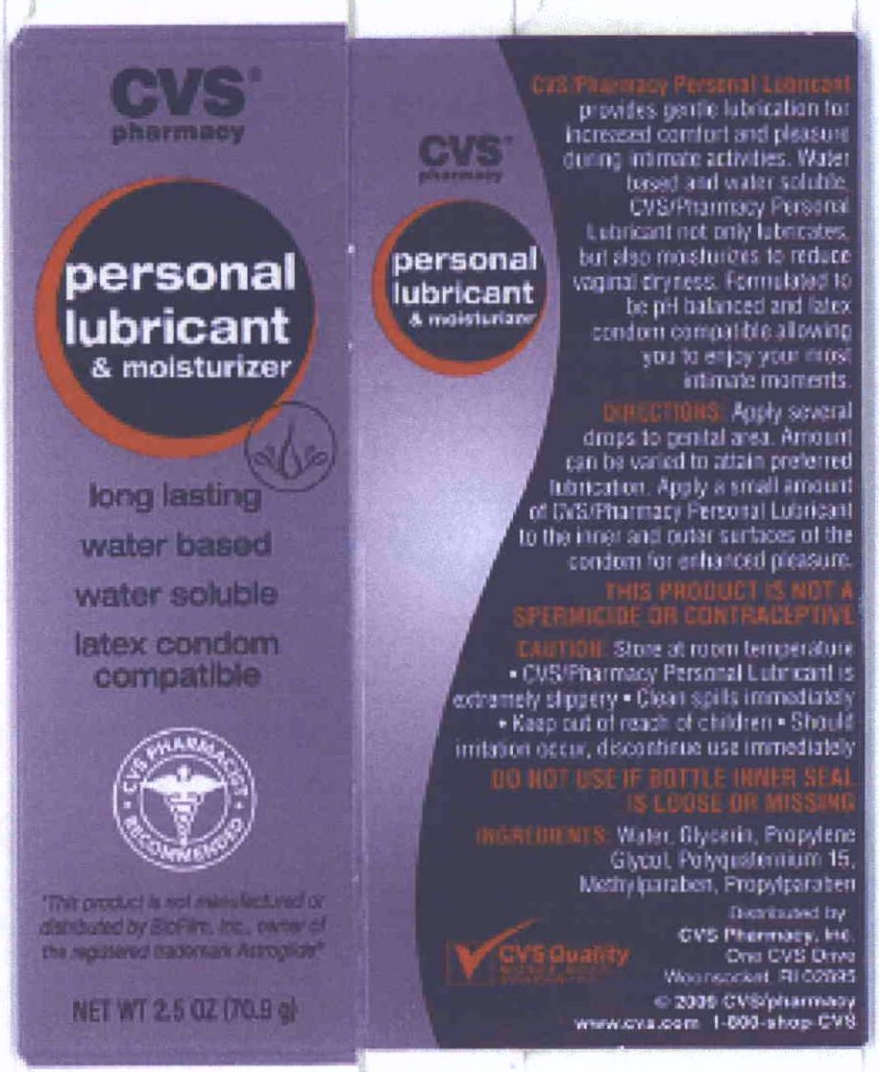
Conclusion

Replens Long-Lasting Vaginal Moisturizer and its predicate device have the same intended use and similar indications and technological characteristics. The only technological differences between Replens and its predicate device are: (1) the applicator method used with Replens for delivery of the vaginal lubricant and moisturizer; (2) minor differences in formulation and (3) the device's preservative system. These differences do not present any new issues of safety or effectiveness. Indeed, test data provided in this 510(k) submission demonstrates that even with these minor differences, Replens is a vaginal lubricant and moisturizer that is biocompatible and does not materially impact condom strength or integrity similar to the predicate device. Therefore, the Replens Long-Lasting Vaginal moisturizer is substantially equivalent to the predicate device, CVS Personal Lubricant & Moisturizer.

Detailed Substantial Equivalence Comparison

Characteristic	Subject Device: Replens Vaginal Moisturizer (35g Tube)	Predicate Device: CVS® Personal Lubricant & Moisturizer (K062682)
Regulatory Classification	21 C.F.R. 880.6375 Product Code MMS	21 C.F.R. 880.6375, 21 C.F.R. 884.5300 Product Code MMS, NUC
Intended Use	Vaginal lubrication and moisturization for the relief of vaginal dryness	Same
Indications for Use	A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity. This device is not a contraceptive or spermicide nor does it contain any such component.	A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to enhance condom use and to facilitate ease and comfort during intimate sexual activity. CVS Personal Lubricant & Moisturizer is compatible with latex condoms. This device is not a contraceptive or spermicide nor does it contain any such component.
Physical Characteristics		
pH appropriate for vaginal use	Yes	Same
Highly Viscous Gel	Yes	Same
Color	White to Off-white	Clear
Density	1.01-1.04	Unknown
Sterile	No	Same
Safe for Long-term Use	Yes	Same
Fragrance Free	Yes	Same
Container	Aluminum Tube with Plastic (Polyethylene Applicator)	Plastic Bottle
Delivery	Applicator	Manually
Formulation		
Vehicle	Water	Water
Humectant	Glycerin, Mineral Oil, Hydrogenated Palm Oil Glyceride	Glycerin, Propylene Glycol
Gel formers	Polycarbophil, Carbomer Homopolymer Type B	Polyquaternium
Preservatives	Methylparaben, Sorbic Acid	Methylparaben, Propylparaben
Buffer	Sodium Hydroxide	

CVS Personal Lubricant & Moisturizer (K062682) labeling samples are provided below. A comparison of the labeling for this device and Replens Long-Lasting Vaginal Moisturizer can be found in the predicate device comparison in section 7.1.



Lil' DRUG STORE PRODUCTS

Replens Vaginal Moisturizer (35g Tube) 510k

K-Y Long Lasting Vaginal Moisturizer

You are not alone:

Vaginal dryness is a natural occurrence for women. It is characterized by discomfort during sexual intercourse and at other times. The most common cause is a decline in the level of the female hormone estrogen, due to menopause, childbirth, or breast feeding. Other factors which can cause or increase vaginal dryness include oral contraceptive use; taking certain medications such as antihistamines, decongestants, or antidepressants; intensive exercising; stress; use of tampons; intercourse; fatigue; frequent douching; and undergoing radiation or chemotherapy treatment. Vaginal dryness symptoms may impact your feelings of confidence and well-being.

How K-Y® Brand *LONG LASTING* Vaginal Moisturizer can help:

K-Y® Brand *LONG LASTING* Vaginal Moisturizer supplements your body's natural moisture for days at a time. Its non-irritating, fragrance-free, and non-hormonal formula is bioadhesive. K-Y® Brand *LONG LASTING* promotes a natural feeling of vaginal health. One application enhances vaginal moisture for up to several days...and with it, comfort, peace of mind, and the freedom to be spontaneous. Each applicator contains a pre-measured amount of pH balanced moisturizer, assuring you comfort and convenience. K-Y® Brand *LONG LASTING* also contains Vitamin E. You can be sure that K-Y® Brand *LONG LASTING* is safe and effective, because it's from K-Y®, the #1 doctor recommended brand*. Clear instructions for K-Y® Brand *LONG LASTING* Vaginal Moisturizer use are displayed on the opposite side of this package insert.

How often should you use K-Y® Brand *LONG LASTING* Vaginal Moisturizer:

K-Y® Brand *LONG LASTING* is safe and gentle. The severity of your vaginal dryness symptoms will largely determine how frequently you use K-Y® Brand *LONG LASTING*. Typically, K-Y® Brand *LONG LASTING* is best reapplied after two or three days. Use K-Y® Brand *LONG LASTING* as often as you need to relieve vaginal dryness. If your symptoms are intermittent, occasional use may be all that is needed. After a few K-Y® Brand *LONG LASTING* applications, you should learn the frequency of use which is best for you. We recommend using it at night, before going to bed, so the moisturizing process is unaffected by exercise.

#1 DOCTOR RECOMMENDED BRAND

K-Y® BRAND

Long Lasting™

VAGINAL MOISTURIZER

Other Important Information:

Douching is not recommended by medical professionals. If you do douche, however, you may decide to stop douching while using K-Y® Brand *LONG LASTING* Vaginal Moisturizer.

For best intercourse results, K-Y® Brand *LONG LASTING* should be used on a regular basis – not just prior to having intercourse.

K-Y® Brand *LONG LASTING* is water-based.

K-Y® Brand *LONG LASTING* is not a contraceptive and does not contain Nonoxynol-9.

If you stop using K-Y® Brand *LONG LASTING*, your vaginal dryness may return. You can resume product use at any time.

DIRECTIONS FOR USE:

Use as needed: one application every 2 to 3 days is recommended. Please carefully read all instructions prior to use.

1 Unscrew and remove blue cap from prefilled applicator.

2 Insert plunger into prefilled applicator by placing small end of plunger into the gray hole at the end of the applicator.

3 Gently insert the applicator into the vagina. This can be done while lying on your back with your knees bent (as shown in the picture), or while standing with your feet apart and your knees bent. With one hand holding the barrel use the other to push the plunger all the way in. Then remove both parts of the applicator from the vagina. Throw away the applicator after each use. Do not flush in toilet.

Each applicator contains a measured amount of K-Y® Brand *LONG LASTING*. If you do not use the entire contents of the applicator, discard the unused product and the applicator.

If you feel discomfort while using K-Y® Brand *LONG LASTING*, you should stop using it. If your symptoms continue or if you are experiencing very severe vaginal dryness, contact your physician.

STORE AT ROOM TEMPERATURE (59° TO 86° F) (15° TO 32° C).

KEEP OUT OF REACH OF CHILDREN.

Distributed by
Personal Products Company
Division of McNeil-PPC, Inc.,
Skillman, NJ 08558-9418 10011100

Made in U.S.A.

? 1-877-KYBRAND 719718

468

CVS Long Lasting Vaginal Moisturizer

469

470

CVS' Long-Lasting Vaginal Moisturizer:
CVS' Long-Lasting Vaginal Moisturizer provides immediate relief from the itching, burning, irritation, soreness and pain associated with vaginal dryness.

The Gentle Formula is:
- Estrogen Free
- Convenient to Use
- Safe for Daily and Long Term Use

Pharmacist Recommended
CVS' Long-Lasting Vaginal Moisturizer is recommended by Pharmacists for immediate relief of the symptoms associated with vaginal dryness.

Frequently Asked Questions...

What Causes Vaginal Dryness?
Most common causes of vaginal dryness are childbirth, breastfeeding, menopause and chemotherapy treatments. Certain medications, douching, use of tampons, excessive exercise and stress can also have an impact on vaginal dryness.

How often should CVS' Long-Lasting Vaginal Moisturizer be used?
CVS' Long-Lasting Vaginal Moisturizer was specifically developed to supplement and replenish a woman's natural vaginal moisturize. The formula is gentle enough to use daily and safe for long term use. To use: start with one applicator every two to three days and adjust as necessary to relieve the symptoms associated with vaginal dryness.

Will there be a discharge when using CVS' Long-Lasting Vaginal Moisturizer?
Yes. Many women notice a small amount of discharge after using CVS' Long-Lasting Vaginal Moisturizer. This is the normal result of shedding older skin cells and replacing with newer, softer vaginal tissue.

Is CVS' Long-Lasting Vaginal Moisturizer the same as a lubricant?
Not at all. CVS' Long-Lasting Vaginal Moisturizer is intended to be used regularly for comfort and relief from vaginal dryness (itching, soreness, etc.). While using CVS' Long-Lasting Vaginal Moisturizer can make sexual activity more comfortable, pharmacists recommend the use of a personal lubricant to achieve the extra lubrication needed to fully enjoy sexual intercourse.

Can CVS' Long-Lasting Vaginal Moisturizer be used as birth control?
No. CVS' Long-Lasting Vaginal Moisturizer does not contain spermicides and should never be used as birth control.

Can I douche while using CVS' Long-Lasting Vaginal Moisturizer?
Douching is found to increase vaginal dryness in many women. While using CVS' Long-Lasting Vaginal Moisturizer, you may choose to discontinue douching.

Can I use CVS' Long-Lasting Vaginal Moisturizer during my period?
No. Discontinue the use of CVS' Long-Lasting Vaginal Moisturizer during the start of your menstrual cycle and resume use after your flow completely stops.

**This product is not manufactured or distributed by LDS Consumer Products, owner of the registered Trademark Replens®*

H1639

Please read the following carefully before use.

Warnings
Keep out of reach of children. CVS' Long-Lasting Vaginal Moisturizer is not a contraceptive.

If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.

Directions for Disposable Applicator

1. Remove the applicator from the sealed wrapper. Hold firmly at the thick end of the applicator and shake down to ensure that the contents are at the thin end.

2. Snap off tab and discard. While sitting or lying on your back with knees bent, gently insert the thin end of the applicator into the vagina.

3. Squeeze the thick end of the applicator firmly to deposit gel. Remove the applicator and discard.

Disposable Applicator

IMPORTANT
If an applicator is unwrapped or the wrapper is torn DO NOT USE. Return entire contents to place of purchase.

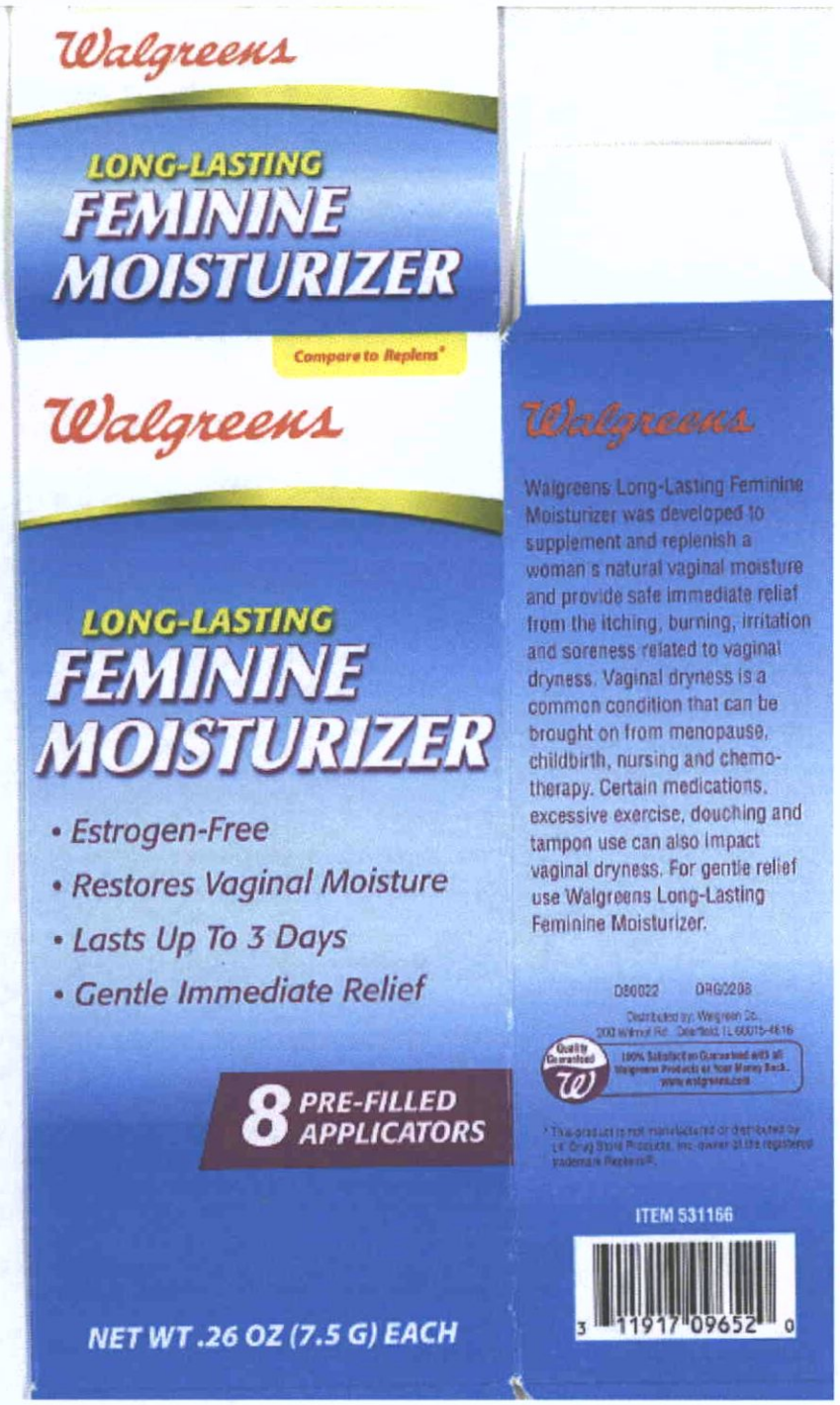
INGREDIENTS
Purified Water, Glycerine, Aloe Vera, Carbomer, Chlorhexidine Gluconate, Citric Acid, Diazolidinyl Urea, Potassium Sorbate, Sodium Benzoate, Sorbic Acid, Triethanolamine

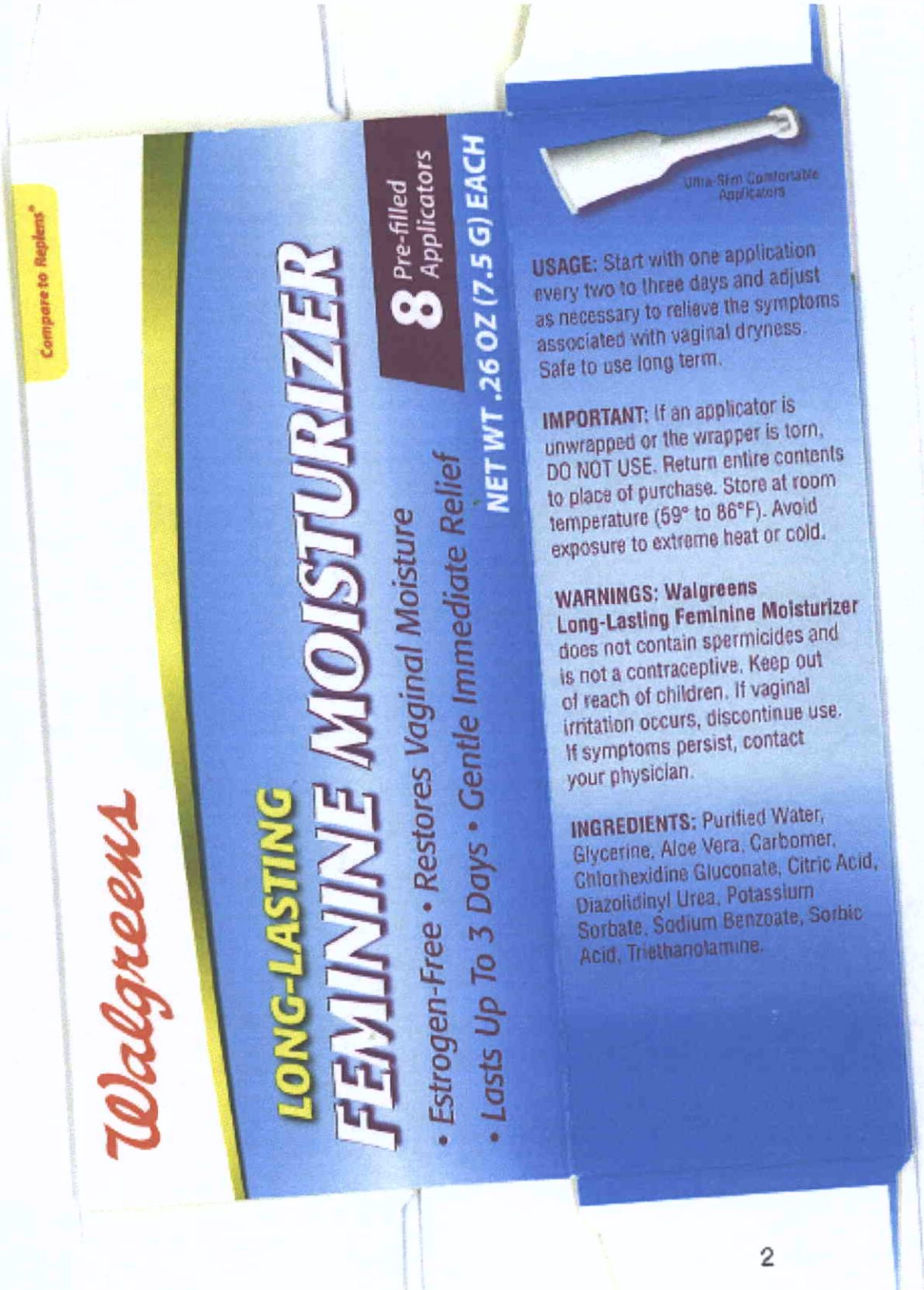
1.

2.

3.

Walgreens Long Lasting Vaginal Moisturizer





Walgreens Long-Lasting Vaginal Moisturizer:
Walgreens Long-Lasting Vaginal Moisturizer provides immediate relief from the itching, burning, irritation, soreness and pain associated with vaginal dryness.

The Gentle Formula is:
- Estrogen Free
- Convenient to Use
- Safe for Daily and Long Term Use

Pharmacist Recommended
Walgreens Long-Lasting Vaginal Moisturizer is recommended by Pharmacists for immediate relief of the symptoms associated with vaginal dryness.

Frequently Asked Questions...

What Causes Vaginal Dryness?
Most common causes of vaginal dryness are childbirth, breastfeeding, menopause and chemotherapy treatments. Certain medications, douching, use of tampons, excessive exercise and stress can also have an impact on vaginal dryness.

How often should Walgreens Long-Lasting Vaginal Moisturizer be used?
Walgreens Long-Lasting Vaginal Moisturizer was specifically developed to supplement and replenish a woman's natural vaginal moisturize. The formula is gentle enough to use daily and safe for long term use. To use: start with one applicator every two to three days and adjust as necessary to relieve the symptoms associated with vaginal dryness.

Will there be a discharge when using Walgreens Long-Lasting Vaginal Moisturizer?
Yes. Many women notice a small amount of discharge after using Walgreens Long-Lasting Vaginal Moisturizer. This is the normal result of shedding older skin cells and replacing with newer, softer vaginal tissue.

Is Walgreens Long-Lasting Vaginal Moisturizer the same as a lubricant?
Not at all. Walgreens Long-Lasting Vaginal Moisturizer is intended to be used regularly for comfort and relief from vaginal dryness (itching, soreness, etc.). While using Walgreens Long-Lasting Vaginal Moisturizer can make sexual activity more comfortable, pharmacists recommend the use of a personal lubricant to achieve the extra lubrication needed to fully enjoy sexual intercourse.

Can Walgreens Long-Lasting Vaginal Moisturizer be used as birth control?
No. Walgreens Long-Lasting Vaginal Moisturizer does not contain spermicides and should never be used as birth control.

Can I douche while using Walgreens Long-Lasting Vaginal Moisturizer?
Douching is found to increase vaginal dryness in many women. While using Walgreens Long-Lasting Vaginal Moisturizer, you may choose to discontinue douching.

Can I use Walgreens Long-Lasting Vaginal Moisturizer during my period?
No. Discontinue the use of Walgreens Long-Lasting Vaginal Moisturizer during the start of your menstrual cycle and resume use after your flow completely stops.

**This product is not manufactured or distributed by LDS Consumer Products, owner of the registered Trademark Replens®*

Please read the following carefully before use.

Warnings

Keep out of reach of children.
Walgreens Long-Lasting Vaginal Moisturizer is not a contraceptive.

If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.

Direction for Disposable Applicator

1. Remove the applicator from the sealed wrapper. Hold firmly at the thick end of the applicator and shake down to ensure that the contents are at the thin end.

2. Snap off tab and discard. While sitting or lying on your back with knees bent, gently insert the thin end of the applicator into the vagina.

3. Squeeze the thick end of the applicator firmly to deposit gel. Remove the applicator and discard.

Disposable Applicator

IMPORTANT
If an applicator is unwrapped or the wrapper is torn DO NOT USE. Return entire contents to place of purchase.

INGREDIENTS
Purified Water, Glycerine, Aloe Vera, Carbomer, Chlorhexidine Gluconate, Citric Acid, Diazolidinyl Urea, Potassium Sorbate, Sodium Benzoate,Sorbic Acid, Triethanolamine

HB002

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actividad sexual, los farmacéuticos recomiendan el uso de un lubricante personal para lograr la lubricación extra que se necesita para disfrutar más delas relaciones sexuales.

¿Puede la Crema Hidratante Vaginal de Duración Prolongada de Walgreens usarse como anticonceptivo?
No. La Crema Hidratante Vaginal de Duración Prolongada de Walgreens no contiene espermicidas y nunca debe de usarse como anticonceptivo.

¿Puedo yo irrigarme mientras uso la Crema Hidratante Vaginal de Duración Prolongada de Walgreens?
Se ha comprobado que la irrigación vaginal aumenta la sequedad en muchas mujeres. Mientras se usa la Crema Hidratante Vaginal de Duración Prolongada de Walgreens, se puede elegir dejar de irrigarse.

¿Puedo utilizar la Crema Hidratante Vaginal de Duración Prolongada de Walgreens durante mi período?
No. Deje de usar la Crema Hidratante Vaginal de Duración Prolongada de Walgreens durante el comienzo de su ciclo menstrual y vuelva a utilizarla después de que su fluido pare completamente.

Crema Hidratante Vaginal de Duración Prolongada de Walgreens:
La Crema Hidratante Vaginal de Duración Prolongada de Walgreens proporciona alivio inmediato a la picazón, ardor, irritación y dolores asociados con la sequedad vaginal.

La Formula Suave es:
- Libre de Estrógeno
- De Uso Conveniente
- Segura para el Uso Diario o de Duración Prolongada

Recomendada por Farmacéuticos
La Crema Hidratante Vaginal de Duración Prolongada de Walgreens es recomendada por farmacéuticos para el alivio inmediato de los síntomas asociados con la sequedad vaginal.

Preguntas Frecuentes...

¿Qué causa la sequedad vaginal?
Las causas más comunes de la sequedad vaginal incluyen el parto, el amamantamiento, la menopausia y los tratamientos de quimioterapia. Ciertos medicamentos, la irrigación vaginal, el uso de tampones, el ejercicio o estrés excesivos pueden también impactar la sequedad vaginal.

¿Qué tan a menudo debo usar la Crema Hidratante Vaginal de Duración Prolongada de Walgreens?
La Crema Hidratante Vaginal de Duración Prolongada de Walgreens fue desarrollada especificamente para complementar y reabastecer la humedad vaginal natural de la mujer. La fórmula es lo suficiente suave para el uso diario y segura para el uso prolongado. Para usar: Empieze con un aplicador cada dos o tres días y ajuste como sea necesario para aliviar los síntomas asociados con la sequedad vaginal.

Habrá secreción al utilizar la Crema Hidratante Vaginal de Duración Prolongada de Walgreens:
Sí. Muchas mujeres se dan cuenta de una pequeña cantidad de secreción después de usar la Crema Hidratante Vaginal de Duración Prolongada de Walgreens. Esto es el resultado normal del cambio de las antiguas células por tejido nuevo vaginal.

¿Es la Crema Hidratante Vaginal de Duración Prolongada de Walgreen's igual que un lubricante?
Por supuesto que no. La Crema Hidratante Vaginal de Duración Prolongada de Walgreens propone ser usada regularmente para la comodidad y el alivio de la sequedad vaginal (picazón, dolor, etc.). Mientras el uso de la Crema Hidratante Vaginal de Larga Duración de Walgreens puede hacer más cómoda la

**Este producto no se fabrica ni se distribuye por LDS Consumer Products, dueña de la marca registrada Replens®*

Por favor lea lo siguiente con cuidado antes de usar.

Precauciones:

Mantenga fuera del alcance de los niños. **La Crema Hidratante Vaginal de Duración Prolongada de CVS no es un anticonceptivo.**

Si ocurre irritación vaginal, descontinúe el uso. Si los síntomas persisten, contacte a su doctor.

Instrucciones para el Aplicador Desechable

1. Saque el aplicador de la envoltura. Agite hacia abajo como un termómetro para asegurarse de que el contenido esté en la punta delgada.

2. Parta la lengüeta y deshágase de ella. Mientras sentada o de espalda con las rodillas dobladas, inserte cuidadosamente la punta, delgada del aplicador dentro de la vagina.

3. Presione la punta gruesa del aplicador firmemente para del depositar el gel. Remueva el aplicador y deseche.

Aplicador Desechable

IMPORTANTE
Si un aplicador está abierto o si la envoltura está rota NO LO USE. Devuelva el contenido completo al lugar donde lo compró.

INGREDIENTS
Purified Water, Glycerine, Aloe Vera, Carbomer, Chlorhexidine Gluconate, Citric Acid, Diazolidinyl Urea, Potassium Sorbate, Sodium Benzoate, Sorbic Acid, Triethanolamine

475

Me Again Long Lasting Vaginal Moisturizer

Me Again™

On average a woman spends one-third of her life post-menopause. As she approaches and transitions through and beyond menopause, a variety of changes occur that, if untreated, can dramatically diminish her quality of life. For example, as a result of fluctuating hormone levels, women commonly suffer from uncomfortable vaginal itching, burning and soreness associated with vaginal dryness.

Me Again Long Lasting Vaginal Moisturizer is a clinically tested, water based gel that uses a patented liposomal technology to deliver natural, long lasting moisture to dry vaginal mucosa. This unique advanced formula is specifically formulated to ease the vaginal dryness and discomfort associated with the reduction in estrogen levels during and after menopause.

Satisfaction Guaranteed:
If you are not completely satisfied with this product after using it, return the unused portion with the sales receipt to Lake Consumer Products, Inc. Please allow 6-8 weeks for a refund.

LAKE CONSUMER PRODUCTS, INC.
a Subsidiary of Wisconsin Pharmacal Company, LLC
1 Pharmacal Way
Jackson, Wisconsin 53037
Questions? Call 800-537-8658
www.MeAgainOnline.com

Relieves Vaginal Dryness
Immediate Natural Relief
Long-lasting Hydration

MENOPAUSE
long lasting
Vaginal Moisturizer

8 Prefilled Individual Applicators

Net Wt. .24 oz. (7g) Each

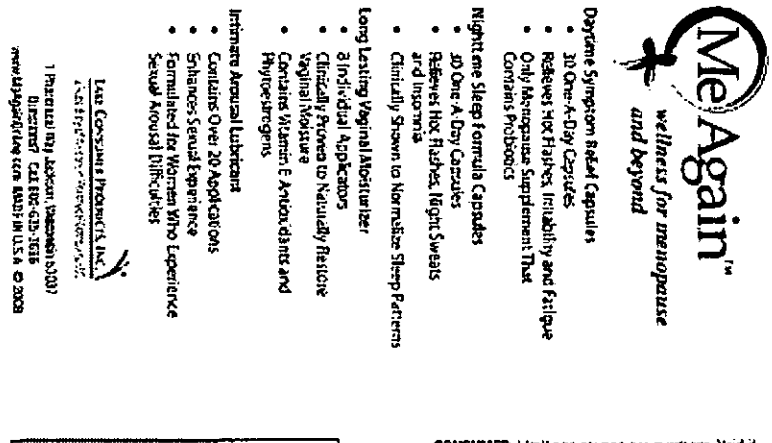
Me Again™
wellness for menopause and beyond

477

478

Replens Vaginal Moisturizer (35g Tube) 510k

Lil' DRUG STORE PRODUCTS



MANUFACTURER'S COUPON | EXPIRES 5/31/10

This coupon valid for

$3.00 off

on ONE package of any Me Again™ product

CONSUMER: Limit one coupon per purchase. Void if copied, sold, exchanged or transferred. Consumer is responsible for any sales tax.

RETAILER: Lake Consumer Products, Inc., will reimburse you the face value of the coupon plus 8¢ handling if submitted in compliance with our Coupon Redemption Policy (available at www.lakeconsumer.com) Cash value 1/20¢.

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Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name — Carol Stamps (Regulatory Technology Services)

Subject: 510(k) Number — K101098/S2

To: The Record

Please list CTS decision code SE

- ☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)
- ☐ Hold (Additional Information or Telephone Hold).
- ☑ Final Decision (SE) SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	*Attach IFU*	✓	
510(k) Summary /510(k) Statement	*Attach Summary*	✓	
Truthful and Accurate Statement.	*Must be present for a Final Decision*	✓	
Is the device Class III? If yes; does firm include Class III Summary?	*Must be present for a Final Decision*		✓
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)		✓	
Is this a combination product? (Please specify category N, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC			✓
this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			✓
Is this device intended for pediatric use only?			✓
Is this a prescription device? (If both prescription & OTC, check both boxes.)			✓
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?		✓	
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (If not, then applicant must be contacted to obtain completed form.)		✓	
Does this device include an Animal Tissue Source?			✓
All Pediatric Patients age<=21			✓
Neonate/Newborn (Birth to 28 days)			✓
Infant (29 days -< 2 years old)			✓
Child (2 years -< 12 years old)			✓
Adolescent (12 years -< 18 years old)			✓
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this ...up, different from adults age ≥ 21 (different device design or testing, different protocol ...ures, etc.)			✓

Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)			✓
Nanotechnology			✓
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC.*		✓

Regulation Number **Class*** **Product Code**

21 CFR 884.5300 II NUC

(*If unclassified, see 510(k) Staff)

Additional Product Codes:

Review: Colleen Pouland (Branch Chief) OGDB (Branch Code) 8/17/10 (Date)

Final Review: (Division Director) 8/17/10 (Date)

 5

Andrews, Sharon M

From: Carole Stamp [stamp.carole@gmail.com]
Sent: Friday, August 13, 2010 5:48 PM
To: Andrews, Sharon M
Cc: 'Mark Job'
Subject: RE: K101241 & K101098, Replens vaginal lubricant
Attachments: 5.1 Tube Carton (87100C-US-08-10) v3.1.doc; 5.1 8ct App Carton (80800C-US-08-10) v3.1.doc

Hi Sharon,

Attached are the revised box labeling for both the 35g Tube and the Applicators incorporating the statement that the product is compatible with natural rubber latex, polyisoprene, and polyurethane condoms.

Thank you,
Carole

From: Andrews, Sharon M [mailto:Sharon.Andrews@fda.hhs.gov]
Sent: Friday, August 13, 2010 3:53 PM
To: 'Carole Stamp'
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Carole,

Thank you for this information. I apologize if I was not clear in my earlier e-mail about this, but when I was referring to the device labeling, I was referring to the box labeling, not the package insert. Therefore, please ask the sponsor to revise the box labeling to state that the device is compatible with natural rubber latex, polyisoprene, and polyurethane condoms.

Thank you.

Sharon

From: Carole Stamp [mailto:stamp.carole@gmail.com]
Sent: Friday, August 13, 2010 4:24 PM
To: Andrews, Sharon M
Cc: 'MARK JOB'; Pollard, Colin M.
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Hello Sharon,

The sponsor has provided the updated documents requested in your emails below. I have reviewed them and they have addressed all of the requested information outlined below. Please find the 6 updated documents attached. If you have any further questions, please let me know.

Thank you,
Carole

From: Andrews, Sharon M [mailto:Sharon.Andrews@fda.hhs.gov]
Sent: Friday, August 13, 2010 10:39 AM
To: 'MARK JOB'; 'Carole Stamp'
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Mark and Carole,

I apologize for not including this in my earlier e-mail, but please also ask the sponsor to submit a revised version the ClinicalTrials.gov (Form 3674), which states that clinical data was submitted in this submission.

Thank you.

Sharon

Sharon M. Andrews
Biomedical Engineer, DRGUD/OGDB
10903 New Hampshire Avenue
WO66, Room G102
Silver Spring, MD 20993
Phone: 301-796-6650
Fax: 301-847-8111
sharon.andrews@fda.hhs.gov

From: Andrews, Sharon M
Sent: Friday, August 13, 2010 11:22 AM
To: 'MARK JOB'; 'Carole Stamp'
Cc: Pollard, Colin M.
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Mark and Carole,

Please ask the sponsor to revise the 510(k) Summary and labeling for both K101241 and K101098 as described below.

1. Please revise the 510(k) Summary as follows:

   a. Under the heading, "Summary of Performance Data," please include a short summary of the published clinical data provided in response to Question 2 of our June 10, 2010 e-mail.
   b. Under the heading, "Summary of Performance Data," regarding the "Stability Data" information, please state that the stability data confirms a 1-year shelf-life for the device.
   c. Under the heading, "Summary of Performance Data," regarding "Condom Compatibility Testing" information, please specify that the synthetic condoms evaluated were polyisoprene and polyurethane.

   Please provide a revised copy of the 510(k) Summary including the above requested revisions for review.

2. Please revise the labeling to state that the product is compatible with natural rubber latex, polyisoprene, and polyurethane condoms. Please also provide a revised copy of the labeling with the revision for review.

In order for use to complete our review of this submission in a timely manner, please provide a response no later that **COB, Monday, August 16, 2010** via e-mail.

Thank you.

Sharon

Sharon M. Andrews
Biomedical Engineer, DRGUD/OGDB
10903 New Hampshire Avenue
WO66, Room G102
Silver Spring, MD 20993
Phone: 301-796-6650
Fax: 301-847-8111
sharon.andrews@fda.hhs.gov

From: MARK JOB [mailto:mark@markjob.com]
Sent: Friday, August 13, 2010 10:40 AM
To: Pollard, Colin M.
Cc: Andrews, Sharon M
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Hello Colin,

I am curious to know if you have any further questions related to the additional information provided for these two submissions.

Please let me know.

Thanks,

Mark

Mark Job
Reviewer
Regulatory Technology Services LLC
Phone: 763 682 4139
FAX: 763 682 4420
Email: mark@markjob.com

 9

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

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

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

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. NAME OF SPONSOR/APPLICANT/SUBMITTER
Lil' Drug Store Products, Inc.

2. DATE OF THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
February 19, 2010

3. ADDRESS *(Number, Street, State, and ZIP Code)*
1201 Continental Place NE
Cedar Rapids, IA 52402, USA

4. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 319-294-3745
(Fax) 319-393-3494

PRODUCT INFORMATION

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

Replens Long-Lasting Vaginal Moisturizer (Pre-filled Applicators), 8 count (83008)

Replens Long-Lasting Vaginal Moisturizer (Pre-filled Applicators), 1 count (83001)

APPLICATION / SUBMISSION INFORMATION

6. TYPE OF APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES

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

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

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

CERTIFICATION STATEMENT / INFORMATION

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

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

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

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

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

NCT Number(s):

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

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

12. NAME AND TITLE OF THE PERSON WHO SIGNED IN NO. 11
(Name) Patricia L. Miller
(Title) Director of Regulatory

13. ADDRESS *(Number, Street, State, and ZIP Code) (of person identified in Nos. 11 and 12)*
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402, USA

14. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
(Tel.) 319-294-3745
(Fax) 319-393-3494

15. DATE OF CERTIFICATION
8/13/10

Form FDA 3674 (11/08) (FRONT)

PSC Graphics (301) 443-1090 ET

 10

510(k) Summary

Submitter:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Contact Person:
Tricia Miller
Director of Regulatory
Telephone: 319-294-3745
Facsimile: 319-393-3494
Email: tmiller@lildrugstore.com

Date:
August 13, 2010

Proprietary Name:
Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Common name:
Personal Lubricant

Classification name:
21 C.F.R. 884.5300 Lubricant, Patient, Vaginal, Latex Compatible
Product Code: NUC
Class: 2
Review Panel: Obstetrics/Gynecology

Predicate Devices:

Device Name: CVS Personal Lubricant & Moisturizer
510(k) Number: K062682
Product Code: NUC, MMS

Intended Use:

Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible

with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.

Description of Device

Replens Vaginal Moisturizer is a non-sterile, water-based, white to off-white, non-irritating, non-greasy, non-staining vaginal gel delivered in a tube with a reusable applicator as a long-lasting moisturizer for vaginal dryness. The use of the reusable applicator provides less mess in application. Replens Vaginal Moisturizer is intended for ongoing use, not exclusively for use during intimate sexual activity.

Replens Vaginal Moisturizer contains ingredients commonly used in other products for vaginal use sold as medical devices and cosmetics. All ingredients are either NF, USP, or are considered "generally recognized as safe for their intended use". The quantitative formulation is considered confidential commercial information.

Technological Characteristics of the Device

Replens Vaginal Moisturizer is substantially equivalent to the identified previously cleared vaginal lubricant predicate with respect to its design and materials, principle of operation, function, formulation, and intended use. It is also substantially equivalent to other water-based vaginal lubricants and personal lubricants being commercially marketed in the U.S.

Summary of Performance Data

Biocompatibility Testing: The following biocompatibility testing has been performed on Replens Long-Lasting Vaginal Moisturizer:

- Cytotoxicity
- Acute Vaginal Irritation
- Subacute Vaginal Irritation
- Subacute Vaginal Irritation with Histological Examination
- Acute Systemic Toxicity
- Hypersensitivity
- Acute Oral Toxicity
- Acute Dermal Toxicity
- Dermal Irritation
- Eye Irritation.

Clinical Studies: The following clinical studies have been performed on Replens Long-Lasting Vaginal Moisturizer:

- Bachmann GA, Notelovitz M, Gonzalez SJ, Thompson C, Morecraft BA. (1991) Vaginal Dryness in Menopausal Women: Clinical Characteristics and Nonhormonal Treatment. Clinical Practice in Sexuality, 7(9): 1-8.
- Bachmann GA, Notelovitz M, Kelly SJ, Owens A, Thompson C. (1992) Long Term Nonhormonal Treatment of Vaginal Dryness. Clinical Practice in Sexuality, 8(8/9): 3-8.
- Zinny MA, Lee S. (1991) Double-Blind Study of the Comparative Effects of Two Gels on Vaginal pH in Postmenopausal Women. Today's Therapeutic Trends, 8(4): 65-72.
- Young R, Goldzieher J, Kaufman R. (1991) A Study of the Effects of Col-1003 In Postmenopausal Women. Unpublished.
- Nakamura R. (1991) Evaluation of Col-1003 in the treatment of vaginal dryness in postmenopausal women. Unpublished.
- Whitehead M. (1991) A Randomised Double Blind Evaluation of Col-1003, a bioadhesive polymer system vaginal moisturizing gel and, KY Brand Lubricating Jelly in the treatment of vaginal dryness in postmenopausal women receiving concomitant oral hormone replacement therapy. Unpublished
- Nachtigall LE. (1994) Comparative study: Replens versus local estrogen in menopausal women. Fertility and Sterility, 61(1): 178-180.
- Gelfand MM, Wendman E. (1994) Treating Vaginal Dryness in Breast Cancer Patients: Results of Applying a Polycarbophil Moisturizing Gel. J. Women's Health, 3(6): 427-433.

The format of the studies listed above is summarized in the table below:

Citation	No. Patients Enrolled (Replens)	Study Design*	Dosage Regimen	Duration
Bachmann et al	89	D-B, X-over	2.5 g per day	5 days
Bachmann et al	54	Open	2.5 g, 3 x weekly	12 months
Zinny and Lee	26	D-B, parallel	2.5 g alternate nights	4 weeks
Young et al	30	Open	2.5 g, 3 x weekly, plus option of additional application prior to intercourse.	12 months
Nakamura	10	Open, X-over between treatment durations	2.5 g daily	1-5 days

Citation	No. Patients Enrolled (Replens)	Study Design*	Dosage Regimen	Duration
Whitehead	32	D-B, X-over	2.5 g, 3 x weekly plus option of additional application prior to intercourse.	8 weeks
Nachtigall	15	Open, parallel	2.5 g, 3 x weekly	3 months
Gelfand and Wendman	25	Open	2.5 g, 3 x weekly, plus option of additional application prior to intercourse.	3 months

* D-B = double-blind; X-over = cross-over design

The parameters employed in the studies included the influence of Replens on vaginal pH and the vaginal mucosa, the relief of the patient's symptoms, the vaginal dryness index, determination of vaginal pH at varying time intervals after single or multiple applications of the gel, PAP smears and the completion of diary cards by the patient. All of the studies concluded that Replens was safe and well-tolerated.

Stability Data: Real-time stability data confirms a shelf life of three (3) years for Replens Long-Lasting Vaginal Moisturizer.
Preservative Effectiveness: Replens Long-Lasting Vaginal Moisturizer has successfully passed the requirements of the USP <51> Antimicrobial Effectiveness Test.
Condom Compatibility Testing: Condom compatibility testing confirms that Replens Long-Lasting Vaginal Moisturizer does not materially affect the strength or integrity of natural rubber latex or synthetic condoms (polyurethane and polyisoprene).

Conclusion

Based on the information presented in the 510(k) notice, it is concluded that Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) for OTC use is safe and effective for its proposed indications and is substantially equivalent in intended use, formulation, safety, and technological characteristics to the identified predicate device and other similar water-based personal lubricants.

Replens LONG-LASTING vaginal moisturizer

Please read the following carefully before use.

Warnings

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of the reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE: For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened. Return entire contents with receipt to place of purchase.

Directions for Reusable Applicator

Note: Do not roll the tube up like a toothpaste tube. This may cause the tube to crack. The applicator should be thrown away when all of the gel in the tube has been used.

1. Remove cap from Replens tube. Break seal on tube opening by puncturing it with the opposite end of the cap. Screw the open end of the applicator onto the tube. (Figure 1).
2. Gently squeeze the tube, pushing Replens into the open barrel of the applicator. DO NOT roll up the tube. The applicator contains the recommended amount when the plunger stops (approx. 1 inch). (Figure 2)
3. Unscrew the applicator from the tube. Replace cap.
4. While sitting, standing or lying on your back with knees bent, gently insert open end of applicator into the vagina as deeply as it will go comfortably. Holding the applicator in place with thumb and middle finger, press the plunger until it stops. (Figure 3) Withdraw the applicator.
5. Immediately after use, pull the plunger all the way out of the barrel (Figure 4) and wash both parts of the applicator in warm, soapy water. Rinse thoroughly and dry. The applicator should be completely dry before reassembly. To reassemble, gently push the plunger back into the barrel as far as it will go.

How Does Replens Work?

Replens Long-Lasting Vaginal Moisturizer contains a patented ingredient for soothing and long-lasting moisture. When you apply Replens, it immediately goes to work to provide long lasting moisture. As the cells of the vaginal wall are regenerated, dry cells are cleared and Replens is eliminated naturally. As with dry skin that you experience on your face and hands, regular moisturizing treatment may be necessary to prevent dryness from recurring.

Commonly Asked Questions...

How often should Replens Long-Lasting Vaginal Moisturizer be used?
For most women, Replens Long-Lasting Vaginal Moisturizer should be used every three days for best results. However, depending on the severity of your dryness, Replens can be used more or less frequently, as necessary. Replens is safe to use daily.

When should Replens Long-Lasting Vaginal Moisturizer be used?
Replens can be used any time of day or night. Replens works best when used on a regular schedule and not just prior to intercourse. Because Replens delivers long lasting moisture, there is no need to apply it just prior to intercourse. We recommend using Replens at least 2 hours prior to intercourse to allow proper moisturization.

Will Replens Long Lasting Moisturizer make intimacy more enjoyable? One of the most common ways that women discover vaginal dryness is during intimacy. When used regularly, Replens helps replenish your natural vaginal moisture, making intimacy more enjoyable. Replens' formula delivers long lasting moisture so sexual intercourse can be more spontaneous. Since Replens does not need to be applied immediately before intercourse, it does not interrupt the moment by being runny, messy or slippery. Instead, Replens provides long-lasting lubrication whenever the moment is right.

What causes vaginal dryness? Nearly every woman will experience vaginal dryness sometime in her life. It is most often associated with the normal decline or fluctuation of the female hormone estrogen. This fluctuation can be triggered by childbirth, breastfeeding or menopause. Dryness can also be caused by taking certain medications, exercising intensively or being under stress. It is also common to experience vaginal dryness when douching, using tampons or at the end of the menstrual cycle.

Can Replens be used as birth control? No. Replens does not contain spermicide. It is not a contraceptive.

Should I use Replens during my period? No. It is best to resume use after your flow completely stops.

Are there any side effects after using Replens? Some women notice a residue or discharge after initial use of Replens. This is caused by the elimination of dead skin cells. Your body naturally sheds dry vaginal tissue that has built up over time. When used on a regular basis, Replens will help prevent the buildup of dead skin cells and the discharge should dissipate. If the discharge does not dissipate, you may wish to wait an extra day or two between applications. While use is recommended every three days, every woman is unique and you may wish to increase or decrease the amount of time between Replens applications to maximize moisture and minimize discharge.

Is Replens compatible with condoms? Yes, Replens is compatible with natural rubber latex, polyisoprene, and polyurethane condoms.

For additional information, visit our website at: www.Replens.com or call toll-free 1-877-507-6516 (M-F 8AM – 4:30PM CST).

Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.

Front & Back Panel

Estrogen Free
Replens Logo
Long-Lasting Vaginal Moisturizer

- Helps Replenish Vaginal Moisture
- Supplements the body's natural lubrication
- Long Lasting Formula

14 Applications
One reusable applicator

NET WT 1.23 OZ (35 G) EACH

Side Panels

- Estrogen Free
- Fragrance Free

Vaginal dryness can be a serious problem for women of menopausal age and beyond, new mothers, cancer/chemotherapy patients and women with dryness due to medications, stress or tampon use. Replens helps replenish vaginal moisture and provides long-lasting results.

Comfortable applicator delivers just the right amount of Replens Long-Lasting Vaginal Moisturizer to provide vaginal moisture at the source of discomfort. The patented formula keeps Replens in place to deliver moisture for long-lasting hydration with less mess.

(Applicator diagram)

Usage: Use one application every three days or as needed for day-to-day comfort and moisture.

Replens is compatible with natural rubber latex, polyisoprene, and polyurethane condoms.

Warnings:

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE:
For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened.

Ingredients:
PURIFIED WATER, GLYCERIN, MINERAL OIL, POLYCARBOPHIL, CARBOMER HOMOPOLYMER TYPE B, HYDROGENATED PALM OIL GLYCERIDE, METHYLPARABEN, SORBIC ACID, SODIUM HYDROXIDE

Questions? 1-877-507-6516 (M-F 8AM-4:30PM CST) or www.replens.com
Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Top Panel
Replens Logo
Long-Lasting vaginal moisturizer

Bottom Panel
Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.
UPC code
LOT #
EXP
Made in Canada

Right Bottom Tab
87100C-US-08-10

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Carole Stamp (Reg. Tech. Services)

Subject: 510(k) Number K101098/S1

To: The Record

Please list CTS decision code _____

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)

☒ Hold (Additional Information or Telephone Hold) E-mail follow-up

☐ Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.)

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):	YES	NO
Indications for Use Page — *Attach IFU*		
510(k) Summary /510(k) Statement — *Attach Summary*		
Truthful and Accurate Statement. — *Must be present for a Final Decision*		
Is the device Class III?		
If yes, does firm include Class III Summary? — *Must be present for a Final Decision*		
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)		
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC		✓
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)		
Is this device intended for pediatric use only?		✓
Is this a prescription device? (If both prescription & OTC, check both boxes.)		✓
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?		
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (If not, then applicant must be contacted to obtain completed form.)		
Does this device include an Animal Tissue Source?		
All Pediatric Patients age<=21		
Neonate/Newborn (Birth to 28 days)		
Infant (29 days -< 2 years old)		
Child (2 years -< 12 years old)		
Adolescent (12 years -< 18 years old)		
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)		

Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)

Nanotechnology

Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html) *Contact OC.*

Regulation Number | Class* | Product Code

(*If unclassified, see 510(k) Staff)

Additional Product Codes:

Review: Colin Pollard (Branch Chief) OGDB (Branch Code) 6/10/10 (Date)

Final Review: (Division Director) (Date)

Pollard, Colin M.

From: Pollard, Colin M.
Sent: Thursday, June 10, 2010 12:04 PM
To: 'Carole Stamp'
Cc: 'Mark Job'
Subject: RE: K101241 & K101098, Replens vaginal lubricant -- ASTM draft standard (protocol)

Carole:

Just to close the loop on the 510(k) reviews and this morning's t-con, here are the remaining deficiencies. I plan to place the two documents back on hold until your revised reviews address the following concerns:

Condom Compatibility

1. The mfr provided the results of condom compatibility testing in terms of percent drop in properties (tensile and airburst) following exposure to the subject lubricant for each condom type evaluated. This testing showed that exposure to Replens caused a significant drop in condom properties, condoms made from natural rubber latex, polyisoprene, and polyurethane. In many cases, the percent drop in properties exceeded 20%. (We sent you a chart yesterday illustrating these results.) Consequently, it appears that Replens is not compatible with condom use. Replens labeling should reflect this as a caution statement.

The mfr stated that the data provided demonstrate that the subject lubricant is condom compatible because (1) following exposure, the condom properties met the requirements outlined in ISO and ASTM standards, and (2) the subject lubricant performed equivalently to KY Jelly, which is labeled condom compatible.

However, please note that FDA evaluates the condom compatibility of all personal lubricants based on percent drop in condom properties (typically tensile and airburst) to determine the physical effect of the lubricant on the condom membrane. Furthermore, KY Jelly is known to be condom compatible and is often used as a negative control in condom compatibility studies. It is possible that the specific test method you used to evaluate condom compatibility may have led to negative results, (e.g., brushing the lubricant onto the condom).

Therefore, please revise the Indications for Use form, 510(k) Summary, and labeling for the subject lubricant to state that it is not condom compatible, and please provide revised copies of these documents for review.

Alternatively, you may provide the results of additional condom compatibility testing to support the condom compatibility of the subject lubricant. However, please note that if the results do not demonstrate that the subject lubricant is condom compatible, you will need to revise your labeling accordingly.

Human Use Data

2. In response to questions 9 and 10 for both 510(k)s that we sent you earlier, the mfr referred to published clinical studies of the proposed Replens gel. However, it is unclear whether the published studies used versions of the device with or without methylparaben. For each published study referenced, please identify the formulation used (with or without methylparaben), the number and

frequency of applications, and negative reports following device use (e.g., irritation, allergic response, adverse events, etc). Sufficient data on the methylparaben version of the device should be provided to support safe use in humans as this version would be expected to have the greater potential for toxic effects based on the results of the acute systemic toxicity studies.

In addition, please provide information from complaint files or MDRs regarding any negative effects associated with use of both versions of the device (please provide results separately). Please also confirm how many samples have been sold and information on where devices have been shipped (e.g., one million in US, two million in Canada, etc.).

If the information provided is not sufficient to demonstrate that use of both versions of the device is safe following use by humans, additional testing as described in question 10 from our previous comments (i.e., combined vaginal irritation/systemic toxicity) will be requested.

Shelf-Life

3. In response to question 5 for K101241, the mfr provided the results of shelf-life. In addition, you state that based on a phone conversation April 30, 2010, there was agreement that the device could be labeled with an initial shelf-life of 17 months that could be extended to one year upon completion of the shelf-life study.

Our review of the data showed that real-time test data is available from one lot for 6 months, and additional lots at 3 months. In addition, accelerated shelf-life testing has been conducted for 6 months on one lot, and multiple lots out to 2 months. However, the protocol does not discuss how the environmental conditions used were developed (e.g., no standards identified), or how long 2 or 6 months at these conditions relates to real-time use. Please provide a detailed discussion how the accelerated conditions were developed, and if a published standard method was not used, please provide data validating the accelerated methods used. In addition, please limit the shelf-life to a duration that is supported by data from three lots of device (accelerated or real-time). All accelerated results will need to be confirmed with real-time results.

From: Pollard, Colin M.
Sent: Thursday, June 10, 2010 11:50 AM
To: 'Carole Stamp'
Cc: 'Mark Job'
Subject: RE: K101241 & K101098, Replens vaginal lubricant -- ASTM draft standard (protocol)

Carole:

It's not an FDA protocol, it's a draft ASTM protocol. I think you'd have to obtain it from ASTM. If Akron Rubber is a member of ASTM, they should be able to get a copy.

I can check internally, but - under ASTM rules - I don't think we're entitled to share that draft with you.

On the other hand, as I mentioned, we certainly are willing to look at any proposed draft protocol you want us to consider.

Colin

From: Carole Stamp [mailto:stamp.carole@gmail.com]
Sent: Thursday, June 10, 2010 11:42 AM
To: Pollard, Colin M.
Cc: 'Mark Job'
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Hello Colin,

For our own reference and internal use doing 510(k) reviews, could you forward the draft protocol that FDA has proposed for the lubricant testing?

Thank you,
Carole

From: Pollard, Colin M. [mailto:Colin.Pollard@fda.hhs.gov]
Sent: Wednesday, June 09, 2010 4:58 PM
To: Mark Job
Cc: Carole Stamp; joseph.levitt@hoganlovells.com; Benesch, Bryan H.
Subject: RE: K101241 & K101098, Replens vaginal lubricant

How about tomorrow morning, Thursday, June 10th, at 10:30 am (EST).

Please send me a list of the names of all participants, including their affiliation and title.

Will you have someone from the test lab available on the call (i.e., Akron Rubber Development Laboratories)? That would definitely be advisable.

Also, please provide call-in information.

Thanks!

Colin

From: Mark Job [mailto:mark@markjob.com]
Sent: Wednesday, June 09, 2010 5:50 PM
To: Pollard, Colin M.
Cc: Carole Stamp; joseph.levitt@hoganlovells.com; Benesch, Bryan H.
Subject: Re: K101241 & K101098, Replens vaginal lubricant

Hi Colin,

We and the sponsor will be available any convenient for you.

Please let me know.

Best regards,

Mark

On Wed, Jun 9, 2010 at 4:36 PM, Pollard, Colin M. <Colin.Pollard@fda.hhs.gov> wrote:
Carole, Mark:

We've looked at the test data on condom compatibility and we find some problems with it.

In particular, there are many instances when the drop in properties exceeds 10%, with quite a few that exceed 20%. (It's not enough to show that the sample condoms meet the standard.) Attached is a chart that illustrates the situation. All values that exceed a 10% drop are highlighted in yellow.

The data shows similar effects with K-Y jelly, and this is puzzling because we don't expect to see that for K-Y jelly. We've seen lots of data on K-Y jelly and there should be minimal effect on condom properties. In addition, no positive control was run (typically done with petroleum jelly).

The only real options that occur to us are:

- re-run testing (after considering source of anomalous test findings); or
- label product as not compatible with condom use

Can we talk about this tomorrow? You are welcome to invite staff from the manufacturer who are familiar with this testing.

Colin Pollard
Chief, Ob/Gyn Devices

From: Levitt, Joseph A. <joseph.levitt@hoganlovells.com>
To: Benesch, Bryan H.
Cc: Spears, Larry D
Sent: Mon Jun 07 11:17:13 2010
Subject: Request for Assistance

Hi Bryan --
My client, Lil' Drug Store Products, Inc., very much appreciates the 30-day extension your office has afforded them--until July 1, 2010--to obtain 510(k) clearance for its two Replens vaginal moisturizer products. I am writing to solicit you help in encouraging ODE to grant a request for an in-person meeting between my client, the Third Party Review organization, and ODE. The request for that meeting was submitted on June 3, 2010 to ODE by the Third Party Review organization.
Our reasons for soliciting your help are as follows:
1. Time is of the essence. As you know, the terms of your 30-day extension provide that the company will need to discontinue marketing of these products as of July 1st if 510(k) clearance is not obtained by then.
2. The company has been working diligently and in good faith. As you can see from the monthly reports, the company has been working earnestly to obtain the necessary clearances, and is working through an authorized Third Party Review organization, Regulatory Technology Services LLC, to do so.
3. A meeting is timely. ODE now has all the information it needs to have a substantive discussion. As of late last week, Lil Drug Store had responded to all of ODE's questions, and the Third Party Review organization had agreed with those responses and forwarded them to ODE.
4. The issues are not readily amenable to a routine paper review. ODE's questions, and Lil' Drug Stores responses, involve a number of detailed scientific issues, such that a personal exchange is likely to be needed in order to resolve the issues in the near term.
5. The meeting is likely to be beneficial. The fact that the company, its outside

experts, and the Third Party Reviewer all believe that ODE's questions have been addressed satisfactorily means this meeting would likely have a positive result in narrowing and/or resolving many, if not all, of ODE's questions.

6. The company is ready. My client is prepared to travel to the DC area to meet, once ODE has reviewed the information and a mutually agreeable time can be arranged.

In summary, given the time constraints of the enforcement discretion period, we believe that an in-person meeting is the best way to approach the matter in a mutually respectful and constructive way. Any help you have provide in encouraging ODE to grant the meeting request would be greatly appreciated. Thanks for your assistance.

Joe

Joseph Levitt
Partner

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004

Tel: +1 202 637 5600
Direct: +1 202 637 5759
Fax: +1 202 637 5910
Email: joseph.levitt@hoganlovells.com
www.hoganlovells.com

--
Mark Job
Reviewer
Regulatory Technology Services LLC
Phone: 763 682 4139

FAX: 763 682 4420
Email: mark@markjob.com

(b)(4) Proprietary Information

Pollard, Colin M.

From: MARK JOB [mark@markjob.com]
Sent: Thursday, June 10, 2010 9:58 AM
To: Pollard, Colin M.
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Hello Colin,

The call in information:

Dial-in information for the conference call is: 877-531-0115, Passcode *1792719* (Please make sure to enter the star * both before and after the passcode.).

Participates:

- Tricia Miller, Director of Regulatory, Lil' Drug Store Products, Inc. (confirmed)
- Jim Drummond, Physical & Plastics Testing Manager, Akron Rubber Development Laboratory (ARDL) ✓

Third Party

- Mark Job ✓
- Carole Stamp ✓

Best regards,

Mark

Mark Job
Reviewer
Regulatory Technology Services LLC
Phone: 763 682 4139
FAX: 763 682 4420
Email: mark@markjob.com

From: Pollard, Colin M. [mailto:Colin.Pollard@fda.hhs.gov]
Sent: Thursday, June 10, 2010 8:55 AM
To: MARK JOB
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Mark:

Please send us the call-in # and the list of participants (with title/affiliation).

Also, please confirm that someone from the test lab will be on the call.

Colin

From: MARK JOB [mailto:mark@markjob.com]
Sent: Thursday, June 10, 2010 9:35 AM
To: Pollard, Colin M.
Subject: RE: K101241 & K101098, Replens vaginal lubricant

Hi Colin,

The conference call has been confirmed with all parties on our end.

I look forward to the call.

Thank you for your time.

Best regards,

Mark

Mark Job
Reviewer
Regulatory Technology Services LLC
Phone: 763 682 4139
FAX: 763 682 4420
Email: mark@markjob.com

From: Pollard, Colin M. [mailto:Colin.Pollard@fda.hhs.gov]
Sent: Wednesday, June 09, 2010 4:58 PM
To: Mark Job
Cc: Carole Stamp; joseph.levitt@hoganlovells.com; Benesch, Bryan H.
Subject: RE: K101241 & K101098, Replens vaginal lubricant

How about tomorrow morning, Thursday, June 10th, at 10:30 am (EST).

Please send me a list of the names of all participants, including their affiliation and title.

Will you have someone from the test lab available on the call (i.e., Akron Rubber Development Laboratories)? That would definitely be advisable.

Also, please provide call-in information.

Thanks!

Colin

From: Mark Job [mailto:mark@markjob.com]
Sent: Wednesday, June 09, 2010 5:50 PM
To: Pollard, Colin M.
Cc: Carole Stamp; joseph.levitt@hoganlovells.com; Benesch, Bryan H.
Subject: Re: K101241 & K101098, Replens vaginal lubricant

Hi Colin,

We and the sponsor will be available any convenient for you.

Please let me know.

Best regards,

Mark

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Carole, Mark:

We've looked at the test data on condom compatibility and we find some problems with it.

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Chief, Ob/Gyn Devices

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Email: joseph.levitt@hoganlovells.com
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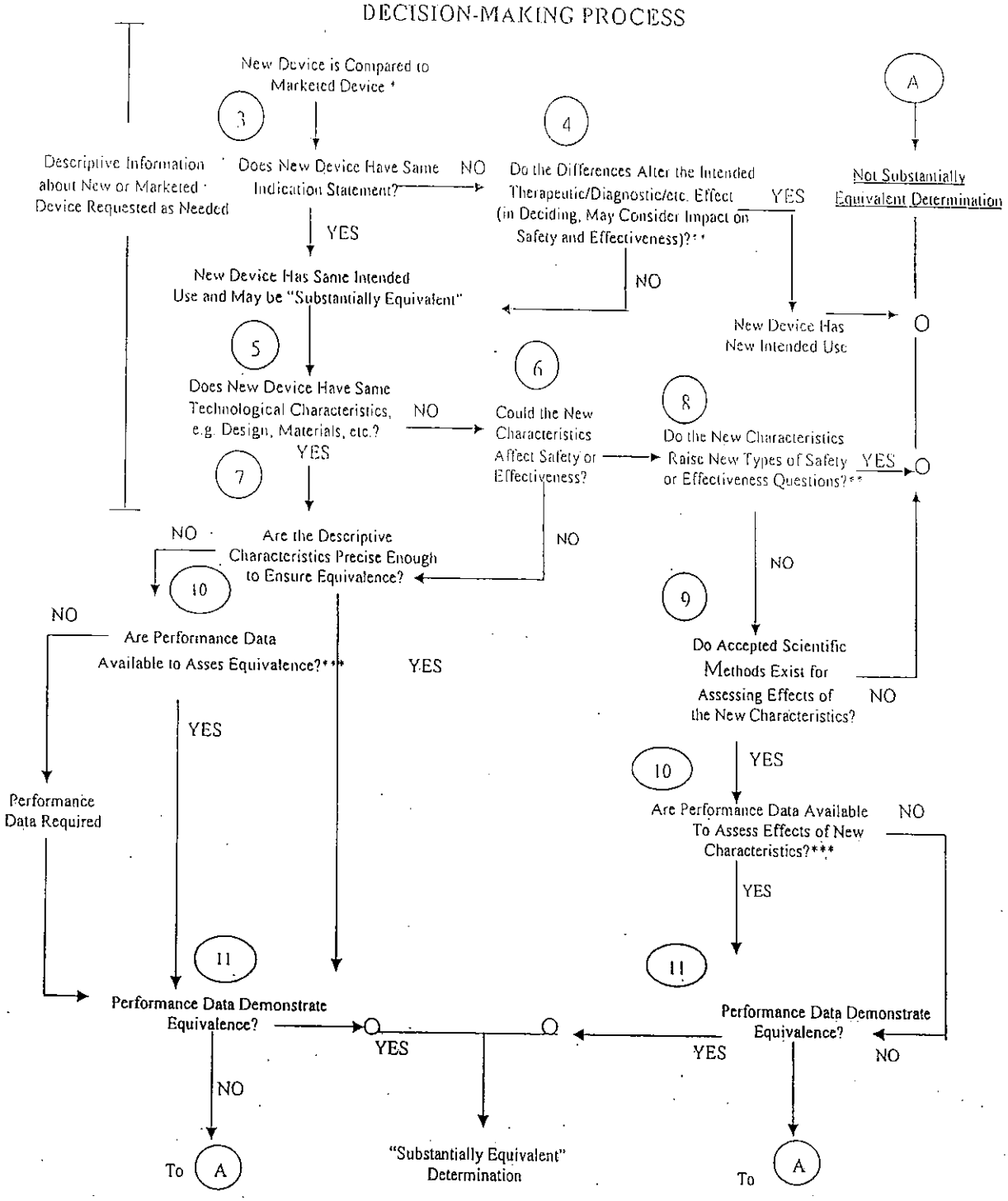
Mark Job
Reviewer
Regulatory Technology Services LLC
Phone: 763 682 4139
FAX: 763 682 4420
Email: mark@markjob.com

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



❖ 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

❖❖ This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

❖❖❖ Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Carole Stamp (RTS, LLC)

Subject: 510(k) Number K101098

To: The Record

Please list CTS decision code A1

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)

☑ Hold (Additional Information or Telephone Hold) — sent Email

☐ Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):	YES	NO
Indications for Use Page — *Attach IFU*		
510(k) Summary /510(k) Statement — *Attach Summary*		
Truthful and Accurate Statement. — *Must be present for a Final Decision*		
Is the device Class III?		
If yes, does firm include Class III Summary? — *Must be present for a Final Decision*		
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)		
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC		
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)		
Is this device intended for pediatric use only?		
Is this a prescription device? (If both prescription & OTC, check both boxes.)		
Did the application include a completed FORM FDA 3674, Certification with Requirements of ClinicalTrials.gov Data Bank?		
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (If not, then applicant must be contacted to obtain completed form.)		
Does this device include an Animal Tissue Source?		
All Pediatric Patients age<=21		
Neonate/Newborn (Birth to 28 days)		
Infant (29 days -< 2 years old)		
Child (2 years -< 12 years old)		
Adolescent (12 years -< 18 years old)		
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)		

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

Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)

Nanotechnology

Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html) *Contact OC.*

Regulation Number	Class*	Product Code
21 CFR 884.5300	II	NUC

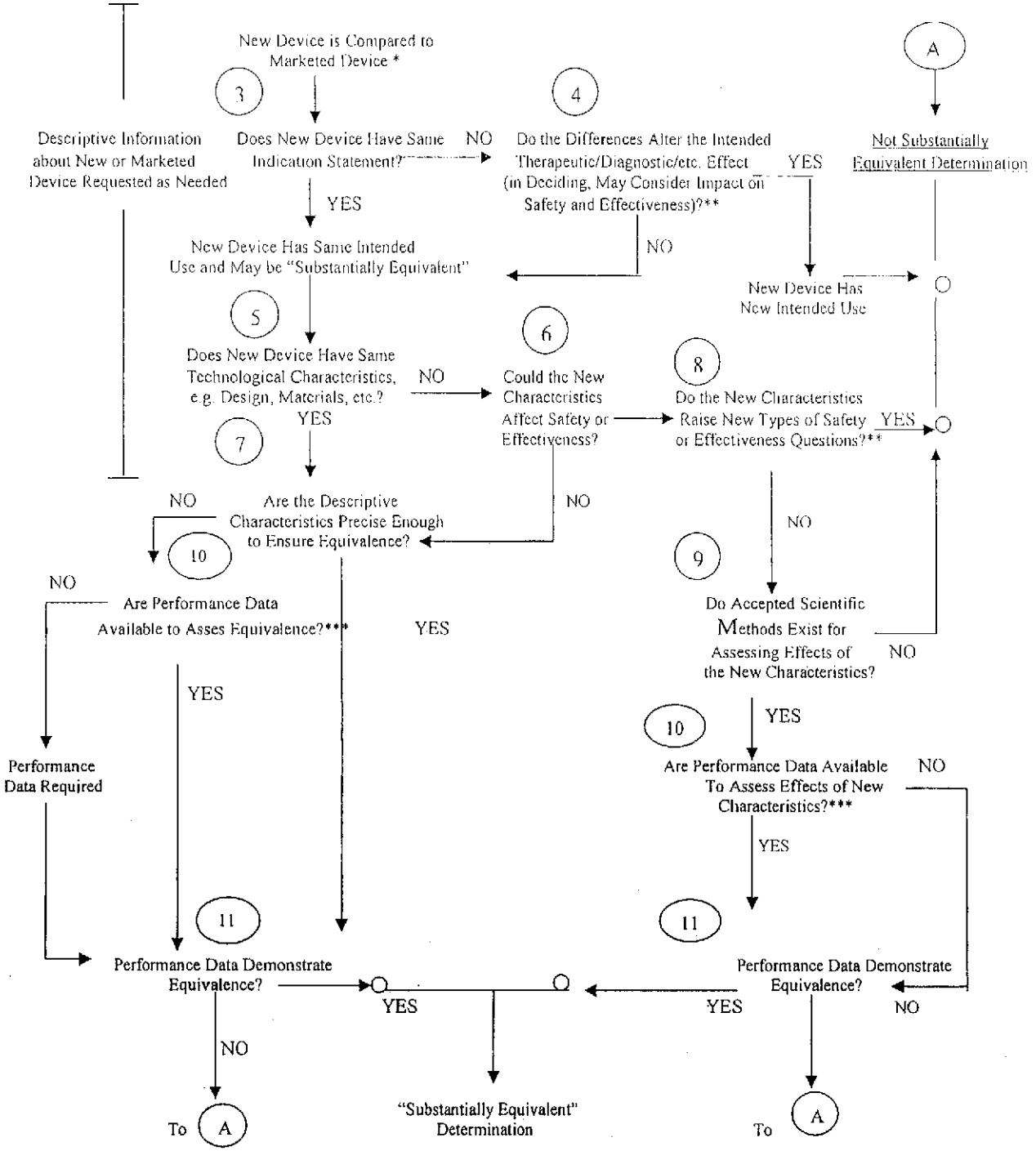
(*If unclassified, see 510(k) Staff)

Additional Product Codes: _____

Review: Colwell Pollard (Branch Chief) OGDB (Branch Code) 5/5/10 (Date)

Final Review: _____ (Division Director) (Date)

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



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❖❖❖ Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

Pollard, Colin M.

[redacted]om: Pollard, Colin M.
Sent: Wednesday, May 05, 2010 12:58 PM
To: 'mark@markjob.com'
Subject: K101098 - Lil' Drug Store Products - Replens Vaginal Moisturizer, FDA comments on 3rd party review

Dear Mr. Job,

I am placing this 510(k) submission on hold. The 3rd party review did not address all relevant aspects, and the mfr will need to provide additional information (listed below). If you need to discuss certain aspects, please contact me and I will make myself and a reviewer here available for discussion.

Thank you.

Colin Pollard
Chief, Ob/Gyn Devices Branch
DRARD/Office of Device Evaluation

Device Description

1. Please note that personal lubricants such as Replens are Class II devices, covered by procode NUC (vaginal patient lubricant), under regulation number 21 CFR 884.5300.

   You state that the pH of the subject lubricant is 2.9 and ranges from 2.3-3.5. You also state that this is in the physiologic range of the normal vagina. However, it appears to us that the pH of the subject lubricant is below normal vaginal pH, which typically ranges from 4.0 – 5.0 in women with active menstrual cycles (M. Garcia-Closas et al. *Epidemiologic determinants of vaginal pH.* AJOG. Volume 180(5). pp.1060-1066.).

   In light of this information, please justify the pH of the subject lubricant. You justification should include, but is not limited to, a discussion of the possible changes to the vaginal microflora that may result from prolonged exposure to this product and if a low pH environment makes the vagina more susceptible to infections of any kind.

Indications for Use

3. Please revise your indications for use statement to that of the standard indication for personal lubricants as follows:

   [Product name] is a personal lubricant, for penile and/or vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is [is not] compatible with natural rubber latex condoms [and/or synthetic condoms (specify specific type(s) of synthetic condoms)].

   Please modify your Indications for Use form, 510(k) Summary, and labeling accordingly, and please provided revised copies of these documents for review. Please note that the last sentence of your indication statement is dependent upon how you choose to address the condom compatibility issues described in Deficiencies 12-13.

Labeling

4. Please revise your package insert as follows:

   a. Please provide information in the labeling regarding when to dispose of the applicator (e.g., when the lubricant has been used up).

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b. Please state that the applicator should be cleaned immediately after use. The cleaning validation testing provided in Appendix D of the 510(k) submission evaluated the applicator after sitting for only 10 minutes following contamination.
c. Please state that the applicator should be completely dry before reassembly.

Please provide a revised copy of your product labeling including the above requested revisions.

Shelf-Life

5. Please clarify if the 36 month accelerated-aging study conducted by Pharmetics evaluated ingredients from the current suppliers and the current product packaging. If not, please justify why any differences between the evaluated product and the current product would not affect shelf-life. Please note that if your justification is not sufficient you will be asked to conduct additional shelf-life testing.

Biocompatibility

6. Four key biocompatibility studies provided in your submission were conducted twenty years ago. These studies are as follows:

- Acute Vaginal Irritation in Rabbits (1989)
- Subacute Vaginal Irritation in Rabbits (1989)
- Subacute Vaginal Irritation with Histological Examination (1990)
- Hypersensitivity (1989)

Please confirm if the current version of the subject lubricant is identical to the product evaluated in the above studies, (i.e., identical ingredient suppliers, identical manufacturing processes, etc.). If not please provide vaginal irritation and sensitization testing on the final, finished version of the subject lubricant. These studies should evaluate appropriate models (e.g., ISO Vaginal Mucosal Irritation, ISO Maximization Sensitization), evaluate both polar and non-polar extracts, and follow the extraction procedures outlined in ISO 10993-12:2007.

You conducted an Agar Overlay test to evaluate the cytotoxicity potential of the subject lubricant, which displayed cytotoxicity scores of 2 and 3. This is a much higher degree of cytotoxicity than typically seen for personal lubricant products. This is especially concerning because an Agar Overlay test is less sensitive than the MEM Elution Cytotoxicity test typically used to evaluate the cytotoxicity potential of personal lubricant products. An Agar Overlay test is less sensitive because the agar acts a barrier between the cells and the test article, allowing less penetration compared to a direct contact method such as MEM Elution.

You state that the negative cytotoxicity result was caused by the low pH of the subject lubricant, and to demonstrate this, you repeated the cytotoxicity study after adjusting the pH of the subject lubricant to 7.0-7.5. You state that this modified cytotoxicity study did not display any signs of cytotoxicity.

We do not believe this is appropriate justification because the marketed product will not have a pH of 7.0-7.5. Please provide justification that supports the safety of the subject lubricant with its intended specifications. In addition, we are unable to locate the test report for the modified cytotoxicity study in your submission. Please provide this information.

8. To assess the sensitization potential of the subject lubricant, your conducted a hypersensitivity test in guinea pigs. This test is not sufficient as it is not an appropriate test for a device in contact with mucosal surfaces such as personal lubricants. This is especially true considering the unfavorable cytotoxicity study results. Please provide the complete protocol, results, and analysis from a sensitization study that is appropriate for materials in contact with mucosal surfaces (e.g., ISO Maximization Study). Please note that testing should be completed with both polar and non-polar extracts of your device.

9. You conducted an Acute Systemic Toxicity test using both IV and IP routes of administration to evaluate the acute systemic toxicity potential of the subject lubricant. While the test animals did not display any signs of toxicity via the IP route of administration, several very concerning adverse effects were seen in the test animals in both studies evaluating the IV route of administration. In the first IV study, the two test animals went into convulsions and were gasping immediately following an injection of the undiluted subject lubricant. Both animals died shortly thereafter. In the second IV study, despite dilution of the subject lubricant in saline (2.9 grams in 15.4 mL), four out of the five animals displayed significant clinical signs of toxicity, three animals lost excess of 10% of their body

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weight, and one animal died. To justify these results, you simply state that the IV route of administration is not an appropriate method for evaluating a vaginal lubricant; however, this does not explain why the subject lubricant caused these reactions in the test animals. Please provide this information.

In addition, please reevaluate the acute systemic toxicity potential of the subject lubricant as described in Deficiency 10.

Furthermore, you did not provided justification for your test dose of 50 mL/kg for either the IV or IP route of administration. Please provide a justification for your test dose that accounts for daily, repeat use.

10. In lieu of conducting both a vaginal irritation study and an acute systemic toxicity study, an alternate testing approach that may be more relevant to the proposed use of your device (i.e., vaginal use) is summarized below. This alternate design is a hybrid between the ISO Vaginal Irritation test and the ISO Acute Systemic Toxicity test and assesses both the systemic toxicity and mucosal irritation potential of your device.

    - Rabbits (n=5 per group) are treated with either the test article extracted in a polar extraction vehicle, the test article extracted in a non-polar extraction vehicle, or saline (negative control) and dosed 1x/day for 10 days. Each animal will receive 1 ml of the test article extracted in a polar extraction vehicle (treatment group 1), the test article extracted in a non-polar extraction vehicle (treatment group 2), or saline (control).

    - The following information should be collected during the study:

        - initial, daily, and terminal body weights;
        - initial baseline and terminal blood samples;
        - daily health observations;
        - food consumption data;
        - macroscopic and microscopic evaluation of vaginal, cervical, and uterine tissues;
        - necropsy including examination of major organs, including organ weights; and
        - tissues from major organs during necropsy.

    If you choose to follow this approach, we recommend that you discuss your protocol with us prior to initiating this study.

11. It appears that you changed applicator material and then conducted additional biocompatibility tests (irritation and sensitization) on the new version of the applicator. However, it is unclear is unclear which version of the applicator was evaluated in the cytotoxicity study conducted. Please provide this information. If the cytotoxicity testing was not completed on the new version of the applicator, please provide additional cytotoxicity testing on the new version of the applicator. Alternatively, you may justify why the cytotoxicity testing already completed is sufficient.

Condom Compatibility

12. You conducted tensile and airburst testing on several brands of latex, polyurethane, and polyisoprene condoms. You evaluated these condoms untreated and following 30 minutes of exposure to the subject lubricant and to KY Jelly. You evaluated 20 samples per condom type per exposure and presented your results in terms of the mean and standard deviation of each parameter evaluated. In order for us to fully evaluate the effect of the subject lubricant on condoms, please provide your condom compatibility results as described in the following table for each parameter evaluated:

Condom Type	**airburst pressure of condoms without additional lubricant (kPa) (n = xx)**	**airburst pressure for condoms lubricated with test lubricant (kPa) (n = xx)**	**difference**	**% decrease**
1	*Insert mean and confidence interval*	*Insert mean and confidence interval*		

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2				
3				

Please note that any drop in condom properties of greater than 10% will need to be justified.

13. You do not make any claims in your product labeling regarding condom compatibility. Please include an appropriate condom compatibility claim based on the results of condom compatibility testing conducted and please modify your Indications for Use form accordingly.

In addition, please revise your review memo to include a detailed discussion of all the performance testing conducting by the sponsor including cleaning validation, all biocompatibility studies, shelf-life, and condom compatibility. This discussion should include a summary of the protocol, the study results, and your reasoning as to why the study results are acceptable.

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Andrews, Sharon M

To: mark@markjob.com
Pollard, Colin M.
Subject: K101098 - Lil' Drug Store Products - Replens Vaginal Moisturizer

Dear Mr. Job,

I am placing this 510(k) submission on hold. Please ask the sponsor to address the following deficiencies:

Device Description

1. Please note that this device should be classified as a Class II vaginal patient lubricant under regulation number 21 CFR 884.5300 and procode NUC.

2. You state that the pH of the subject lubricant is 2.9 and ranges from 2.3-3.5. You also state that this is in the physiologic range of the normal vagina. However, it appears to us that the pH of the subject lubricant is below normal vaginal pH, which typically ranges from 4.0 – 5.0 in women with active menstrual cycles (M. Garcia-Closas et al. *Epidemiologic determinants of vaginal pH.* AJOG. Volume 180(5). pp.1060-1066.).

   In light of this information, please justify the pH of the subject lubricant. You justification should include, but is not limited to, a discussion of the possible changes to the vaginal microflora that may result from prolonged exposure to this product and if a low pH environment makes the vagina more susceptible to infections of any kind.

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3. Please revise your indications for use statement to that of the standard indication for personal lubricants as follows:

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   Please modify your Indications for Use form, 510(k) Summary, and labeling accordingly, and please provided revised copies of these documents for review. Please note that the last sentence of your indication statement is dependent upon how you choose to address the condom compatibility issues described in Deficiencies 12-13.

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5. Please clarify if the 36 month accelerating aging study conducted by Pharmetics evaluated ingredients from the current suppliers and the current product packaging. If not, please justify why any differences between the evaluated product and the current product would not affect shelf-life. Please note that if your justification is not sufficient you will be asked to conduct additional shelf-life testing.

Biocompatibility

238

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7. You conducted an Agar Overlay test to evaluate the cytotoxicity potential of the subject lubricant, which displayed cytotoxicity scores of 2 and 3. This is a much higher degree of cytotoxicity than typically seen for personal lubricant products. This is especially concerning because an Agar Overlay test is less sensitive than the MEM Elution Cytotoxicity test typically used to evaluate the cytotoxicity potential of personal lubricant products. An Agar Overlay test is less sensitive because the agar acts a barrier between the cells and the test article, allowing less penetration compared to a direct contact method such as MEM Elution.

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We do not believe this is appropriate justification because the marketed product will not have a pH of 7.0-7.5. Please provide justification that supports the safety of the subject lubricant with its intended specifications. In addition, we are unable to locate the test report for the modified cytotoxicity study in your submission. Please provide this information.

8. To assess the sensitization potential of the subject lubricant, your conducted a hypersensitivity test in guinea pigs. This test is not sufficient as it is not an appropriate test for a device in contact with mucosal surfaces such as personal lubricants. This is especially true considering the unfavorable cytotoxicity study results. Please provide the complete protocol, results, and analysis from a sensitization study that is appropriate for materials in contact with mucosal surfaces (e.g., ISO Maximization Study). Please note that testing should be completed with both polar and non-polar extracts of your device.

9. You conducted an Acute Systemic Toxicity test using both IV and IP routes of administration to evaluate the acute systemic toxicity potential of the subject lubricant. While the test animals did not display any signs of toxicity via the IP route of administration, several very concerning adverse effects were seen in the test animals in both studies evaluating the IV route of administration. In the first IV study, the two test animals went into convulsions and were gasping immediately following an injection of the undiluted subject lubricant. Both animals died shortly thereafter. In the second IV study, despite dilution of the subject lubricant in saline (2.9 grams in 15.4 mL), four out of the five animals displayed significant clinical signs of toxicity, three animals lost excess of 10% of their body weight, and one animal died. To justify these results, you simply state that the IV route of administration is not an appropriate method for evaluating a vaginal lubricant; however, this does not explain why the subject lubricant caused these reactions in the test animals. Please provide this information.

In addition, please reevaluate the acute systemic toxicity potential of the subject lubricant as described in Deficiency 10.

Furthermore, you did not provided justification for your test dose of 50 mL/kg for either the IV or IP route of administration. Please provide a justification for your test dose that accounts for daily, repeat use.

10. In lieu of conducting both a vaginal irritation study and an acute systemic toxicity study, an alternate testing approach that may be more relevant to the proposed use of your device (i.e., vaginal use) is summarized below. This alternate design is a hybrid between the ISO Vaginal Irritation test and the ISO Acute Systemic Toxicity test and assesses both the systemic toxicity and mucosal irritation potential of your device.

- Rabbits (n=5 per group) are treated with either the test article extracted in a polar extraction vehicle, the test article extracted in a non-polar extraction vehicle, or saline (negative control) and dosed 1x/day for 10 days. Each animal will receive 1 ml of the test article extracted in a polar extraction vehicle (treatment

group 1), the test article extracted in a non-polar extraction vehicle (treatment group 2), or saline (control).

- The following information should be collected during the study:
  - initial, daily, and terminal body weights;
  - initial baseline and terminal blood samples;
  - daily health observations;
  - food consumption data;
  - macroscopic and microscopic evaluation of vaginal, cervical, and uterine tissues;
  - necropsy including examination of major organs, including organ weights; and
  - tissues from major organs during necropsy.

If you choose to follow this approach, we recommend that you discuss your protocol with us prior to initiating this study.

11. It appears that you changed applicator material and then conducted additional biocompatibility tests (irritation and sensitization) on the new version of the applicator. However, it is unclear is unclear which version of the applicator was evaluated in the cytotoxicity study conducted. Please provide this information. If the cytotoxicity testing was not completed on the new version of the applicator, please provide additional cytotoxicity testing on the new version of the applicator. Alternatively, you may justify why the cytotoxicity testing already completed is sufficient.

Condom Compatibility

12. You conducted tensile and airburst testing on several brands of latex, polyurethane, and polyisoprene condoms. You evaluated these condoms untreated and following 30 minutes of exposure to the subject lubricant and to KY Jelly. You evaluated 20 samples per condom type per exposure and presented your results in terms of the mean and standard deviation of each parameter evaluated. In order for us to fully evaluate the effect of the subject lubricant on condoms, please provide your condom compatibility results as described in the following table for each parameter evaluated:

Condom Type	airburst pressure of condoms without additional lubricant (kPa) (n = xx)	airburst pressure for condoms lubricated with test lubricant (kPa) (n = xx)	difference	% decrease
1	*Insert mean and confidence interval*	*Insert mean and confidence interval*		
2				
3				

Please note that any drop in condom properties of greater than 10% will need to be justified.

13. You do not make any claims in your product labeling regarding condom compatibility. Please include an appropriate condom compatibility claim based on the results of condom compatibility testing conducted and please modify your Indications for Use form accordingly.

In addition, please revise your review memo to include a detailed discussion of all the performance testing conducting by the sponsor including cleaning validation, all biocompatibility studies, shelf-life, and condom compatibility. This discussion should include a summary of the protocol, the study results, and your reasoning as to why the study results are acceptable.

Thank you.

[redacted]haron

Sharon M. Andrews
Biomedical Engineer, DRARD/OGDB

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10903 New Hampshire Avenue
WO66, Room G102
Silver Spring, MD 20993
Phone: 301-796-6650
:: 301-847-8111
aron.andrews@fda.hhs.gov

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THIRD PARTY REVIEW CHECKLIST

1. Is this 510(k) eligible for third party review, i.e.:		
a. Is the device on the list of eligible devices?*	(Yes)	No
b. Can a determination of substantial equivalence be made without clinical data?	(Yes)	No
c. Are you aware of the 510(k) holder being the subject of an Integrity Investigation?	Yes	(No)

IF THE ANSWER IS "NO" TO A or B above, or "YES" to C above, PLEASE BRING THE SUBMISSION TO POS IMMEDIATELY.

Are the following elements included in the submission:

2. A cover letter signed by the third party's official correspondent clearly identifying:		
a. The purpose of the submission	(Yes)	No
b. The name and address of the third party	(Yes)	No
c. The name and address of the 510(k) holder	(Yes)	No
d. The name of the device (trade name, common or usual name, and FDA classification name)	(Yes)	No
e. The third party's recommendation with respect to the substantial equivalence of the device	(Yes)	No
f. The date the third party first received the 510(k) from the 510(k) holder	(Yes)	No

3. A letter signed by the 510(k) holder authorizing the third party to submit the 510(k) on its behalf and to discuss its contents with FDA.	(Yes)	No

4. The complete 510(k) conforming to FDA's established requirements relating to content and form of such submissions.	(Yes)	No

5. A complete review of the 510(k), signed by all personnel who conducted the third party review and by an individual within the third party responsible for supervising third party reviews, with a recommendation concerning the substantial equivalence of the device.	(Yes)	No

6. A certification that:		
a. The third party continues to meet the personnel qualifications and prevention of conflict of interest criteria reviewed by FDA	(Yes)	No
b. Statements made in the third party's review are true and accurate to the best knowledge of the third party	(Yes)	No
c. The third party's review is based on the 510(k) that it is submitting with the review	(Yes)	No
d. The third party understands that the submission to the government of false information is prohibited	(Yes)	No

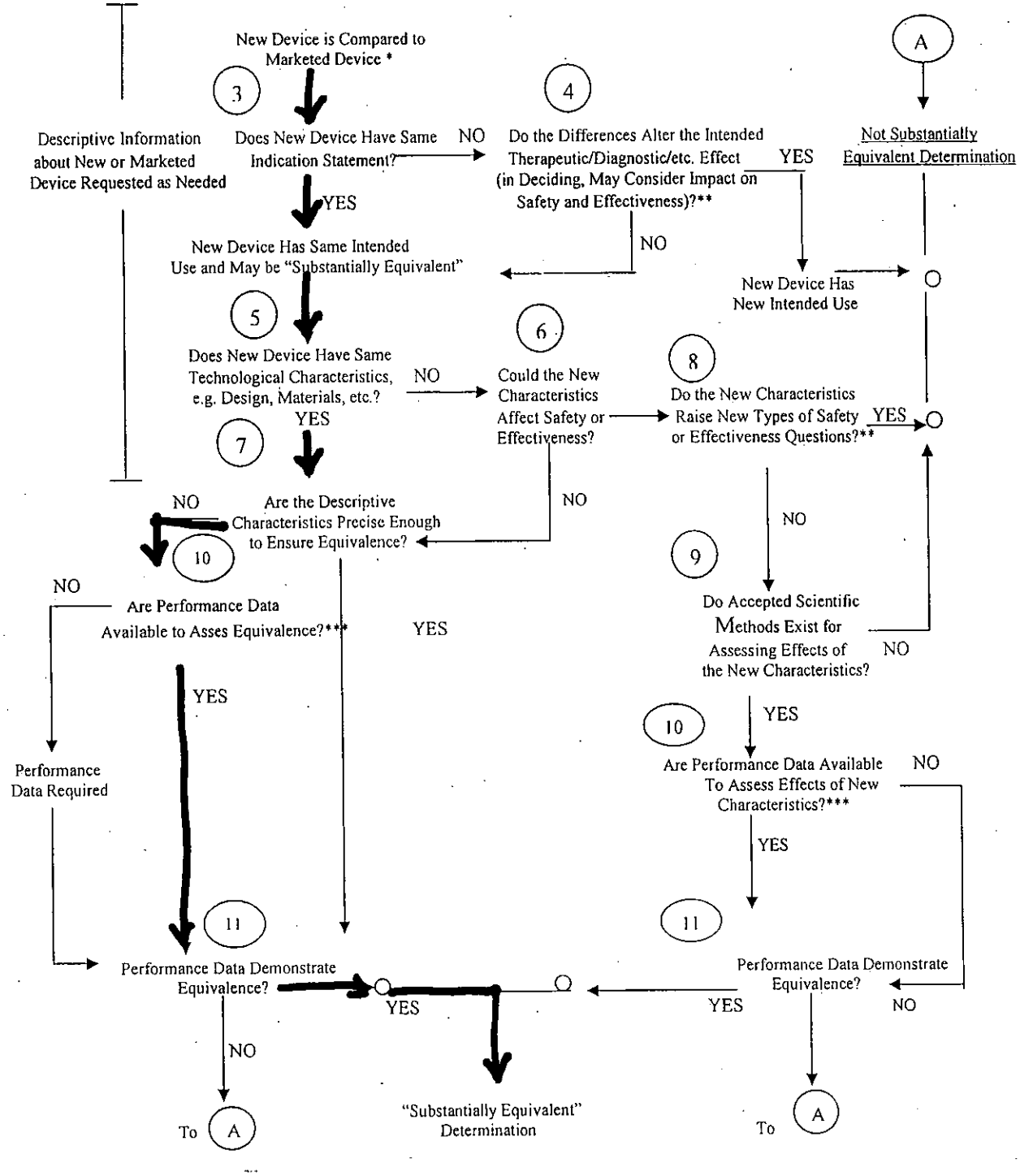
7. Are the following forms included in the submission as discussed in the Center's guidance document entitled Third Party Review-An Instruction Manual for Conducting Reviews of Premarket Notifications:		
a. Third Party Premarket Notification (510(k)) Checklist for Acceptance Decision (Parts I and II)	(Yes)	No
b. Record of Deficiencies, if applicable (attachment 1a)	(Yes)	No
c. Indications for Use Form	(Yes)	No
d. 510(k) Summary or Statement (attachment 1c)	(Yes)	No
e. 510(k) Truthful and Accurate Statement (attachment 1d)	(Yes)	No
f. Third Party "Substantial Equivalence" (SE) Decision Making Documentation (attachment 2)	(Yes)	No

IF ANY OF THE ABOVE INFORMATION IS NOT INCLUDED WITH THE THIRD PARTY'S SUBMISSION OR IS NOT ADEQUATE, CONTACT THE THIRD PARTY AND ATTEMPT TO RESOLVE THE DEFICIENCY. PLEASE INCLUDE A MEMORANDUM TO THE RECORD OF THE TELEPHONE CALL. WHEN THE INFORMATION IS RECEIVED PLEASE REVISE THIS CHECKLIST OR COMPLETE A NEW ONE.

COMMENTS: Reviewed by Sharon Andrews 5/4/10

*If the third party incorrectly classified the device and it is not a device type eligible for third party review please bring to POS.

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS



❖ 510(k) Submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

❖❖ This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

❖❖❖ Data maybe in the 510(k), other 510(k)s, the Center's classification files, or the literature.

DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

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

May 28, 2010

LIL DRUG STORE PRODUCTS, INC.
c/o REGULATORY TECHNOLOGY SERVICES, LLC
1394 25TH STREET, NW
BUFFALO, MINNESOTA 55313
UNITED STATES
ATTN: MARK JOB

510k Number: K101098

Product: REPLENS LONG-LASTING VAGINAL M

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Pleaseremember that all correspondence concerning your submission MUST be sent to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff

K101098 1 31

Date: May 27, 2010

FDA CDRH DMC

MAY 28 2010

Received

U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Additional Information for **K101098**
Lil' Drug Store Products Inc..
Long-Lasting Vaginal Moisturizer Gel

To Whom It May Concern:

Enclosed in duplicate is the following information:

As requested by a letter from Colin Pollard dated May 5, 2010, requesting additional information for this submission. The review memo has been revised. The sponsor provided additional information to support the revision of the memo. This information addresses the items raised in the request. Based on this review of the additional information, a decision of substantially equivalence is recommended.

If you should have any further questions regarding this submission please contact me at 763 682 4139 or fax 763 682 4420 or email at mark@markjob.com. Please fax any correspondence regarding this submission to Regulatory Technology Services LLC.

Sincerely,

Mark Job
Responsible Third Party Official

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Addendum to the Review Memo for K101098

Third Party Reviewer: Mark Job - Regulatory Technology Services LLC

Dated: May 26, 2010

Replens Long-Lasting Vaginal Moisturizer Gel

Deficiencies from a letter dated May 5, 2010 from Colin M. Pollard

Device Description

1. Please note that personal lubricants such as Replens are Class II devices, covered by procode NUC (vaginal patient lubricant), under regulation number 21 CFR 884.5300.

   Reviewer comments: The sponsor has provided the updated CDRH cover sheet, 510(k) Summary and the Device Information (section 4.0) with the corrected product code and regulation number. These documents are provided with this response.

2. You state that the pH of the subject lubricant is 2.9 and ranges from 2.3-3.5. You also state that this is in the physiologic range of the normal vagina. However, it appears to us that the pH of the subject lubricant is below normal vaginal pH, which typically ranges from 4.0 – 5.0 in women with active menstrual cycles (M. Garcia-Closas et al. Epidemiologic determinants of vaginal pH. AJOG. Volume 180(5). pp.1060-1066.). In light of this information, please justify the pH of the subject lubricant. You justification should include, but is not limited to, a discussion of the possible changes to the vaginal microflora that may result from prolonged exposure to this product and if a low pH environment makes the vagina more susceptible to infections of any kind.

   Reviewer comments: The sponsor has provided an extensive summary from numerous articles that supports their selection of the pH range of 2.5 to 3.5 for the Replens product. In developing Replens, the company noted that products with pH ranges around 3 to 5 are commonly used as vaginal moisturizers. This may be due to the observed pH ranges in pre-menopausal women (as cited in the FDA's reference above), as well as the clinical observation that post-menopausal women (many of whom report an increase in vaginal dryness discomfort) frequently are shown to have an upward shift in vaginal pH. Replens, therefore, was formulated at a pH that, in addition to providing moisture to the vaginal environment, could act as a mild buffering agent. While the sponsor does not intend to seek pH adjustment or maintenance claims for Replens, they have summarized pH data in their response from both pre- and post-menopausal women using the product that demonstrates that the pH of the Replens vaginal moisturizer does not have a negative impact on vaginal pH or vaginal microflora. The company provided references from the clinical literature that describe the normal pH of a healthy vagina as weakly acidic, having a pH lower than 4.5 in pre-menopausal women and generally in a range of 3.5 to 4.5. The acidic condition is maintained by the normal lactobacillus-dominated flora producing lactic acid. The low vaginal pH restricts the growth of anaerobic microflora that can produce abnormal vaginal discharge and odors when the discharge amines are volatilized at pH > 5. During menopause, the vaginal pH becomes less acidic and rises to almost 7.0 in the post-menopausal female.

   There is a body of literature demonstrating a linkage between high pH and unfavorable changes in the balance of flora that comprise the normal vaginal ecosystem and corresponding risk of vaginal infections. In vitro studies have shown that acidification by lactobacilli can inhibit the proliferation of pathogenic microorganisms, such as *C. albicans*, *E. Coli*, *G. vaginalis*, *Mobiluncus* spp., and other bacteria. In addition, published literature has demonstrated that locally-

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administered products with a low pH (lactic acid, low-pH lactate gel, polycarbophil acidic gels) can help restore normal vaginal acidity and facilitate recolonization with normal vaginal flora in patients with bacterial vaginosis. The clinical literature supports the view that it is desirable to maintain normally acidic vaginal pH and to preserve the normal balance of flora in the vaginal ecosystem.

Effect of Replens in Post-Menopausal Women

Bachmann et al performed a double-blind evaluation of Replens and KY Brand Lubricating Jelly in the treatment of vaginal dryness in peri-menopausal and post-menopausal women. Five consecutive days application of Replens resulted in a reduction in mean pH from 5.6 to 4.9.

Zinny and Lee performed a double-blind evaluation of Replens and KY Jelly on pH and normal vaginal flora in post-menopausal women. Replens or KY Jelly was applied on alternate nights for twenty eight days. The mean pH values at baseline and at the end of treatment were 5.8 and 4.8, respectively.

Two longer studies were conducted by Nachtigall (treatment of vaginal dryness in post-menopausal women) and Gelfand and Wendman (treatment of vaginal dryness in women with a history of breast cancer in whom hormone replacement therapy was contraindicated). The first demonstrated the vaginal pH after 3 months of use dropped from 5.8 to 4.8. The second demonstrated the vaginal pH after 4 months dropped from 6.9 to 4.1. .

Young performed a long-term (12 month) open study of the effects of Replens use (3 applications per week) in post-menopausal women. There was a small decrease in mean and median pH values; mean pH value decreased from 5.1 at baseline to 4.7 at 12 months. Minimum pH was consistently 4.0 at baseline, week 12, month 6, and month 12.

The long-term extension of the Bachmann study reported that over a twelve month treatment period (3 applications per week) there was a sustained reduction in vaginal pH associated with use of Replens. Mean pH values declined from 5.1 at day 16 (entry to open extension phase) to 4.7 at month 6, and remained at 4.7 at 12 months. Minimum pH was 3.5 at baseline and remained at 3.5 after 12 months.

All of these studies resulted in acceptable pH values within the normal vaginal pH range of 3.5 to 4.5. The lower pH of the Replens product (2.5 to 3.5) did not result in any vaginal pH values lower than 3.5 indicating it has no negative effect on the vaginal pH.

In addition, limited data show that Replens does not have a negative impact on vaginal flora or risk of vaginal infection in post-menopausal women. The impact of Replens on vaginal flora (lactobacillus colony counts) was studied by Zinny et al (1991) in post-menopausal women. Replens was applied on alternate nights for twenty eight days. Four weeks of application of Replens did not have a

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significant effect on lactobacillus counts in this study.

Effect of Replens in Pre-Menopausal Women

There is limited data regarding the use of Replens in pre-menopausal women, primarily because vaginal dryness, which the product is intended to treat, tends to disproportionally affect post-menopausal women.

With regard to pre-menopausal women with a healthy (low) pH at baseline, the company does not have clinical data on changes in pH associated with Replens use in this population. However, the two long-term (12 month) studies described above reported minimum pH in addition to mean pH. In the Young study, minimum pH reported in the population treated with Replens remained constant at 4.0 at baseline, week 12, month 6 and month 12. In the Bachmann extension study, minimum pH was 3.5 at baseline, 4.0 at day 16, and 3.5 at months 6 and 12. Although these studies included primarily post-menopausal women, they show that in women with low baseline pH treated with Replens, pH stays relatively constant and remains within the normal, healthy range. Lil' Drug Store believes that this data demonstrates that the product will not adversely affect pH in pre-menopausal women.

Effect of Replens on Microflora

There is limited data showing that Replens does not have a negative impact on vaginal flora or risk of vaginal infection in pre-menopausal women. Wu performed a pilot study to assess the effect of Replens use every third day on bacterial vaginosis. At week four, there was improvement in Nugent scores, vaginal odor and clue cell count ($p < 0.05$). Eleven women converted from amine positive to negative (73 +/- 20%). There was no significant change in vaginal pH.

References to publications that were used for this summary are provided in the sponsor's response. The sponsor's summary provides adequate justification for the pH range of the product and that the product has no negative impact on vaginal pH or vaginal microflora. This deficiency has been addressed.

Indications for Use

3. Please revise your indications for use statement to that of the standard indication for personal lubricants as follows: *[Product name] is a personal lubricant, for penile and/or vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is [is not] compatible with natural rubber latex condoms [and/or synthetic condoms (specify specific type(s) of synthetic condoms)].* Please modify your Indications for Use form, 510(k) Summary, and labeling accordingly, and please provided revised copies of these documents for review. Please note that the last sentence of your indication statement is dependent upon how you choose to address the condom compatibility issues described in Deficiencies 12-13.

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Reviewer comments: The sponsor has provided an updated Indications for Use Form and 510(k) Summary with the corrected indication statement. The updated indication statement is acceptable.

Labeling

4. Please revise your package insert as follows:

   a) Please provide information in the labeling regarding when to dispose of the applicator (e.g., when the lubricant has been used up).

      Reviewer comments: The package insert has been updated with a sentence that adequately addresses this item.

   b) Please state that the applicator should be cleaned immediately after use. The cleaning validation testing provided in Appendix D of the 510(k) submission evaluated the applicator after sitting for only 10 minutes following contamination.

      Reviewer comments: The package insert has been updated with a sentence that adequately addresses this item.

   c) Please state that the applicator should be completely dry before reassembly.

      Reviewer comments: The package insert has been updated with a sentence that adequately addresses this item.

   Please provide a revised copy of your product labeling including the above requested revisions

   Reviewer comments: The revised package insert is acceptable.

Shelf Life

5. Please clarify if the 36 month accelerated-aging study conducted by Pharmetics evaluated ingredients from the current suppliers and the current product packaging. If not, please justify why any differences between the evaluated product and the current product would not affect shelf-life. Please note that if your justification is not sufficient you will be asked to conduct additional shelf-life testing.

   Reviewer comments: The 36 month real time study conducted by Pharmetics evaluated the current product packaging and materials with equivalent grades to those indicated in the 510(k). The real time testing of the product (summarized in the review memo) demonstrates that it meets the product specifications and supports the proposed 3 year shelf life. This item has been addressed.

Biocompatibility

6. Four key biocompatibility studies provided in your submission were conducted twenty years

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ago. These studies are as follows:

Acute Vaginal Irritation in Rabbits (1989)
Subacute Vaginal Irritation in Rabbits (1989)
Subacute Vaginal Irritation with Histological Examination (1990)
Hypersensitivity (1989)

Please confirm if the current version of the subject lubricant is identical to the product evaluated in the above studies, (i.e., identical ingredient suppliers, identical manufacturing processes, etc.). If not please provide vaginal irritation and sensitization testing on the final, finished version of the subject lubricant. These studies should evaluate appropriate models (e.g., ISO Vaginal Mucosal Irritation, ISO Maximization Sensitization), evaluate both polar and non-polar extracts, and follow the extraction procedures outlined in ISO 10993-12:2007.

Reviewer comments: According to the sponsor, the Replens formulation used in these four studies is essentially identical to the product as it is marketed today. Specifically:

1. **The product has an equivalent formulation with the exception of insignificant variations in the amount of purified water and glycerin in the gel (refer to material percentage table in sponsor's response);**
2. **The product has comparable product specifications (appearance, color, pH, sorbic acid identity and content, density, no leakage);**
3. **The product has used the same grade of raw materials (all are GRAS or USP-NF grade materials); and**
4. **The manufacturing process used today is comparable to the manufacturing process used to produce the Replens formulation used in these four biocompatibility studies. Minor changes include mixing the gel in two vessels instead of three, using a tighter temperature range during a particular mixing step, and changing sampling protocol.**

Therefore, although the material suppliers have changed, they provide the identical grade of ingredients and the changes to the manufacturing processes as described would not be considered significant as it relates to the biocompatibility studies. This deficiency has been addressed adequately and further vaginal irritation and sensitization testing on the current version of the product is not warranted.

7. You conducted an Agar Overlay test to evaluate the cytotoxicity potential of the subject lubricant, which displayed cytotoxicity scores of 2 and 3. This is a much higher degree of cytotoxicity than typically seen for personal lubricant products. This is especially concerning because an Agar Overlay test is less sensitive than the MEM Elution Cytotoxicity test typically used to evaluate the cytotoxicity potential of personal lubricant products. An Agar Overlay test is less sensitive because the agar acts a barrier between the cells and the test article, allowing less penetration compared to a direct contact method such as MEM Elution.

   You state that the negative cytotoxicity result was caused by the low pH of the subject lubricant, and to demonstrate this, you repeated the cytotoxicity study after adjusting the pH

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of the subject lubricant to 7.0-7.5. You state that this modified cytotoxicity study did not display any signs of cytotoxicity.

We do not believe this is appropriate justification because the marketed product will not have a pH of 7.0-7.5. Please provide justification that supports the safety of the subject lubricant with its intended specifications. In addition, we are unable to locate the test report for the modified cytotoxicity study in your submission. Please provide this information.

Reviewer comments: The sponsor consulted with their primary GLP testing laboratory (Nelson Labs) and consulting toxicologist (Dr. Dan McLain, Walker Downey & Associates, Inc) regarding the methodology for testing cytotoxicity of personal lubricants. Both Nelson Labs and Dr. McLain believe that the Agar Overlay test is more appropriate to determine the cytotoxicity of an acidic lubricant material (such as Replens) than the direct contact MEM Elution test. A reasonable justification for this position is summarized in the response. In addition, the sponsor explained that the pH adjustment would be considered appropriate per ISO 10993-5 and the test results demonstrate the issue is related to pH and not chemically- or toxicologically-induced. Considering the passing cytotoxicity result with pH adjustment and the passing results from the GLP sensitization and vaginal mucosal cell irritation testing which are more reflective of the clinical intended use of the product, the sponsor has demonstrated acceptable biocompatibility of Replens. The GLP test report for the modified cytotoxicity study was provided. This deficiency has been adequately addressed.

8. To assess the sensitization potential of the subject lubricant, your conducted a hypersensitivity test in guinea pigs. This test is not sufficient as it is not an appropriate test for a device in contact with mucosal surfaces such as personal lubricants. This is especially true considering the unfavorable cytotoxicity study results. Please provide the complete protocol, results, and analysis from a sensitization study that is appropriate for materials in contact with mucosal surfaces (e.g., ISO Maximization Study). Please note that testing should be completed with both polar and non-polar extracts of your device.

Reviewer comments: The sponsor believes that the hypersensitivity test performed on Replens (the modified Maguire sensitization test) is comparable to the two sensitization methods currently used to test personal lubricants (the ISO Maximization Study and the Buehler method) in terms of procedure and sensitivity and, therefore, that further testing of Replens is not warranted.

The sponsor consulted with Nelson Laboratories regarding these test methodologies. According to Nelson Labs the Buehler method has historically been the preferred method for personal lubricants for the following reasons: 1) they are applied topically (as administered in the Buehler method); 2) the ISO maximization test requires the test article to be a liquid, suspendable powder, or extract (and lubricants are not liquids or suspendable powders and they are difficult to extract); and 3) injecting the lubricant "neat" (i.e., directly) by intradermal means is in contrast with the test method and has not been studied to know if it is a valid method that will accurately measure sensitization without harm to the test animals. Therefore, while the ISO Maximization test is generally considered more sensitive

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than the Buehler method, it has inherent limitations that the company believes prevent it from being an appropriate test method for lubricants such as Replens. As described in the response, the sponsor believes that the modified Maguire method used in the Replens hypersensitivity test is a better alternative to both the ISO Maximization and Buehler methods.

The modified Maguire sensitization test method involves topical application of the test material as in the Buehler method, but it also involves injection of an adjuvant to stimulate the immune system response as in the ISO Maximization method. Because the Maguire method only involves topical application of the test material, it eliminates the issues involved in either creating extracts of the lubricant or injecting it neat in the ISO Maximization test.

The sponsor has provided a reasonable justification of their use of the modified Maguire sensitization test for the Replens product. The modified Maguire sensitization test is more sensitive than the Buehler method and potentially more consistent than the ISO Maximization test, and it does not have the same technical limitations as the ISO Maximization test for use with personal lubricants. This deficiency has been addressed and no further hypersensitivity testing (e.g., ISO Maximization test) is necessary.

9. You conducted an Acute Systemic Toxicity test using both IV and IP routes of administration to evaluate the acute systemic toxicity potential of the subject lubricant. While the test animals did not display any signs of toxicity via the IP route of administration, several very concerning adverse effects were seen in the test animals in both studies evaluating the IV route of administration. In the first IV study, the two test animals went into convulsions and were gasping immediately following an injection of the undiluted subject lubricant. Both animals died shortly thereafter. In the second IV study, despite dilution of the subject lubricant in saline (2.9 grams in 15.4 mL), four out of the five animals displayed significant clinical signs of toxicity, three animals lost excess of 10% of their body weight, and one animal died. To justify these results, you simply state that the IV route of administration is not an appropriate method for evaluating a vaginal lubricant; however, this does not explain why the subject lubricant caused these reactions in the test animals. Please provide this information.

   In addition, please reevaluate the acute systemic toxicity potential of the subject lubricant as described in Deficiency 10.

   Furthermore, you did not provided justification for your test dose of 50 mL/kg for either the IV or IP route of administration. Please provide a justification for your test dose that accounts for daily, repeat use.

   Reviewer comments: The sponsor provided a detailed explanation why the lubricant caused the adverse effects noted during the IV study. Replens is a nonsterile, primarily aqueous product composed of approximately 8% waxes and/or fat. After two expert toxicology consultations the sponsor learned that this latter property should have immediately exempted it from acute toxicity testing by the intravenous route. Additionally, the non-sterile nature of the product is not ideal for dosing by an

intravenous route and the test solution should have been sterilized prior to administration. The experts they consulted indicated that it is not scientifically appropriate or advisable to administer a nonsterile, lipid-containing solution with potential for micro-emboli formation via intravenous administration.

Their consulting toxicologist (Dr. Dan McLain, Walker Downey & Associates, Inc) retrospectively reviewed the data from these Acute Systemic Toxicity studies. Dr. McLain and a different testing laboratory concurred that the described clinical signs (i.e. convulsions, gasping, and death after administration) of the test animals in the first two studies are classical signs of pulmonary embolism most likely caused, in this case, by the embolic fatty micelles formed following test article extraction.

A third IV test was conducted after the 510(k) was submitted and produced passing results (see final test report provided in the response). In this protocol, they further diluted the test article to 1/20th the original dosing concentration. Based on the absorption rate provided in the response, this dosage represented over 120 million times the amount of the product that would be expected to make its way into the blood stream. Thus, this dosage more than adequately reflects daily, repeat use of the device. This final test demonstrated that in the absence of significant quantities of embolism-causing fatty micelles, Replens does not exhibit toxic effects when delivered intravenously even in a non-sterile form.

This response adequately addresses this deficiency and supports the acceptable biocompatibility of the product.

10. In lieu of conducting both a vaginal irritation study and an acute systemic toxicity study, an alternate testing approach that may be more relevant to the proposed use of your device (i.e., vaginal use) is summarized below. This alternate design is a hybrid between the ISO Vaginal Irritation test and the ISO Acute Systemic Toxicity test and assesses both the systemic toxicity and mucosal irritation potential of your device.

    Rabbits (n=5 per group) are treated with either the test article extracted in a polar extraction vehicle, the test article extracted in a non-polar extraction vehicle, or saline (negative control) and dosed 1x/day for 10 days. Each animal will receive 1 ml of the test article extracted in a polar extraction vehicle (treatment group 1), the test article extracted in a non-polar extraction vehicle (treatment group 2), or saline (control).

    The following information should be collected during the study:
    initial, daily, and terminal body weights;
    initial baseline and terminal blood samples;
    daily health observations;
    food consumption data;
    macroscopic and microscopic evaluation of vaginal, cervical, and uterine tissues;
    necropsy including examination of major organs, including organ weights; and
    tissues from major organs during necropsy.

    If you choose to follow this approach, we recommend that you discuss your protocol with us prior to initiating this study.

Reviewer comments: The sponsor provided justification that the Vaginal Irritation Studies, including the Vaginal Irritation with Histological Examination, already performed are substantially equivalent in terms of methodology to the test requested above. This test was: 1) performed on six rabbits; 2) involved "neat" (i.e., direct) administration of the product for 14 days; 3) included targeted microscopic evaluation of the vaginal, cervical, uterine, and ovarian tissues; 4) included macroscopic evaluation of major organs; and 5) included observation for behavioral or toxic signs, food consumption and body weights. These vaginal irritation tests demonstrated that the product is non-irritating in the target tissue.

The sponsor provided support for the safety of Replens through the acute toxicity studies. Test results for IP administration were consistent with the biocompatibility profile of the product and indicate that it is non-toxic when delivered by the IP route. The company maintains that the results observed in the IV portion of the test are not relevant, due to the wax/fat content of the product that could reasonably be expected to cause emboli. It is noted that test results were provided, however, that indicate Replens is non-toxic when delivered by the IV route when embolic fatty micelles are minimized (e.g., further diluted).

This response adequately addresses this deficiency and supports the acceptable biocompatibility of the product. No further testing using the alternate testing approach described above is required.

11. It appears that you changed applicator material and then conducted additional biocompatibility tests (irritation and sensitization) on the new version of the applicator. However, it is unclear is unclear which version of the applicator was evaluated in the cytotoxicity study conducted. Please provide this information. If the cytotoxicity testing was not completed on the new version of the applicator, please provide additional cytotoxicity testing on the new version of the applicator. Alternatively, you may justify why the cytotoxicity testing already completed is sufficient.

    Reviewer comments: The sponsor has stated that all of the applicator biocompatibility tests (cytotoxicity, vaginal irritation, and sensitization) were conducted on the current version of the reusable applicator. The vaginal irritation and sensitization studies were not complete at the time of the initial 510(k) submission and were provided as supplemental information in response to a deficiency from the Third Party Reviewer. This deficiency is adequately addressed.

Condom Compatibility

12. You conducted tensile and airburst testing on several brands of latex, polyurethane, and polyisoprene condoms. You evaluated these condoms untreated and following 30 minutes of exposure to the subject lubricant and to KY Jelly. You evaluated 20 samples per condom type per exposure and presented your results in terms of the mean and standard deviation of each parameter evaluated. In order for us to fully evaluate the effect of the subject lubricant on condoms, please provide your condom compatibility results as described in the following table for each parameter evaluated:

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Condom Type
airburst pressure of condoms without additional lubricant (kPa)
(n = xx)
airburst pressure for condoms lubricated with test lubricant (kPa)
(n = xx)
difference
Insert mean and confidence interval
% decrease
Insert mean and confidence interval

Please note that any drop in condom properties of greater than 10% will need to be justified.

Reviewer comments: The sponsor provided a revised table with the requested condom compatibility testing data. Values that decreased following treatment with either Replens or KY Jelly by more than 10% compared to untreated condoms are highlighted in orange and those that decreased by more than 20% are highlighted in red.

Latex Condom Test Results:
Five out of 15 test sets across 3 brands of latex condoms treated with Replens (n≥20 each) resulted in decreases from the untreated condoms greater than 20%. These 5 results were 22% and 25% for air burst pressure, 27% for air burst volume, 30% for tensile strength, and 29% for breaking force. For each of these 5 results, the corresponding minimum value compared to the ISO/ASTM latex condom standard goal were 173%, 120%, 152%, 104%, and 268%, respectively. Since the latex condoms treated with Replens still met the ISO/ASTM standard and they performed equivalent to the condoms treated with the latex condom compatible predicate (K-Y Jelly), the Replens vaginal lubricant is considered compatible with latex condoms.

Synthetic Condom Test Results:
Two out of 10 test sets across 2 brands of synthetic condoms treated with Replens (n≥20 each) resulted in decreases from the untreated condoms greater than 20%. These 2 results were 25% for air burst pressure and 23% for tensile strength. For each of these 2 results, the corresponding minimum value compared to the ISO/ASTM latex condom standard goal were 128% and 169%, respectively. Since the synthetic condoms treated with Replens still met the ISO/ASTM standard and they performed equivalent to the condoms treated with the synthetic condom compatible predicate (K-Y Jelly), the Replens vaginal lubricant is considered compatible with synthetic condoms.

This response adequately addresses this deficiency and supports the latex and synthetic condom compatibility of the Replens product.

13. You do not make any claims in your product labeling regarding condom compatibility. Please include an appropriate condom compatibility claim based on the results of condom compatibility testing conducted and please modify your Indications for Use form

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accordingly.

Reviewer comments: The sponsor has updated the Indications for Use form to include a condom compatibility statement. The package insert has been updated to include a Frequently Asked Question that states: "*Is Replens compatible with condoms? Yes, Replens is compatible with latex and synthetic condoms*"

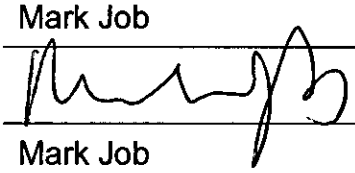
In addition, please revise your review memo to include a detailed discussion of all the performance testing conducting by the sponsor including cleaning validation, all biocompatibility studies, shelf-life, and condom compatibility. This discussion should include a summary of the protocol, the study results, and your reasoning as to why the study results are acceptable.

Reviewer comments: The cleaning validation discussion was presented in the Sterilization/Shelf Life/Reuse section VII of the review memo. The summary of the biocompatibility testing was in the Biocompatibility section VIII. The summary of shelf life testing was in the Sterilization/Shelf Life/Reuse section VII of the review memo. The condom compatibility testing was summarized in the Performance Testing – Bench section XI. The Performance Testing – Bench section of the review memo was updated with a reference to these other sections. This item is complete.

REVISED
Third Party Review
Reviewer Memorandum

Third Party Organization: Regulatory Technology Services LLC

Primary Reviewer: Mark Job

Signature:  Date: May 26, 2010

Print Name: Mark Job Title: Reviewer

510(k) Applicant's Name: **Lil' Drug Store Products, Inc.**

Device Name: **Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reusable Applicator)**

Contact Person: **Patricia L. Miller**

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I. Purpose and Submission Summary:

The 510(k) holder **Lil' Drug Store Products, Inc.** would like to introduce the **Replens Long-Lasting Vaginal Moisturizer** into interstate commerce as a vaginal patient lubricant device. This product, **Replens**, has been sold as a cosmetic in the U.S. since 1989 based on its intended use as a moisturizer. The sponsor has been marketing **Replens** with the understanding that it did not fall under the definition of a medical device under Section 201(h) of the Federal Food, Drug, and Cosmetic Act ("the Act") and was therefore not subject to the requirements for premarket clearance or approval under the Act. Based on recent discussions with CDRH, the sponsor understands that the Center's current position is that claims for relief of vaginal dryness may render a product a medical device under 21 C.F.R. § 884.5300 (Class II, Product Code MMS, NUC). **Lil' Drug Store Products, Inc.** has submitted a 510(k) premarket notification to support the marketing of Replens as a medical device for over-the-counter (OTC) use. During the review of the original submission dated February 25, 2010 one round of deficiencies was issued (March 16, 2010). Additional information was provided April 9, 2010 to respond to the deficiencies. FDA review resulted in another round of deficiencies on May 5, 2010. Additional information was provided May 24, 2010. All deficiencies have been adequately addressed.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use = **Over-the-Counter** Page Number: **Additional Information dated May 24, 2010**	X		
Truthful and Accuracy Statement Page Number: **Section 3.0**	X		
510(k) Summary Page Number: **Additional Information dated May 24, 2010**	X		
Standards Form (FDA Form 3654) Page Number: **Section 0.5**	X		

III. Device Description

	Yes	No	N/A
Is the device life-supporting or life sustaining?		X	
Is the device an implant (implanted longer than 30 days)?		X	
Does the device design use software?		X	
Is the device sterile?		X	
Is the device reusable (not reprocessed single use)?		X	
Are "cleaning" instructions included for the end user?		X	

The submission describes the **Replens Long-Lasting Vaginal Moisturizer Gel** as a non-sterile, water-based, vaginal moisturizing gel for vaginal dryness and personal lubrication of

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Contains Polyquaternium 15	No	Yes
Contains Methylparaben	Yes	Yes
Contains Polyparaben	No	Yes
Contains Mineral Oil NF	Yes	No
Contains Polycarbophil USP	Yes	No
Contains Carbomer Homopolymer Type B NF	Yes	No
Contains Hydrogenated Palm Oil Glyceride (GRAS per 21 CFR 184.1505)	Yes	No
Contains Sodium Hydroxide NF	Yes	No
Contains Sorbic Acid	Yes	No
Container	Aluminum Tube with Plastic (Polyethylene Applicator)	Plastic Bottle
Delivery	Applicator	Manually
Sterile	No	No

Both products are composed of similar ingredients and the technological characteristics are very similar. Replens is delivered in a reusable polyethylene applicator designed for vaginal use. The safety of the applicator has been demonstrated through its commercial use in the Replens Vaginal Moisturizer cosmetic product. Additionally, a vaginal applicator is used with RepHresh Vaginal Gel (K021737).

The formulation of Replens is similar to that of the CVS Personal Lubricant & Moisturizer. Water and glycerin represent approximately 92% of the Replens formulation and provide the primary lubrication and moisturizer characteristics of both Replens and the predicate device. While certain of the other ingredients differ between the two formulations, these other ingredients perform equivalent functions that can be safely accomplished via a variety of ingredients. Each product has ingredients that perform the following functions: vehicle, humectant, gel former and preservative. All ingredients included in Replens are either NF, USP, or are considered "generally recognized as safe for their intended use". In addition, these other Replens ingredients are commonly used in other devices and cosmetics for vaginal use.

Although they perform the same functions as analogous ingredients included in the CVS Personal Lubricant & Moisturizer, Replens contains the following ingredients that are not utilized in the predicate: polycarbophil, Carbomer Homopolymer Type B, mineral oil, hydrogenated palm oil glyceride, sorbic acid, and sodium hydroxide. All of these ingredients are well characterized and are used in other vaginal lubricants. Each ingredient and its characteristics are discussed in detail in section 7.1 of the submission.

Intended Use:

The Replens Long-Lasting Vaginal Moisturizer is intended for the same use as the over-the-counter predicate device, CVS Lubricant & Moisturizer. Both devices are non-sterile, aqueous gels intended for use as a vaginal lubricant and moisturizer for vaginal dryness and personal lubrication of the vaginal area to facilitate ease and comfort during intimate sexual activity.

The comparison of the indications for use statements is provided in the following table.

[illegible]

Replens Vaginal Moisturizer (35g Tube) New Device	CVS® Personal Lubricant & Moisturizer (K062682)
Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.	A non-sterile personal lubricant for OTC consumer use, as a moisturizer for vaginal dryness and personal lubrication of the vaginal area to enhance condom use and to facilitate ease and comfort during intimate sexual activity. CVS Personal Lubricant & Moisturizer is compatible with latex condoms. This device is not a contraceptive or spermicide nor does it contain any such component.

The updated indications for Replens are consistent with the current FDA recommended content of the standard indication for personal lubricants:
[Product name] is a personal lubricant, for penile and/or vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is [is not] compatible with natural rubber latex condoms [and/or synthetic condoms (specify specific type(s) of synthetic condoms)].

Conclusion

The differences in formulations between the predicate device and the new device have been adequately addressed by the biocompatibility testing, condom compatibility testing, and preservative effectiveness testing of the new device. Performance testing demonstrates that Replens is as safe as the predicate and other vaginal moisturizers. Therefore, based on the comparison of the device technological characteristics, the indications for use, and the safety and performance testing results, the Replens Long-Lasting Vaginal Moisturizer is substantially equivalent to the predicate device and does not raise new questions of safety or effectiveness.

VI. Labeling

The labeling is provided in section 5.4 and in the additional information that was provided April 9 and May 24, 2010. The labeling includes all the appropriate instructions for use of this over-the-counter device and the applicable warnings to the user. Based on biocompatibility testing results that indicated the device was an eye irritant, a warning stating, "Keep out of eyes and ears" was added to the instructions for use. There are detailed instructions and diagrams to assist the user in understanding the proper use of the device, cleaning of the reusable applicator, along with a description of how the device works and a list of commonly asked questions with answers. The instructions were updated May 24, 2010 to include the following FAQ: *Is Replens compatible with condoms? Yes, Replens is compatible with latex and synthetic condoms.* No other specific claims are made which would raise questions of safety and effectiveness.

VII. Sterilization/Shelf Life/Reuse

The device is provided non-sterile and the applicator is intended to be reused.

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Verification & Validation Testing:		
Revision level history:		
Unresolved anomalies:		

The device does not employ software.

X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

The device is not electrically powered.

XI. Performance Testing – Bench

Refer to the cleaning validation discussion and the summary of shelf life testing presented in the Sterilization/Shelf Life/Reuse section VII of this review memo. Refer to the summary of the biocompatibility testing in the Biocompatibility section VIII.

Condom Compatibility Testing

The overview of the condom compatibility testing is presented in section 8.2 of the submission and the full test report is provided in Appendix C.1. Condom compatibility was evaluated by measuring burst pressure, burst volume, breaking force, tensile strength and elongation. 5 different brands of condoms were used. Three brands were latex, with two non-lubricated and one lubricated. The other two brands were lubricated synthetic condoms – one was polyurethane and one was polyisoprene. Condoms treated with Replens were used as the test group; untreated condoms and condoms treated with KY Jelly (K810310) were used as the control and comparator, respectively, across all brands. KY Jelly was chosen as the comparator since it is a widely used international brand, like Replens, and because it has a condom compatibility claim that is not limited to latex condoms.

Forty (40) condoms / brand / treatment protocol were tested for Burst Volume and Burst Pressure using the Airburst Testing procedure identified in the FDA recognized standard, ISO 4074:2002(E). Twenty (20) condoms / brand / treatment protocol were tested for Tensile Strength, Elongation, and Breaking Force using the Tensile Testing procedure identified in ISO 4074:2002(E). Acceptance criteria were utilized from both the ISO 4074:2002 and the ASTM D3492-93.

Results from this testing:

- Replens treated condoms met recognized standards on 22 of 25 measures with the following exceptions:
    - The untreated Durex Natural Feeling (lubricated latex) condoms did not meet ASTM standards for Tensile Testing – Tensile Strength. Both the Replens and KY Jelly treated condoms also did not meet the standard and showed equivalent performance declines.
    - The untreated Durex Avanti (polyurethane) condoms did not meet ISO standard for Airburst Testing – Burst Volume. The Replens treated condoms also did not meet

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the standards, but they performed better than the untreated condoms and performed equivalent to KY Jelly.
  - The untreated Durex Avanti (polyurethane) condoms did not meet ASTM standards for Tensile Testing – Elongation at Break. The Replens treated condoms also did not meet the standard, but they performed better than the untreated condoms and also better than KY Jelly.
- As compared to expected test results, performance of Replens treated condoms in air burst and tensile testing exceeded test standards and was substantially equivalent to performance of the untreated and KY Jelly treated condoms.

Conclusions from this testing:
The results of this testing demonstrate that condom strength and integrity are not materially affected by Replens. Therefore, Replens is safe for use with both lubricated and non-lubricated latex condoms and also synthetic condoms. Replens performs comparably to other lubricants with approved claims of condom compatibility.

Preservative Effectiveness Testing

A Preservative Effectiveness Test (PET) was conducted according to USP 32 <51> to verify the effectiveness of the preservative system (methylparaben and sorbic acid). This study tests anti-microbial preservatives against the following organisms: Candida albicans (ATCC 10231), Aspergillus niger (ATCC 16404), Escherichia coli (ATCC 8739), Pseudomonas aeruginosa (ATCC 9027), and Staphylococcus aureus (ATCC 6538).

After inoculation and 0 hour assay, the samples were stored in a 20-25°C incubator for the duration of the test. At 14 days and 28 days, the samples were removed from the incubator and assayed for growth. At each of these time points, an aliquot is removed from the samples and the concentration of organism remaining in the sample is determined by standard plate count procedure.

Plate counts from each time point were compared to those seen in the 0 hour positive control. Reductions in CFU/mL were converted to log reduction values for assessing the antimicrobial effectiveness of the samples, according to USP 32 <51> criteria. Replens was compared against the criteria for category 2 type products (topically used products made with aqueous bases or vehicles, nonsterile nasal products, and emulsions, including those applied to mucous membranes) as follows:

Bacteria:	Not less than 2.0 log reduction from the initial count at 14 days, and no increase from the 14 days' count at 28 days.
Yeast and Molds:	No increase from the initial calculated count at 14 and 28 days.

The results for Replens in the table below demonstrated conformance with the criteria above and the preservative was determined to be effective.

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XIV. Substantial Equivalence Discussion

	Yes	No	
1. Same Indication Statement?	X		If **YES** = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If **YES** = Stop **NSE**
3. Same Technological Characteristics?	X		If **YES** = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If **YES** = Go To 6
5. Descriptive Characteristics Precise Enough?		X	If **NO** = Go To 8 If **YES** = Stop **SE**
6. New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NSE**
7. Accepted Scientific Methods Exist?			If **NO** = Stop **NSE**
8. Performance Data Available?	X		If **NO** = Request Data
9. Data Demonstrate Equivalence?	X		Final Decision: **SE**

Note: Document the decision path by marking the arrows followed on the FDA flowchart.

Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

1. Explain how the new indication differs from the predicate device's indication:

2. Explain why there is or is not a new effect or safety or effectiveness issue:

3. Describe the new technological characteristics:

4. Explain how new characteristics could or could not affect safety or effectiveness:

5. Explain how descriptive characteristics are not precise enough:

   The submission includes the descriptive characteristics but the performance testing is needed to support substantial equivalence and demonstrate the similarities between the new device and the predicate device.

6. Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:

7. Explain why existing scientific methods cannot be used:

8. Explain what performance data is needed:

9. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

   As the reviewer of this submission I have reviewed the instructions for use, the sponsor's description of the device and compared this information against the information for the predicate device that was provided by the sponsor. The specifications for the predicate device and the new device have been compared. They are very similar. The comparison table demonstrates the similarities and differences between the new device and predicate device. The submission includes biocompatibility and performance testing which demonstrates the new device and the predicate device have similar performance characteristics. The labeling included in the submission was reviewed and found to be similar to the predicate labeling. There are no new questions of safety and effectiveness raised during this review.

   Based upon the above summary, a substantially equivalent decision is recommended.

XV. Deficiencies

During the review of the original submission dated February 25, 2010 one round of deficiencies was issued (March 16, 2010). Additional information was provided April 9, 2010 to respond to the deficiencies. FDA review resulted in another round of deficiencies on May 5, 2010. Additional information was provided May 24, 2010. All deficiencies have been adequately addressed.

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XVI. Contact History

All correspondence is included in the submission.

XVII. Recommendation

Classification Name:	**Lubricant, Patient, Vaginal**
Regulatory Class:	**II**
Product Code:	**MMS, NUC**
Classification Number:	**21 CFR 884.5300**

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Lil' Drug Store Products

Response to 510(k) Deficiency Letter

May 24, 2010

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

Reference: **Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) 510(k) (K101098) Deficiency Letter dated May 5, 2010**
Applicant: **Lil' Drug Store Products, Inc.**

Dear Sir or Madam:

Further to your deficiency letter dated May 5, 2010 for the Traditional 510(k) Premarket Notification for Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) ("Replens"), a vaginal moisturizer for treatment of vaginal dryness, please see below the response from the applicant. Your comments are restated in bold followed by the response.

Device Description

1. **Please note that personal lubricants such as Replens are Class II devices, covered by prodcode NUC (vaginal patient lubricant), under regulation number 21 CFR 884.5300.**

   Please find attached revised versions of the following documents that have been modified to reflect the indicated product categorization:

   - 0.1 FDA Form 3514
   - 2.0 510(k) Summary
   - 4.0 Device Information

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

2. **You state that the pH of the subject lubricant is 2.9 and ranges from 2.3-3.5. You also state that this is in the physiologic range of the normal vagina. However, it appears to us that the pH of the subject lubricant is below normal vaginal pH, which typically ranges from 4.0 – 5.0 in women with active menstrual cycles (M. Garcia-Closas et al. Epidemiologic determinants of vaginal pH. AJOG. Volume 180(5). pp.1060-1066.).**
In light of this information, please justify the pH of the subject lubricant. Your justification should include, but is not limited to, a discussion of the possible changes to the vaginal microflora that may result from prolonged exposure to this product and if a low pH environment makes the vagina more susceptible to infections of any kind.

   Please find attached a detailed response regarding Replens' effect on vaginal pH and vaginal flora.

Indications for Use

3. **Please revise your indications for use statement to that of the standard indication for personal lubricants as follows:**

   [Product name] is a personal lubricant, for penile and/or vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is [is not] compatible with natural rubber latex condoms [and/or synthetic condoms (specify specific type(s) of synthetic condoms)].

   Please modify your Indications for Use form, 510(k) Summary, and labeling accordingly, and please provided revised copies of these documents for review. Please note that the last sentence of your indication statement is dependent upon how you choose to address the condom compatibility issues described in Deficiencies 12-13.

   Please find attached revised versions of the following documents that have been modified to reflect an indications for use statement consistent with the standard indication for personal lubricants:

   - 0.1 FDA Form 3514
   - 1.0 Indications for Use Statement
   - 2.0 510(k) Summary

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

The revised indications for use statement for Replens is as follows:

"Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms."

As Replens is intended only for direct vaginal application, the portion of the suggested statement related to "penile application" has been removed.

Labeling

4. **Please revise your package insert as follows:**
   a. Please provide information in the labeling regarding when to dispose of the applicator (e.g., when the lubricant has been used up).
   b. Please state that the applicator should be cleaned immediately after use. The cleaning validation testing provided in Appendix D of the 510(k) submission evaluated the applicator after sitting for only 10 minutes following contamination.
   c. Please state that the applicator should be completely dry before reassembly.
   Please provide a revised copy of your product labeling including the above requested revisions.

   Please find attached a revised copy of the package insert. The package insert has been revised to include: a) instructions to dispose of the applicator after the tube of lubricant has been used; b) to instruct the user to clean the applicator immediately after use; and c) to state that the applicator should be completely dry before reassembly.

Shelf Life

5. **Please clarify if the 36 month accelerated-aging study conducted by Pharmetics evaluated ingredients from the current suppliers and the current product packaging. If not, please justify why any differences between the evaluated product and the current product would not affect shelf-life. Please note that if your justification is not sufficient you will be asked to conduct additional shelf-life testing.**

Lil' Drug Store Products, Inc. | 1201 Continental Place NE | Cedar Rapids, IA 52402
Phone: 319-294-3745 | Fax: 319-393-3494 | Internet: www.lildrugstore.com | E-mail: tmiller@lildrugstore.com

The 36 month real time study conducted by Pharmetics evaluated the current product packaging and materials with equivalent grades to those indicated in this 510(k). While this data independently supports the proposed shelf life, an ongoing stability study is in progress as described in the protocol provided in appendix E.1 of the original 510(k) notice.

Biocompatibility

6. **Four key biocompatibility studies provided in your submission were conducted twenty years ago. These studies are as follows:**

    - **Acute Vaginal Irritation in Rabbits (1989)**
    - **Subacute Vaginal Irritation in Rabbits (1989)**
    - **Subacute Vaginal Irritation with Histological Examination (1990)**
    - **Hypersensitivity (1989)**

    Please confirm if the current version of the subject lubricant is identical to the product evaluated in the above studies, (i.e., identical ingredient suppliers, identical manufacturing processes, etc.). If not please provide vaginal irritation and sensitization testing on the final, finished version of the subject lubricant. These studies should evaluate appropriate models (e.g., ISO Vaginal Mucosal Irritation, ISO Maximization Sensitization), evaluate both polar and non-polar extracts, and follow the extraction procedures outlined in ISO 10993-12:2007.

    The Replens product has been sold as a cosmetic in the U.S. since 1989 and in Europe initially as a drug and later as a Class IIa Medical Device since 1992 (it is still sold as a drug in some countries around the world). Therefore, certain of the biocompatibility tests of the product were conducted to support its approval in Europe as a drug and marketing in the U.S. at that time.

    The Replens formulation used in the acute and subacute vaginal irritation studies and hypersensitivity study included in the 510(k) notice is essentially identical to the product as it is marketed today. Specifically:

(b)(4) Proprietary Information

The formulation ingredients of Replens (all are GRAS or USP-NF grade materials) have not changed since the subject GLP biocompatibility testing was completed. Moreover, when new suppliers were selected they were required to provide the same GRAS or USP-NF grade materials. It is noted that all of the ingredients in Replens are included in the FDA Drug Inactive Ingredients database[3] as appropriate for vaginal gels or emulsions in percentages lower than the "maximum potency" allowed.

Minor changes in the manufacturing process (e.g., mixing the gel in two vessels instead of three, using a tighter temperature range during a particular mixing step, changing sampling protocol) were determined to have no expected effect on product quality or integrity.

The company does not believe any of the changes in raw material suppliers or manufacturing processes would be expected to have any effect on the product's biocompatibility. Changing raw material suppliers is common in the production of medical devices, and does not typically necessitate repeating biocompatibility testing, particularly for the same GRAS or USP-NF grade materials. In addition, minor changes in manufacturing would not be expected to affect the biocompatibility of the product, or necessitate additional testing.

In addition, the biocompatibility of the Replens product is confirmed by a significant amount of testing, including testing that was conducted on the current product (cytotoxicity and acute systemic toxicity). See **Section 8.1** of the 510(k) for more detail.

Therefore, Lil' Drug Store believes that the vaginal irritation and hypersensitivity studies included in the 510(k) notice are applicable to the current product, and do not need to be repeated.

Finally, in considering the biocompatibility of Replens, it is important to note that the formulation of Replens is substantially equivalent to that of the predicate, CVS Personal Lubricant & Moisturizer (K062682). Water and glycerin represent approximately 92% of the Replens formulation and provide the primary lubrication and moisturizer characteristics of both Replens and the predicate device. While certain of the other, minor ingredients differ between the two formulations, these other ingredients perform equivalent functions that can be safely accomplished via a variety of ingredients. All ingredients included in Replens are either NF, USP, or are considered "generally recognized as

[3] http://www.accessdata.fda.gov/scripts/cder/iig/index.cfm (Note: Carbomer Homopolymer Type B is a new name for Carbomer 974P, as listed in the database.)

safe for their intended use". In addition, these other Replens ingredients are commonly used in other devices and cosmetics for vaginal use (see **Section 7.1** of the 510(k) for additional detail).[4] Therefore, Lil' Drug Store Products believes that any differences in formulation between Replens and the predicate do not affect the safety or effectiveness of the device and do not raise new questions of safety or effectiveness with regard to the Replens product.

7. **You conducted an Agar Overlay test to evaluate the cytotoxicity potential of the subject lubricant, which displayed cytotoxicity scores of 2 and 3. This is a much higher degree of cytotoxicity than typically seen for personal lubricant products. This is especially concerning because an Agar Overlay test is less sensitive than the MEM Elution Cytotoxicity test typically used to evaluate the cytotoxicity potential of personal lubricant products. An Agar Overlay test is less sensitive because the agar acts a barrier between the cells and the test article, allowing less penetration compared to a direct contact method such as MEM Elution.**

   You state that the negative cytotoxicity result was caused by the low pH of the subject lubricant, and to demonstrate this, you repeated the cytotoxicity study after adjusting the pH of the subject lubricant to 7.0-7.5. You state that this modified cytotoxicity study did not display any signs of cytotoxicity.

   We do not believe this is appropriate justification because the marketed product will not have a pH of 7.0-7.5. Please provide justification that supports the safety of the subject lubricant with its intended specifications. In addition, we are unable to locate the test report for the modified cytotoxicity study in your submission. Please provide this information.

   Lil' Drug Store consulted with our primary GLP testing laboratory (Nelson Labs) and our consulting toxicologist (Dr. Dan McLain, Walker Downey & Associates, Inc) regarding the methodology for testing cytotoxicity of personal lubricants. For the reasons described below,

[4] Replens' formulation is also very similar to Crinone (NDA 20-701 and NDA 20-756), a gel with progesterone as the active ingredient, marketed in the U.S. since 1997 for vaginal use during the first trimester of pregnancy to support embryo implantation and maintain pregnancies as part of assisted reproductive technology treatment regimens. With the exception of water, methylparaben, and the active ingredient, the two gels have the same weight to weight ratio of all Replens ingredients, including the ones not in the identified predicate. Replens was used as the non-drug control in several Crinone clinical studies. Together, this provides further evidence of the safety of these ingredients.

both Nelson Labs and Dr. McLain believe that the Agar Overlay test is more appropriate to determine the cytotoxicity of an acidic lubricant material (such as Replens) than the direct contact MEM Elution test.

In the MEM Elution test, the test sample is applied directly to the cells; however, the test sample is an extract of the test article, not the actual test article. Extraction must be used because dosing a lubricant "neat" (i.e., directly) on the cell cultures is not a viable option because the cell cultures would not survive without the nutrients in the MEM solution. For lubricants, the sample partially dissolves into the MEM solution during the extraction process creating a diluted or lower dose (4g/20ml or 25% solution) of the sample rather than an extract. There is no practical way to determine a dose ratio for this test since the cells do not have a basis to compare to patient use (e.g. animal dosing can be compared to human dosing based on weight). As a result, this dilution effect makes it difficult to determine the true cytotoxic effect of the test material. Additionally, the extraction process has a pH buffering effect due to the higher pH (~7.3) of the extraction media, which matches the pH of the cultured cells. Cells are very sensitive and can be killed by minor changes in pH, salinity, or temperature. Therefore, because the pH of a lubricant is buffered by the extraction process, the MEM test would not detect cell changes due to the original pH of the test article. As a result, acidic vaginal lubricants tested with the MEM elution test are less likely to show reactivity due to both the dilution and the pH buffering effects.

For these reasons, Nelson Labs prefers the Agar Overlay method to test the cytotoxicity of lubricants despite the following limitations of this method: 1) the ability of lubricants to spread beyond the filter disks making it difficult to grade the zone of reactivity; and 2) significant differences in pH, salinity, osmolarity, etc. from the cell cultures will show reactivity that may not be reflective of the test substance's actual use.

The original negative cytotoxic results associated with Replens on the Agar Overlay test were entirely mitigated following pH adjustment of the product, using an otherwise-identical test methodology. It can be concluded, therefore, that the unfavorable results were caused by the gel's pH. It is noted that adjusting the pH of a test sample is allowable per ISO 10993-5 and is appropriate given the intended use of the product and pH range of the normal, healthy vagina, which is also acidic (see response to deficiency #2 for a discussion of vaginal pH). Because of the naturally acidic environment, cells in the vaginal mucosa would not be expected to exhibit the same reaction to low pH

as the L-929 cell line used in the cytotoxicity testing. Finally, the pH adjustment in the Agar Overlay test is equivalent to the pH buffering effect that occurs with an extract in the MEM Elution test, without also having a dilution effect. The favorable results on the final test with the pH-adjusted Replens (GLP report attached) are therefore more representative of the product in actual use.

In conclusion, the company believes that the Agar Overlay test is the most appropriate method for testing cytotoxicity of personal lubricants such as Replens. We have demonstrated through a series of mechanistic cytotoxicity studies that the observed effects of Replens were physical in nature (due to pH), and not chemically- or toxicologically-induced. Finally, the company believes that the GLP sensitization and vaginal mucosal cell irritation testing included in the 510(k) notice are more reflective of the clinical intended use of the product and provide clear evidence of the biocompatibility of Replens in vivo.

8. **To assess the sensitization potential of the subject lubricant, your conducted a hypersensitivity test in guinea pigs. This test is not sufficient as it is not an appropriate test for a device in contact with mucosal surfaces such as personal lubricants. This is especially true considering the unfavorable cytotoxicity study results. Please provide the complete protocol, results, and analysis from a sensitization study that is appropriate for materials in contact with mucosal surfaces (e.g., ISO Maximization Study). Please note that testing should be completed with both polar and non-polar extracts of your device.**

As described in detail below, we believe that the hypersensitivity test performed on Replens (the modified Maguire sensitization test) is comparable to the two sensitization methods currently used to test personal lubricants (the ISO Maximization Study and the Buehler method) in terms of procedure and sensitivity and, therefore, that further testing of Replens is not warranted.

As hypersensitivity testing requires visual scoring for any reaction, our understanding is that the conventional ISO protocols, including the ISO Maximization Study, are not amenable to administration in any of the standard mucosal cell surface models (e.g., vaginal or oral). Therefore, we assume that FDA's request for the ISO Maximization test over the commonly-used Buehler method, both of which employ dermal administration of the test article, is because the ISO

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Maximization test is considered the more sensitive of the two tests and not a request to test the product directly on mucosal surfaces.

A recent article by the biocompatibility director at a major testing laboratory (Toxikon Corporation) summarized the difference between these two tests as follows: "Two primary test methods are used for medical devices to satisfy the sensitization testing requirement. The first is the guinea pig maximization test (GPMT[5]); the second is the closed patch test, also known as the Buehler. Due to the use of an adjuvant to stimulate the immune system, the GPMT has been considered the more sensitive test. The GPMT has intradermal injections in the beginning of the study and topical applications at the conclusion. The Buehler consists of all topical applications. Due to the intradermal injections in the GPMT, the requirements specify that the test article be a liquid, suspendable powder, or extract. The Buehler is better performed with surface contact devices as they are used, if possible, and chemicals."[6] Following administration, these tests both evaluate dermal sensitization to the test material.

Lil' Drug Store has consulted with Nelson Laboratories regarding these test methodologies. We understand from Nelson Labs that the Buehler method has historically been the preferred method for personal lubricants for the following reasons: 1) they are applied topically (as administered in the Buehler method); 2) the ISO maximization test requires the test article to be a liquid, suspendable powder, or extract (and lubricants are not liquids or suspendable powders and they are difficult to extract); and 3) injecting the lubricant "neat" (i.e., directly) by intradermal means is in contrast with the test method and has not been studied to know if it is a valid method that will accurately measure sensitization without harm to the test animals. Therefore, while the ISO Maximization test is generally considered more sensitive than the Buehler method, it has inherent limitations that the company believes prevent it from being an appropriate test method for lubricants such as Replens. As described in more detail below, we believe that the modified Maguire method used in the Replens hypersensitivity test is a better alternative to both the ISO Maximization and Buehler methods.

As previously stated, the method used for the guinea pig hypersensitivity study of Replens submitted in the 510(k) notice was

[5] The guinea pig maximization test (GPMT) is also known as either the ISO Maximization test or the Magnussen-Kligman Maximization test.
[6] Lister L. (2010) Biocompatibility Testing: Tips for Avoiding Pitfalls, Part 2. MD&DI, 32(2). (http://www.mddionline.com/article/testing_tips2)

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the modified Maguire sensitization test[7]. This method involves topical application of the test material as in the Buehler method, but it also involves injection of an adjuvant to stimulate the immune system response as in the ISO Maximization method. Because the Maguire method only involves topical application of the test material, it eliminates the issues involved in either creating extracts of the lubricant or injecting it neat in the ISO Maximization test. In addition, a study comparing the sensitivity of guinea pig test models (Marzulli and Maguire (1982)) showed that the modified Maguire method is significantly more sensitive than the Buehler method for weak sensitizers[8]. Marzulli and Maguire did not show the Maguire method to be as sensitive as the Magnusson-Kligman test (ISO Maximization), but another study reported it to be more consistent in detecting the sensitizing effects of materials in the predicted order than the Magnusson-Kligman test[9]. Therefore, as the modified Maguire sensitization test is more sensitive than the Buehler method and potentially more consistent than the ISO Maximization test, and it does not have the same technical limitations as the ISO Maximization test for use with personal lubricants, we consider the submitted test to remain a valid assessment of the sensitization potential of Replens.

Moreover, it is noted that no significant allergenicity/sensitization has been observed in the numerous clinical studies performed on Replens (see the response to FDA deficiency #2).

For these reasons, the company does not believe that additional hypersensitivity testing of Replens is necessary.

9. **You conducted an Acute Systemic Toxicity test using both IV and IP routes of administration to evaluate the acute systemic toxicity potential of the subject lubricant. While the test animals did not display any signs of toxicity via the IP route of administration, several very concerning adverse effects were seen in the test animals in both studies evaluating the IV route of administration. In the first IV study, the two test animals went into convulsions and were gasping immediately following**

[7] Maguire HC. (1973) The Bioassay of Contact Allergens in the Guinea Pig. J. Soc. Cosmet. Chem., 24: 151-162.
[8] Marzulli F, Maguire HC. (1982) Usefulness and Limitations of Various Guinea-Pig Test Methods in Detecting Human Skin Sensitizers—Validation of Guinea-Pig Tests for Skin Hypersensitivity. *Fd Chem. Toxic.* 20:67-74.
[9] Horton JR, MacEwen JD, Vernot EH. (1981) Comparison of Skin Sensitization Methods: Landsteiner, Maguire and Guinea Pig Maximization. Air Force Aerospace Medical Research Laboratory, report # AFAMRL-TR-81-131.

an injection of the undiluted subject lubricant. Both animals died shortly thereafter. In the second IV study, despite dilution of the subject lubricant in saline (2.9 grams in 15.4 mL), four out of the five animals displayed significant clinical signs of toxicity, three animals lost excess of 10% of their body weight, and one animal died. To justify these results, you simply state that the IV route of administration is not an appropriate method for evaluating a vaginal lubricant; however, this does not explain why the subject lubricant caused these reactions in the test animals. Please provide this information.

In addition, please reevaluate the acute systemic toxicity potential of the subject lubricant as described in Deficiency 10.

Furthermore, you did not provided justification for your test dose of 50 mL/kg for either the IV or IP route of administration. Please provide a justification for your test dose that accounts for daily, repeat use.

In the 510(k) notice, we identified two primary reasons why the Acute Systemic Toxicity by IV route is not an appropriate measure of the biocompatibility or toxicity of the product. First, the viscosity of the product and the lack of a homogenous test solution because the product is not completely soluble in water raise significant questions as to the scientific validity of testing acute systemic toxicity with IV administration for vaginal lubricants. Second, while it is difficult to model the differential absorption rates for the vaginal membrane and blood, in testing the absorption rate through the vaginal membrane of a variety of substances, the worst case absorption rate measured was 0.095 µg/g.[10] Using this absorption rate, the dosage administered in the second test represented 705 million times the amount of a vaginally-delivered dose that might make its way into the blood stream of a user. These two points are further discussed below.

Replens is a nonsterile, primarily aqueous product composed of approximately 8% waxes and/or fat. The company now understands from two expert toxicology consultations that this latter property should have immediately exempted it from acute toxicity testing by the intravenous route. Additionally, the non-sterile nature of the

[10] Pharmaceutical Society of Japan; Vol 12 (1964) The Absorption of Organomercurial Compounds from the Vaginal Route of the Rabbits. I. Comparative Study on the Effect of Suppository Vehicles on the Absorption of ω-Ethylmercurithio-n-undecanoic Acid, Phenylmercuric Acetate and Ethylmercuric Chloride after Single Dose Administration.

product is also not ideal for dosing by an intravenous route and the test solution should have been sterilized prior to administration. The experts we consulted indicated that it is not scientifically appropriate or advisable to administer a nonsterile, lipid-containing solution with potential for micro-emboli formation via intravenous administration.

Nelson Laboratories, who conducted these tests, did not investigate the cause of death of the animals. Therefore, Lil' Drug Store asked our consulting toxicologist (Dr. Dan McLain, Walker Downey & Associates, Inc) to retrospectively review the data from these Acute Systemic Toxicity studies. Dr. McLain and a different testing laboratory concurred that the described clinical signs (i.e. convulsions, gasping, and death after administration) of the test animals in the first two studies are classical signs of pulmonary embolism most likely caused, in this case, by the embolic fatty micelles formed following test article extraction. Based on this conclusion, they indicated that filtering of the 0.2 g/mL test article solution would have been the only logical recourse (other than dilution) for intravenous administration, but viewed this as a potentially significant departure from standard ISO testing practice.

While we now believe that the intravenous test should not have been conducted based on the information presented above, we attempted three different protocol modifications in our effort to satisfy this assumed requirement. The third test was completed after the 510(k) was submitted and produced passing results (see final test report attached). In this protocol, we further diluted the test article to 1/20th the original dosing concentration. Based on the absorption rate provided above, this dosage still represented over 120 million times the amount of the product that would be expected to make its way into the blood stream. Thus, this dosage more than adequately reflects daily, repeat use of the device. It should be noted that this dilution rate also reduced the potential microbial and fatty micelle burden to $1/20^{th}$ of the original amount so that it did not affect the animals in this particular test. This final test demonstrates that in the absence of significant quantities of embolism-causing fatty micelles, Replens does not demonstrate toxic effects when delivered intravenously even in a non-sterile form.

Finally, while the acute systemic toxicity test is not designed to address the effects of repeat administration, the dosages administered by both the IP and IV route represented many multiples of individual doses. The dosage delivered in both tests was based on ISO 10993-11:2006, which recommends a 50-mL/kg dose for systemic toxicity

evaluation for both IP and IV administrations. As noted above, at the dilution used, the dosage delivered via the IV route in the last (successful) test represented 120 million times the amount that might possibly make its way into the bloodstream based on the weight of the animal. At the dilution used in the IP test, the dosage delivered via the IP route represents >10x dosage based on the weight of the animal. Additionally, the company has submitted other data in the 510(k) notice that demonstrate the biocompatibility of the gel following repeat administration, specifically the *Subacute Vaginal Irritation with Histological Examination* study.

In summary, as concluded by two different and independent expert sources, the observed clinical signs of the test animals in the first two studies administered the product via the IV route are classic signs of pulmonary embolism, most likely caused by intravenous administration of embolic fatty micelles. We respectfully submit, therefore, that the intravenous administration test was not scientifically appropriate and that the intraperitoneal administration test should be sufficient to demonstrate the safety of the product in the acute systemic toxicity test. It is noted, however, that Replens, after dilution to essentially eliminate the embolic fatty micelles, successfully passed the Acute Systemic Toxicity test by IV administration, demonstrating that without this factor, the product is not toxic by the IV route.

10. In lieu of conducting both a vaginal irritation study and an acute systemic toxicity study, an alternate testing approach that may be more relevant to the proposed use of your device (i.e., vaginal use) is summarized below. This alternate design is a hybrid between the ISO Vaginal Irritation test and the ISO Acute Systemic Toxicity test and assesses both the systemic toxicity and mucosal irritation potential of your device.

Rabbits (n=5 per group) are treated with either the test article extracted in a polar extraction vehicle, the test article extracted in a non-polar extraction vehicle, or saline (negative control) and dosed 1x/day for 10 days. Each animal will receive 1 ml of the test article extracted in a polar extraction vehicle (treatment group 1), the test article extracted in a non-polar extraction vehicle (treatment group 2), or saline (control).

The following information should be collected during the study:
-initial, daily, and terminal body weights;
-initial baseline and terminal blood samples;

-daily health observations;
-food consumption data;
-macroscopic and microscopic evaluation of vaginal, cervical, and uterine tissues;
-necropsy including examination of major organs, including organ weights; and
-tissues from major organs during necropsy.

If you choose to follow this approach, we recommend that you discuss your protocol with us prior to initiating this study.

In response to deficiency #6, we have provided justification that the Vaginal Irritation Studies, including the Vaginal Irritation with Histological Examination are applicable to the current Replens product. The Vaginal Irritation with Histological Examination test is substantially equivalent in terms of methodology to the test requested above. This test was: 1) performed on six rabbits; 2) involved "neat" (i.e., direct) administration of the product for 14 days; 3) included targeted microscopic evaluation of the vaginal, cervical, uterine, and ovarian tissues; 4) included macroscopic evaluation of major organs; and 5) included observation for behavioral or toxic signs, food consumption and body weights. These tests demonstrate that the product is non-irritating in the target tissue. This conclusion is further supported by: 1) the clinical studies performed on Replens, including two long-term, protracted use studies (see the response to deficiency #2 for a discussion of the clinical studies conducted using Replens) and 2) the extensive use of Replens over 20 years with over 100 million doses used. The significant clinical experience with the product confirms that the product is non-irritating when used as intended.

Additionally, in response to deficiency #9, we have provided support for the safety of Replens through acute toxicity studies. Test results for IP administration were consistent with the biocompatibility profile of the product and indicate that it is non-toxic when delivered by the IP route. The company maintains that the results observed in the IV portion of the test are not relevant, due to the wax/fat content of the product that could reasonably be expected to cause emboli. It is noted that test results were provided, however, that indicate Replens is non-toxic when delivered by the IV route when embolic fatty micelles are minimized.

For these reasons, the company believes that the vaginal irritation studies and the acute systemic toxicity study support the biocompatibility of the current product, that no further testing is

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required, and that further testing would be a redundant and unnecessary use of laboratory animals. In addition, the significant clinical experience with the product, including seven clinical studies and the extensive commercial use of Replens for over 20 years with no safety concerns, clearly demonstrate that the product is non-irritating and non-toxic when used as intended.

11. **It appears that you changed applicator material and then conducted additional biocompatibility tests (irritation and sensitization) on the new version of the applicator. However, it is unclear is unclear which version of the applicator was evaluated in the cytotoxicity study conducted. Please provide this information. If the cytotoxicity testing was not completed on the new version of the applicator, please provide additional cytotoxicity testing on the new version of the applicator. Alternatively, you may justify why the cytotoxicity testing already completed is sufficient.**

This question appears to result from a misunderstanding of the materials submitted. All of the applicator biocompatibility tests (cytotoxicity, vaginal irritation, and sensitization) were conducted on the current version of the reusable applicator. The vaginal irritation and sensitization studies were not complete at the time of the initial 510(k) submission and were provided as supplemental information in response to a deficiency from the Third Party Reviewer.

Condom Compatibility

12. **You conducted tensile and airburst testing on several brands of latex, polyurethane, and polyisoprene condoms. You evaluated these condoms untreated and following 30 minutes of exposure to the subject lubricant and to KY Jelly. You evaluated 20 samples per condom type per exposure and presented your results in terms of the mean and standard deviation of each parameter evaluated. In order for us to fully evaluate the effect of the subject lubricant on condoms, please provide your condom compatibility results as described in the following table for each parameter evaluated:**

Condom Type	airburst pressure of condoms without additional lubricant (kPa)

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(n = xx) airburst pressure

for condoms

lubricated with test lubricant

(kPa)

	(n = xx)	difference	% decrease
1	Insert mean and confidence interval		Insert mean and confidence interval
2			
3			

Please note that any drop in condom properties of greater than 10% will need to be justified.

Please find attached a revised table with the requested condom testing data. Values that decreased following treatment with either Replens or KY Jelly by more than 10% compared to untreated condoms are highlighted in orange and those that decreased by more than 20% are highlighted in red. It is noted that, even with untreated condoms, significant variability in results are observed. Specifically, the following can be seen from the table provided: 1) condoms from different brands perform differently from each other on the same test; 2) condoms made from different materials perform differently from each other on the same test; 3) the same brand of condoms perform differently on the various tests; and 4) results for untreated condoms compared to ISO/ASTM standards vary for the various tests, brands, and materials.

As described in Section 8.2 of the original 510(k) notice, the company believes that the most appropriate way to determine whether a lubricant is compatible with condoms is by comparing the performance of the treated and untreated condoms with the FDA recognized ISO/ASTM requirement for latex condoms for the particular test parameter (Note: no standards currently exist for synthetic condoms). These requirements are also provided in the attached condom testing data table. Where performance exceeded the requirement in the standard, the cell is highlighted in green; where performance did not meet the requirement, the cell is highlighted in red.

The company does not believe that simply assessing the percentage decline following treatment against a specific cutoff (for example 10%

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or 20%) provides adequate information to determine whether a lubricant is compatible with condoms. This is because a lubricant can have an effect on condoms, but if the condoms continue to meet or exceed specifications for the various properties, the lubricant would not be considered to have a significant deleterious effect on condoms and therefore would be compatible with condoms. For example, we can see that a 30% decline in performance for lubricant-treated condoms on a test where the untreated condom performed at 480% of the standard is not a significant effect. However, a 5% decline in performance for lubricant-treated condoms on a test where the untreated condom performed at 34% of the standard may or may not be significant. The company believes these factors must be taken into account in assessing the condom compatibility of Replens, or any other vaginal lubricant.

The following results were observed in this testing:

- Replens-treated condoms met recognized standards in every case, with the exception of three cases in which the particular condom *had not met the standard in the untreated condition* (specifically, Durex Natural Feeling (lubricated latex) condoms for Tensile Testing—Tensile Strength, Durex Avanti (polyurethane) condoms for Airburst Testing—Burst Volume, and Durex Avanti (polyurethane) condoms for Tensile Testing—Elongation at Break). In these three cases, the Replens-treated condoms performed equivalently to or better than both the untreated condoms and the KY Jelly-treated condoms.
- As compared to expected test results, performance of Replens treated condoms in air burst and tensile testing exceeded test standards and was substantially equivalent to performance of the untreated and KY Jelly treated condoms. KY Jelly is labeled as compatible with condoms.

In conclusion, the results of this testing demonstrate that condom strength and integrity are not materially affected by Replens, as condoms treated with Replens were in compliance with recognized standards in every case in which the untreated condom also was in compliance with the standard. In the cases where the untreated condom did not meet the standard, Replens-treated condoms performed equivalently to or better than both the untreated condoms and the K-Y Jelly-treated condoms. Across all measures, Replens-treated condoms exhibited a 9.8% average performance decline compared to untreated condoms and performed at 185% of the relevant ISO or ASTM goal (K-Y Jelly-treated condoms had a 9.2%

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average performance decline and performed at 184% of goal). Therefore, Replens is safe for use with both lubricated and non-lubricated latex condoms and also synthetic (polyurethane and polyisoprene) condoms.

13. You do not make any claims in your product labeling regarding condom compatibility. Please include an appropriate condom compatibility claim based on the results of condom compatibility testing conducted and please modify your Indications for Use form accordingly.

As described in the response to #3 above, the documents that include the indications for use statement have been modified to reflect a statement consistent with the standard indication for personal lubricants, including a claim of condom compatibility with both latex and synthetic (polyurethane and polyisoprene) condoms. Additionally, please find attached the revised package insert, which has been modified to include an FAQ related to compatibility with condoms.

In addition, please revise your review memo to include a detailed discussion of all the performance testing conducting by the sponsor including cleaning validation, all biocompatibility studies, shelf-life, and condom compatibility. This discussion should include a summary of the protocol, the study results, and your reasoning as to why the study results are acceptable.

Please note that this information has been previously provided and should be available from the Third Party Reviewer.

Please do not hesitate to contact me at (319) 294-3745 or by email at tmiller@lildrugstore.com should you require any clarification regarding this response.

Sincerely,

Patricia L. Miller

Patricia L. Miller
Lil' Drug Store Products, Inc.
Director of Regulatory

Lil' Drug Store Products

Attachments:

0.1 FDA Form 3514

1.0 Indications for Use

2.0 510(k) Summary

4.0 Device Information

5.2 Instructions for Use

Replens Effect on Vaginal pH and Vaginal Flora

Final Cytotoxicity Report with pH Adjusted Replens

Final Acute Systemic Injection Test (IV) Report

Condom Compatibility Tables

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 0910-0120
Expiration Date: August 31, 2010.
See OMB Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
February 25, 2010	n/a, using 3rd Party Review	

SECTION A TYPE OF SUBMISSION

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

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

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

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
Lil' Drug Store Products, Inc.	3003491851		
Division Name *(if applicable)*	**Phone Number *(including area code)***		
	319-294-3745		
Street Address	**FAX Number *(including area code)***		
1201 Continental Place NE	319-393-3494		
City	**State / Province**	**ZIP/Postal Code**	**Country**
Cedar Rapids	IA	52402	USA
Contact Name			
Patricia (Tricia) L. Miller			
Contact Title	**Contact E-mail Address**		
Director of Regulatory	TMiller@lildrugstore.com		

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

Company / Institution Name			
Division Name *(if applicable)*	**Phone Number *(including area code)***		
Street Address	**FAX Number *(including area code)***		
City	**State / Province**	**ZIP Code**	**Country**
Contact Name			
Contact Title	**Contact E-mail Address**		

PSC Graphics (301) 443-1090 EF

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

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

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

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

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

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

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

- ☐ Response to FDA correspondence:

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

- ☐ Other Reason *(specify):*

SECTION D2 REASON FOR APPLICATION - IDE

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

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

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

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

- ☐ Other Reason *(specify):*

SECTION D3 REASON FOR SUBMISSION - 510(k)

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

- ☐ Other Reason *(specify):*

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SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	MMS	2	NUC	3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

☒ 510 (k) summary attached
☐ 510 (k) statement

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

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K062682	1	CVS® Personal Lubricant &Moisturizer	1	Lake Consumer Products, Inc.
2		2		2	
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification name

Lubricant, Patient, Vaginal

	Trade or Proprietary or Model Name for This Device		Model Number
1	Replens Long-Lasting Vaginal Moisturizer (35g Tube with Reusable Applicator)	1	83035
2		2	
3		3	
4		4	
5		5	

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

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

☒ Laboratory Testing ☐ Animal Trials ☐ Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
NUC	21 C.F.R. 884.5300	☐ Class I ☒ Class II ☐ Class III ☐ Unclassified

Classification Panel

Obstetrics/Gynecology

Indications *(from labeling)*

Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number *(if known)*

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

☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number (b)(4)	☐ Manufacturer ☐ Contract Sterilizer ☒ Contract Manufacturer ☐ Repackager / Relabeler
☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number (b)(4)	☐ Manufacturer ☐ Contract Sterilizer ☒ Contract Manufacturer ☐ Repackager / Relabeler
☒ Original ☐ Add ☐ Delete	Facility Establishment Identifier (FEI) Number (b)(4)	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☒ Repackager / Relabeler

SECTION I — UTILIZATION OF STANDARDS

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

	Standards No.	Standards Organization	Standards Title	Version	Date
1	10993	ISO	Biological evaluation of medical devices	current	
2	32 <51>	USP	Antimicrobial Effectiveness Testing	2009	
3	32 <61>	USP	Microbial Examination of Nonsterile Products: Microbial Enumeration Tests	2009	
4	32 <62>	USP	Microbial Examination of Nonsterile Products: Tests for Specified Microorganisms	2009	
5	D3492	ASTM	Standard Specification for Rubber Contraceptives (Male Condoms)	1993	
6	4074	ISO	Natural latex rubber condoms —Requirements and test methods	2002	
7					

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

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer (HFA-710)
5600 Fishers Lane
Rockville, Maryland 20857

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

STATEMENT OF INDICATIONS FOR USE

510(k) Number: _____

Device Name: Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Indications for Use: Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.

Prescription Use _____ OR Over-the-Counter Use __X__
(Per 21 CFR 801.109) (Optional Format 1-2-96)

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)
Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) Summary

Submitter:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Contact Person:
Tricia Miller
Director of Regulatory
Telephone: 319-294-3745
Facsimile: 319-393-3494
Email: tmiller@lildrugstore.com

Date:
May 12, 2010

Proprietary Name:
Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)

Common name:
Personal Lubricant

Classification name:
21 C.F.R. 884.5300 Lubricant, Patient, Vaginal, Latex Compatible
Product Code: NUC
Class: 2
Review Panel: Obstetrics/Gynecology

Predicate Devices:

Device Name: CVS Personal Lubricant & Moisturizer
510(k) Number: K062682
Product Code: NUC, MMS

Intended Use:

Replens is a personal lubricant for vaginal application, intended to moisturize and lubricate, to enhance the ease and comfort of intimate sexual activity and supplement the body's natural lubrication. This product is compatible

with natural rubber latex condoms and synthetic (polyurethane and polyisoprene) condoms.

Description of Device

Replens Vaginal Moisturizer is a non-sterile, water-based, white to off-white, non-irritating, non-greasy, non-staining vaginal gel delivered in a tube with a reusable applicator as a long-lasting moisturizer for vaginal dryness. The use of the reusable applicator provides less mess in application. Replens Vaginal Moisturizer is intended for ongoing use, not exclusively for use during intimate sexual activity.

Replens Vaginal Moisturizer contains ingredients commonly used in other products for vaginal use sold as medical devices and cosmetics. All ingredients are either NF, USP, or are considered "generally recognized as safe for their intended use". The quantitative formulation is considered confidential commercial information.

Technological Characteristics of the Device

Replens Vaginal Moisturizer is substantially equivalent to the identified previously cleared vaginal lubricant predicate with respect to its design and materials, principle of operation, function, formulation, and intended use. It is also substantially equivalent to other water-based vaginal lubricants and personal lubricants being commercially marketed in the U.S.

Summary of Performance Data

Biocompatibility Testing: The following biocompatibility testing has been performed on Replens Long-Lasting Vaginal Moisturizer:

- Cytotoxicity
- Acute Vaginal Irritation
- Subacute Vaginal Irritation
- Subacute Vaginal Irritation with Histological Examination
- Acute Systemic Toxicity
- Hypersensitivity
- Acute Oral Toxicity
- Acute Dermal Toxicity
- Dermal Irritation
- Eye Irritation.

Stability Data: Real-time stability data confirms a shelf life of three (3) years for Replens Long-Lasting Vaginal Moisturizer.

Preservative Effectiveness: Replens Long-Lasting Vaginal Moisturizer has successfully passed the requirements of the USP <51> Antimicrobial Effectiveness Test.

Condom Compatibility Testing: Condom compatibility testing confirms that Replens Long-Lasting Vaginal Moisturizer does not materially affect the strength or integrity of latex or synthetic condoms.

Conclusion

Based on the information presented in the 510(k) notice, it is concluded that Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) for OTC use is safe and effective for its proposed indications and is substantially equivalent in intended use, formulation, safety, and technological characteristics to the identified predicate device and other similar water-based personal lubricants.

DEVICE INFORMATION

Proprietary name of the new device	Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator)
Generic name of the device	Lubricant, Patient, Vaginal, Condom Compatible
Proposed regulatory class for the new device	2
Review Panel	Obstetrics/Gynecology
Product Code	NUC
Regulation Number	884.5300
Previous/Concurrent Submissions	New, initial submission
Previously submitted to the FDA for identical or different indications	No
Currently being reviewed for different indications by the same or different branch within ODE	No
Previously cleared by the FDA for different indications	No

Replens LONG-LASTING vaginal moisturizer

Please read the following carefully before use.

Warnings

- Replens is not a contraceptive and does not contain a spermicide.
- Keep out of the reach of children.
- Keep out of eyes and ears.
- If vaginal irritation occurs, discontinue use. If symptoms persist, contact your physician.
- If pregnant or breast-feeding, consult your healthcare provider before use.
- Store at room temperature.

TAMPER EVIDENT FEATURE: For your protection, the opening of the aluminum tube is sealed and must be punctured before use. DO NOT USE this product if the aluminum seal of the tube is damaged or opened. Return entire contents with receipt to place of purchase.

Directions for Reusable Applicator

Note: Do not roll the tube up like a toothpaste tube. This may cause the tube to crack. The applicator should be thrown away when all of the gel in the tube has been used.

1. Remove cap from Replens tube. Break seal on tube opening by puncturing it with the opposite end of the cap. Screw the open end of the applicator onto the tube. (Figure 1).
2. Gently squeeze the tube, pushing Replens into the open barrel of the applicator. DO NOT roll up the tube. The applicator contains the recommended amount when the plunger stops (approx. 1 inch). (Figure 2)
3. Unscrew the applicator from the tube. Replace cap.
4. While sitting, standing or lying on your back with knees bent, gently insert open end of applicator into the vagina as deeply as it will go comfortably. Holding the applicator in place with thumb and middle finger, press the plunger until it stops. (Figure 3) Withdraw the applicator.
5. Immediately after use, pull the plunger all the way out of the barrel (Figure 4) and wash both parts of the applicator in warm, soapy water. Rinse thoroughly and dry. The applicator should be completely dry before reassembly. To reassemble, gently push the plunger back into the barrel as far as it will go.

How Does Replens Work?

Replens Long-Lasting Vaginal Moisturizer contains a patented ingredient for soothing and long-lasting moisture. When you apply Replens, it immediately goes to work to provide long lasting moisture. As the cells of the vaginal wall are regenerated, dry cells are cleared and Replens is eliminated naturally. As with dry skin that you experience on your face and hands, regular moisturizing treatment may be necessary to prevent dryness from recurring.

Commonly Asked Questions...

How often should Replens Long-Lasting Vaginal Moisturizer be used?
For most women, Replens Long-Lasting Vaginal Moisturizer should be used every three days for best results. However, depending on the severity of your dryness, Replens can be used more or less frequently, as necessary. Replens is safe to use daily.

When should Replens Long-Lasting Vaginal Moisturizer be used?
Replens can be used any time of day or night. Replens works best when used on a regular schedule and not just prior to intercourse. Because Replens delivers long lasting moisture, there is no need to apply it just prior to intercourse. We recommend using Replens at least 2 hours prior to intercourse to allow proper moisturization.

Will Replens Long Lasting Moisturizer make intimacy more enjoyable? One of the most common ways that women discover vaginal dryness is during intimacy. When used regularly, Replens helps replenish your natural vaginal moisture, making intimacy more enjoyable. Replens' formula delivers long lasting moisture so sexual intercourse can be more spontaneous. Since Replens does not need to be applied immediately before intercourse, it does not interrupt the moment by being runny, messy or slippery. Instead, Replens provides long-lasting lubrication whenever the moment is right.

What causes vaginal dryness? Nearly every woman will experience vaginal dryness sometime in her life. It is most often associated with the normal decline or fluctuation of the female hormone estrogen. This fluctuation can be triggered by childbirth, breastfeeding or menopause. Dryness can also be caused by taking certain medications, exercising intensively or being under stress. It is also common to experience vaginal dryness when douching, using tampons or at the end of the menstrual cycle.

Can Replens be used as birth control? No. Replens does not contain spermicide. It is not a contraceptive.

Should I use Replens during my period? No. It is best to resume use after your flow completely stops.

Are there any side effects after using Replens? Some women notice a residue or discharge after initial use of Replens. This is caused by the elimination of dead skin cells. Your body naturally sheds dry vaginal tissue that has built up over time. When used on a regular basis, Replens will help prevent the buildup of dead skin cells and the discharge should dissipate. If the discharge does not dissipate, you may wish to wait an extra day or two between applications. While use is recommended every three days, every woman is unique and you may wish to increase or decrease the amount of time between Replens applications to maximize moisture and minimize discharge.

Is Replens compatible with condoms? Yes, Replens is compatible with latex and synthetic condoms.

For additional information, visit our website at: www.Replens.com or call toll-free 1-877-507-6516 (M-F 8AM – 4:30PM CST).

Manufactured for:
Lil' Drug Store Products, Inc.
1201 Continental Place NE
Cedar Rapids, IA 52402

Replens is a registered U.S. trademark of Lil' Drug Store Products, Inc.

2. You state that the pH of the subject lubricant is 2.9 and ranges from 2.3-3.5. You also state that this is in the physiologic range of the normal vagina. However, it appears to us that the pH of the subject lubricant is below normal vaginal pH, which typically ranges from 4.0 – 5.0 in women with active menstrual cycles (M. Garcia-Closas et al. Epidemiologic determinants of vaginal pH. AJOG. Volume 180(5). pp.1060-1066.).
In light of this information, please justify the pH of the subject lubricant. Your justification should include, but is not limited to, a discussion of the possible changes to the vaginal microflora that may result from prolonged exposure to this product and if a low pH environment makes the vagina more susceptible to infections of any kind.

Lil' Drug Store understands from FDA's question about pH values and the impact of Replens on vaginal flora that FDA appears to be concerned that the product may have a significant impact on vaginal pH, as well as vaginal microflora. The specific intended use of Replens, its pH value, and the ability of the product to influence vaginal pH (and microflora) are each addressed in greater detail below. The company, however, would like to note that the specification for Replens' pH range is 2.5 to 3.5 (rather than 2.3 to 3.5).

As previously described by the company to FDA, Replens gel is intended as a vaginal moisturizer only. As advertised, Replens is intended for any woman seeking relief from discomfort due to vaginal dryness. Lil' Drug Store does not intend the product as an aid in modifying vaginal pH, nor does the company make any claims regarding the product's impact on vaginal pH or vaginal microflora.

In developing Replens, the company, nevertheless, noted that products with pH ranges around 3 to 5 are commonly used as vaginal moisturizers. This may be due to the observed pH ranges in pre-menopausal women (as cited in the agency's reference), as well as the clinical observation that post-menopausal women (many of whom report an increase in vaginal dryness discomfort) frequently are shown to have a shift in vaginal pH (1,2). Replens, therefore, was formulated at a pH that, in addition to providing moisture to the vaginal environment, could act as a mild buffering agent.

While Lil' Drug Store does not intend to seek pH adjustment or maintenance claims for Replens, the company has gathered pH data, described below, from both pre- and post-menopausal women using the product that demonstrates that the pH of the company's vaginal moisturizer does not have a negative impact on vaginal pH or vaginal microflora.

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1 Kistner RW. (1994) Physiology of the vagina. In: E.S.E. Hafex and T.N. Evans (Eds.) Human Reproductive Medicine: The Human Vagina, North-Holland Publishing Company, 2: 109-120.
2 R.W. Steger and E.S.E. Hafex. (1978) Age-associated changes in the vagina. In: EXE. Hafez and T.N. Evans (Eds.) Human Reproductive Medicine: The Human Vagina. North-Holland Publishing Company. New York, 2: 95-106.

Background

The company understands from the clinical literature that the normal pH of a healthy vagina is weakly acidic, having a pH lower than 4.5 in pre-menopausal women and generally in a range of 3.5 to 4.5. (3) The acidic condition is maintained by the normal lactobacillus-dominated flora producing lactic acid. The low vaginal pH restricts the growth of anaerobic microflora that can produce abnormal vaginal discharge and odors when the discharge amines are volatilized at pH > 5. (4) During menopause, the vaginal pH becomes less acidic and rises to almost 7.0 in the post-menopausal female. (5)

There is a body of literature demonstrating a linkage between high pH and unfavorable changes in the balance of flora that comprise the normal vaginal ecosystem and corresponding risk of vaginal infections. The vaginal ecosystem contains a variety of microorganisms that compete for nutrients and space by various mechanisms. Healthy vaginal pH, as discussed briefly above, is mildly acidic, generally < 4.5. Recent studies have demonstrated that the vaginal flora, namely the lactobacillus population, and not the vaginal epithelial cells, are responsible for maintaining the acidity of the vaginal environment (6). The low pH is the first line of defense used by the lactobacilli to dominate the vaginal ecosystem, thereby preventing or minimizing growth of other undesirable organisms. In vitro studies have shown that acidification by lactobacilli can inhibit the proliferation of pathogenic microorganisms, such as *C. albicans*, *E. Coli*, *G. vaginalis*, *Mobiluncus* spp., and other bacteria (7,8). In addition, published literature has demonstrated that locally-administered products with a low pH (lactic acid, low-pH lactate gel, polycarbophil acidic gels) can help restore normal vaginal acidity and facilitate recolonization with normal vaginal flora in patients with bacterial vaginosis. (9,10,11,12,13)

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3 Owen DH, Katz DF. (1999) A Vaginal Fluid Simulant. Contraception 59: 91-95 (see Table 2).
4 Andersch B, Forssman L, Lincoln K, Torstensson P. (1986) Treatment of bacterial vaginosis with an acid cream: a comparison between the effect of lactate-gel and metronidazole. Gynecol. Obstet. Investig. 21:19-25.
5 Kistner RW. (1994) Physiology of the vagina. In: E.S.E. Hafex and T.N. Evans (Eds.) Human Reproductive Medicine: The Human Vagina, North-Holland Publishing Company, 2: 109-120.
6 Boskey ER, Telsch KM, Whaley KJ, Moench TR, Cone RA. (1999) Acid production by vaginal flora in vitro is consistent with the rate and extent of vaginal acidification. *Infect Immun.*, 67: 5170-5175.
7 Skarin A and Sylwan J. (1986) Vaginal Lactobacilli Inhibiting Growth of *Gardnerella Vaginalis*, *Mobiluncus* and other bacterial species cultured from vaginal content of women with bacterial vaginosis. *Acta Pathologica Microbiologica Scandinavica Series B: Microbiology*, 94B(1-6): 399-403.
8 Boris S, Barbés C. (2000). Role played by lactobacilli in controlling the population of vaginal pathogens. *Microbes and Infection*, 2: 543-546.
9 Andersch B, Forssman L, Lincoln K, Torstensson P. (1986) Treatment of bacterial vaginosis with an acid cream: a comparison between the effect of lactate-gel and metronidazole. Gynecol. Obstet. Investig. 21:19-25.
10 Holst E, Brandberg Å. (1990) Treatment of Bacterial Vaginosis in Pregnancy with a Lactate Gel. Scandinavian J Infectious Diseases, 22(5): 625-626.
11 Milani M, Molteni B. (2000) Effects of Miphil, a new polycarbophil vaginal gel, in suspected bacterial vaginosis: a randomized study versus vaginal douche. *Obstet Gynecol*, 95: S58.

The clinical literature therefore supports the view that it is desirable to maintain normally acidic vaginal pH and, thereby, to preserve the normal balance of flora in the vaginal ecosystem.

Effect of Replens in Post-Menopausal Women

During menopause, the vaginal pH becomes less acidic and can rise to almost 7.0 in the post-menopausal female, (14) due to hormonal differences, lack of cellular sloughing and nutrients needed to maintain lactobacilli.

As described below, Replens has been shown in clinical studies over time periods ranging up to one year to lower vaginal pH from > 5 to a more healthy range (around 4.6-4.9) in primarily peri- and post-menopausal women with elevated vaginal pH at baseline. In addition, the product has not been shown to significantly lower vaginal pH that is already low (for example pH 4.0) below the normal range, even with repeat application. The company theorizes that this capacity of Replens may be due to the difference in volume of material (gel vs. vaginal fluid), and a buffering effect.

Bachmann et al (15) performed a double-blind evaluation of Replens and KY Brand Lubricating Jelly in the treatment of vaginal dryness in peri-menopausal and post-menopausal women. Five consecutive days application of Replens resulted in a reduction in mean pH from 5.6 to 4.9 (Table 1).

Table 1: Vaginal pH Values (Bachmann et al, 1991)

	Baseline	Replens
N	80	78
Mean	5.6 ± 1.1	4.9 ± 1.1

Zinny and Lee (16) performed a double–blind evaluation of Replens and KY Jelly on pH and normal vaginal flora in post-menopausal women. Replens or KY Jelly was applied on alternate nights for twenty eight days. The mean pH values at baseline and at the end of treatment are listed in Table 2. These show varying decreases in pH associated with Replens use. Note that the larger percentage declines seen at

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12 Paternoster DM, Tudor L, Milani M, Magino T, Ambrosini A. (2004) Efficacy of an acidic vaginal gel on vaginal pH and interleukin-6 levels in low-risk pregnant women: a double-blind, randomized placebo-controlled trial. *J Mater Fet Neonat Med*, 15: 198-201.
13 Fiorilli A, Molteni B, Milani M. (2005) Successful treatment of bacterial vaginosis with a polycarbophil-carbopol acid vaginal gel: results from a randomized, double-blind, placebo-controlled trial. *Eur J Obstet Gynecol Reprod Biol*, 120: 202-205.
14 Kistner RW. (1994) Physiology of the vagina. In: E.S.E. Hafex and T.N. Evans (Eds.) Human Reproductive Medicine: The Human Vagina, North-Holland Publishing Company, 2: 109-120.
15 Bachmann GA, Notelovitz M, Gonzalez SJ, Thompson C, Morecraft BA. (1991) Vaginal Dryness in Menopausal Women: Clinical Characteristics and Nonhormonal Treatment. Clinical Practice in Sexuality, 7(9): 1-8.
16 Zinny MA, Lee S. (1991) Double-Blind Study of the Comparative Effects of Two Gels on Vaginal pH in Postmenopausal Women. Today's Therapeutic Trends, 8(4): 65-72.

weeks 1 and 3 may be due to the gel being inserted the previous night whereas at weeks 2 and 4 the gel had been inserted two nights earlier.

Table 2: Mean Observed pH Values (Zinny and Lee, 1991)

Week	Replens		
	n	Mean	% Change from Baseline
0	25	5.8	
1	25	4.8	-16.7
2	23	5.3	-9.9
3	25	4.5	-20.8
4	25	4.8	-17.0

Nakamura (17) performed an evaluation of Replens in the treatment of dryness in post-menopausal women. Vaginal pH was measured at varying time intervals after nightly applications of Replens for 1, 2, 3 or 5 days. Multiple applications of the gel resulted in a reduction in pH from a range of 5.2-5.6 to a range of 4.6-5.3 for each number of applications (Table 3).

Table 3: Mean pH following single and multiple applications of Replens (Nakamura, 1991)

	0 hrs	24 hrs	48 hrs	72 hrs	120 hrs	144 hrs	168 hrs	240 hrs
1 Application								
N	10	10	10	9	9			
Mean	5.2	4.9	4.7	4.9	5.1			
SE	0.24	0.11	0.15	0.15	0.2			
p-value		0.246	0.109	0.289	0.516			
2 Applications								
N	10	10	10	9	9	9		
Mean	5.6	5.3	4.8	4.8	5.0	5.2		
SE	0.25	0.21	0.20	0.15	0.18	0.19		
p-value		0.063	0.0121	0.008	0.31	0.094		
3 Applications								
N	10	10	10	10	10	10	10	
Mean	5.6	4.9	4.8	4.6	4.6	4.6	4.9	
SE	0.27	0.16	0.15	0.12	0.17	0.13	0.15	
p-value		0.016	0.008	0.008	0.010	0.002	0.004	
5 Applications								
N	10	10	10	10	10	10	10	10
Mean	5.4	5.0	4.8	4.6	4.8	4.6	4.8	5.1
SE	0.24	0.13	0.15	0.15	0.20	0.18	0.16	0.09
p-value		0.031	0.008	0.016	0.070	0.031	0.031	0.297

17 Nakamura R. (1991) Evaluation of Col-1003 in the treatment of vaginal dryness in postmenopausal women.

Nachtigall (18) performed a three month evaluation of Replens and Premarin Cream in the treatment of vaginal dryness in post-menopausal women. Replens use (3 applications per week) resulted in a reduction in pH from 5.8 to a range of 4.8-5.3 at the different time points (Table 4).

Table 4: pH values following Replens application (Nachtigall, 1994):

	Treatment		Baseline	Week 4	Week 8	Week 12
Mean Vaginal pH	Replens	N	14	11	15	15
		Mean	5.8	4.8	5.3	4.8
		p-value		0.004	0.102	0.022

Gelfand and Wendman (19) performed a prospective evaluation of Replens in the treatment of vaginal dryness in women with a history of breast cancer in whom hormone replacement therapy was contraindicated. Replens was applied three applications per week for three months, plus the option of an additional application prior to intercourse. From the assessment at the end of the first month of treatment onwards, pH was reduced from 6.8 to 4.1 (Table 5) compared with the value at the end of the first month's evaluation without treatment.

Table 5: pH values following Replens application (Gelfand & Wendman, 1994):

	Baseline	Month 1	Month 2	Month 3	Month 4
Mean vaginal pH (SE)	6.9 (0.15)	6.8 (0.12)	5.5 (0.21)	4.9 (0.19)	4.1 (0.07)
p-value			<0.001	<0.001	<0.001

Young et al (20) performed a long-term (12 month) open study of the effects of Replens use (3 applications per week) in post-menopausal women. There was a small decrease in mean and median pH values; mean pH value decreased from 5.1 at baseline to 4.7 at 12 months (Table 6). Minimum pH was consistently 4.0 at baseline, week 12, month 6, and month 12.

18 Nachtigall L. (1994) Comparative study: Replens versus local estrogen in menopausal women. Fertility and Sterility, 61(1): 178-180.
19 Gelfand MM, Wendman E. (1994) Treating Vaginal Dryness in Breast Cancer Patients: Results of Applying a Polycarbophil Moisturizing Gel. J. Women's Health, 3(6): 427-433.
20 Young RL, Kumar NS, Goldzieher JW. (1990) Management of Menopause When Estrogen Cannot Be Used. Drugs, 40(2): 220-230.

Table 6: pH values following Replens application (Young et al, 1990):

	Baseline	Week 12	Month 6	Month 12
N	30	25	24	22
Mean	5.1	4.9	5.0	4.7
SE	0.17	0.16	0.16	0.09
Median	4.9	4.7	4.7	4.7
Minimum	4.0	4.0	4.0	4.0
Maximum	7.0	7.0	7.0	5.7
p-value		0.492	0.834	0.337

The long-term extension of the Bachmann et al (21) trial described above reported that over a twelve month treatment period (3 applications per week) there was a sustained reduction in vaginal pH associated with use of Replens (Table 7). pH value declined from 5.1 at day 16 (entry to open extension phase) to 4.7 at month 6, and remained the constant at 12 months.

Table 7: pH values following Replens application (Bachmann et al, 1992):

	Baseline	Day 16	Month 6	Month 12
N	81	80	52	45
Mean	5.6	5.1	4.7	4.7
SE	0.12	0.11	0.10	0.12
Median	5.5	4.6	4.5	4.5
Minimum	3.5	4.0	3.5	3.5
Maximum	8.0	7.5	6.5	7.5
p-value			<0.001	<0.001

Finally, Whitehead (22) performed a randomized double-blind evaluation of Replens and KY Lubricating Jelly in the treatment of vaginal dryness in post-menopausal women receiving concomitant oral hormone replacement therapy. pH was not recorded as an absolute value, but the number of pH values falling into the following ranges were recorded: ≥ 6.0, 4.6-5.9 and 3.5-4.5. Although Replens did not significantly change pH, the percentage of patients treated with Replens falling into the lower range (3.5-4.5) progressively increased during treatment.

In each of these published studies, application of Replens was shown to lower vaginal pH in women who exhibited baseline pH values >5, without significantly impacting more acidic baseline values. In addition, limited clinical data show that Replens does not have a negative impact on vaginal flora or risk of vaginal infection in post-menopausal women. The impact of Replens on vaginal flora (lactobacillus colony counts) was studied by Zinny et al (1991) in post-menopausal women. Replens was applied on alternate nights for twenty eight days. Four weeks of

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21 Bachmann GA, Notelovitz M, Kelly SJ, Owens A, Thompson C. (1992) Long Term Nonhormonal Treatment of Vaginal Dryness. Clinical Practice in Sexuality, 8(8/9): 3-8.
22 Whitehead M. (1991) A Randomised Double Blind Evaluation of Col-1003, a bioadhesive polymer system vaginal moisturizing gel and, KY Brand Lubricating Jelly in the treatment of vaginal dryness in postmenopausal women receiving concomitant oral hormone replacement therapy.

application of Replens did not have a significant effect on lactobacillus counts in this study.

Effect of Replens in Pre-Menopausal Women

Normal vaginal pH in healthy pre-menopausal women varies depending on a number of factors, including age, stage in the menstrual cycle (day in the month), and site within the vagina where the pH measurement is taken. (23,24)

There is limited clinical data regarding the use of Replens in pre-menopausal women, primarily because vaginal dryness, which the product is intended to treat, tends to disproportionally affect post-menopausal women.

Two of the studies cited in the section above did not specify post-menopausal women in the inclusion criteria for the trial, therefore, it is expected they included some pre-menopausal women. (25,26) Both of these studies reported reductions in mean pH that was > 5.0 at baseline to within a healthier range (4.1 and 4.9). The company believes this data supports the conclusion that the product can lower vaginal pH from > 5 to around 4.6-4.9 in either post- or pre-menopausal women.

With regard to pre-menopausal women with a healthy (low) pH at baseline, the company does not have clinical data on changes in pH associated with Replens use in this population. However, the two long-term (12 month) studies described above reported minimum pH in addition to mean pH. (27,28) In the Young et al study, minimum pH reported in the population treated with Replens remained constant at 4.0 at baseline, week 12, month 6 and month 12. In the Bachmann et al extension study, minimum pH was 3.5 at baseline, 4.0 at day 16, and 3.5 at months 6 and 12. Although these studies included primarily post-menopausal women, they show that in women with low baseline pH treated with Replens, pH stays relatively constant and remains within the normal, healthy range. Lil' Drug Store believes that this data demonstrate that the product will not adversely affect pH in pre-menopausal women.

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23 Wagner G, Otteson B. (1982) Vaginal Physiology During Menstruation. Ann. Int. Med. 96(2): 921-23.
24 Owen DH, Katz DF. (1999) A Vaginal Fluid Simulant. Contraception 59: 91-95 (see Table 2).
25 Bachmann GA, Notelovitz M, Gonzalez SJ, Thompson C, Morecraft BA. (1991) Vaginal Dryness in Menopausal Women: Clinical Characteristics and Nonhormonal Treatment. Clinical Practice in Sexuality, 7(9): 1-8.
26 Gelfand MM, Wendman E. (1994) Treating Vaginal Dryness in Breast Cancer Patients: Results of Applying a Polycarbophil Moisturizing Gel. J. Women's Health, 3(6): 427-433.
27 Young RL, Kumar NS, Goldzieher JW. (1990) Management of Menopause When Estrogen Cannot Be Used. Drugs, 40(2): 220-230.
28 Bachmann GA, Notelovitz M, Kelly SJ, Owens A, Thompson C. (1992) Long Term Nonhormonal Treatment of Vaginal Dryness. Clinical Practice in Sexuality, 8(8/9): 3-8.

Finally, limited clinical data shows that Replens does not have a negative impact on vaginal flora or risk of vaginal infection in pre-menopausal women. Wu et al (29) performed a pilot study to assess the effect of Replens use every third day on bacterial vaginosis. At week four, there was improvement in Nugent scores, vaginal odor and clue cell count ($p < 0.05$). Eleven women converted from amine positive to negative (73 +/- 20%). There was no significant change in vaginal pH.

Conclusion

Although the company seeks clearance of Replens only as a vaginal moisturizer, and does not make claims with regard to the impact of the product on pH values, the available data demonstrate that Replens does not have an adverse impact either on vaginal pH or on vaginal microflora.

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29 Wu JP, Fielding SL, Fiscella K. (2006) The effect of polycarbophil gel (Replens™) on bacterial vaginosis: A pilot study. European J Obstetrics and Gynecology and Reproductive Biology, 130(1): 132-136.

(b)(4) Proprietary Information, Test Data

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DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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

August 03, 2010

LIL DRUG STORE PRODUCTS, INC.
c/o REGULATORY TECHNOLOGY SERVICES, LLC
1394 25TH STREET, NW
BUFFALO, MINNESOTA 55313
UNITED STATES
ATTN: MARK JOB

510k Number: K101098

Product: REPLENS LONG-LASTING VAGINAL M

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

Please ensure that whether you submit a 510(k) Summary as per 21 CFR 807.92, or a 510(k) Statement as per 21 CFR 807.93, it meets the content and format regulatory requirements.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (301)796-7100 or at their toll-free number (800)638-2041, or contact the 510k staff at (301)796-5640.

Sincerely,

510(k) Staff

K101098/S2

Date: July 30, 2010

U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-0609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC
AUG 02 2010
Received

RE: Additional Information for **K101098**
Lil' Drug Store Products Inc..
Long-Lasting Vaginal Moisturizer Gel

To Whom It May Concern:

Enclosed in duplicate is the following information:

As requested by a letter from Colin Pollard dated June 10, 2010, requesting additional information for this submission. The sponsor provided additional information in response to the questions raised. This information addresses the items raised in the request. This additional information has been reviewed and documented in an addendum to the review memo enclosed. Based on this review of the additional information, a decision of substantially equivalence is recommended.

If you should have any further questions regarding this submission please contact me at 763 682 4139 or fax 763 682 4420 or email at mark@markjob.com. Please fax any correspondence regarding this submission to Regulatory Technology Services LLC.

Sincerely,

Mark Job
Responsible Third Party Official

K33

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Addendum to the Review Memo for K101098

Third Party Reviewer: Mark Job - Regulatory Technology Services LLC

Dated: July 29, 2010

Replens Long-Lasting Vaginal Moisturizer Gel

Deficiencies from a letter dated June 10, 2010 from Colin M. Pollard

Condom Compatibility

1. The mfr provided the results of condom compatibility testing in terms of percent drop in properties (tensile and airburst) following exposure to the subject lubricant for each condom type evaluated. This testing showed that exposure to Replens caused a significant drop in condom properties, condoms made from natural rubber latex, polyisoprene, and polyurethane. In many cases, the percent drop in properties exceeded 20%. (We sent you a chart yesterday illustrating these results.) Consequently, it appears that Replens is not compatible with condom use. Replens labeling should reflect this as a caution statement.

   The mfr stated that the data provided demonstrate that the subject lubricant is condom compatible because (1) following exposure, the condom properties met the requirements outlined in ISO and ASTM standards, and (2) the subject lubricant performed equivalently to KY Jelly, which is labeled condom compatible.

   However, please note that FDA evaluates the condom compatibility of all personal lubricants based on percent drop in condom properties (typically tensile and airburst) to determine the physical effect of the lubricant on the condom membrane. Furthermore, KY Jelly is known to be condom compatible and is often used as a negative control in condom compatibility studies. It is possible that the specific test method you used to evaluate condom compatibility may have led to negative results, (e.g., brushing the lubricant onto the condom).

   Therefore, please revise the Indications for Use form, 510(k) Summary, and labeling for the subject lubricant to state that it is not condom compatible, and please provide revised copies of these documents for review.

   Alternatively, you may provide the results of additional condom compatibility testing to support the condom compatibility of the subject lubricant. However, please note that if the results do not demonstrate that the subject lubricant is condom compatible, you will need to revise your labeling accordingly.

   Reviewer comments: The sponsor made some changes to their condom compatibility test protocol, included both positive and negative controls, applied the lubricants manually (rather than brushed on), and utilized a different laboratory (Nelson Laboratories) to conduct additional condom compatibility testing. The revised protocol resulted in the expected results for both the negative control (KY Jelly) and the positive control (Mineral Oil). Testing consisted of Air Burst Testing (pressure and volume) and Tensile Testing (breaking force, tensile strength, and elongation at break) on 20 samples of each condom and treatment group. The condoms tested included:

   Durex® Avanti Non-Latex Lubricated Condoms, Lot #T3621G
   Durex® Latex Non-Lubricated Condoms, Lot #21108385
   LifeStyles SKYN Lubricated Non-Latex Condoms, Lot #090941PI16
   LifeStyles Ultra Sensitive Non-Lubricated Latex Condoms, Lot #0906172116
   Trojan® Non-Lubricated Latex Condoms, Lot #TT0022TZ219

   The condom treatment groups included untreated, KY Jelly (negative control),

(b)(4) Proprietary Information

(b)(4) Proprietary Information

Addendum to the Review Memo for K101098

Third Party Reviewer: Mark Job - Regulatory Technology Services LLC

Dated: July 29, 2010

Replens Long-Lasting Vaginal Moisturizer Gel

Deficiencies from a letter dated June 10, 2010 from Colin M. Pollard

Shelf-Life

3. In response to question 5 for K101241, the mfr provided the results of shelf-life. In addition, you state that based on a phone conversation April 30, 2010, there was agreement that the device could be labeled with an initial shelf-life of 17 months that could be extended to one year upon completion of the shelf-life study.

   Our review of the data showed that real-time test data is available from one lot for 6 months, and additional lots at 3 months. In addition, accelerated shelf-life testing has been conducted for 6 months on one lot, and multiple lots out to 2 months. However, the protocol does not discuss how the environmental conditions used were developed (e.g., no standards identified), or how long 2 or 6 months at these conditions relates to real-time use. Please provide a detailed discussion how the accelerated conditions were developed, and if a published standard method was not used, please provide data validating the accelerated methods used. In addition, please limit the shelf-life to a duration that is supported by data from three lots of device (accelerated or real-time). All accelerated results will need to be confirmed with real-time results.

   Reviewer comments: This question is not applicable to K101098.

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Lil' Drug Store Products

Response to 510(k) Deficiency Letter

July 28, 2010

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

Reference: **Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) 510(k) (K101098) Deficiency Letter dated June 10, 2010**
Applicant: **Lil' Drug Store Products, Inc.**

Dear Sir or Madam:

In response to the Food and Drug Administration's ("FDA" or the "agency") deficiency letter dated June 10, 2010 for the Traditional 510(k) Premarket Notification, K101098, for Replens Long-Lasting Vaginal Moisturizer (in 35g Tube with Reusable Applicator) ("Replens"), a vaginal moisturizer for treatment of vaginal dryness, please see below the response from the applicant. Your comments are restated in bold followed by the response.

Condom Compatibility

1. **The mfr provided the results of condom compatibility testing in terms of percent drop in properties (tensile and airburst) following exposure to the subject lubricant for each condom type evaluated. This testing showed that exposure to Replens caused a significant drop in condom properties, condoms made from natural rubber latex, polyisoprene, and polyurethane. In many cases, the percent drop in properties exceeded 20%. (We sent you a chart yesterday illustrating these results.) Consequently, it appears that Replens is not compatible with condom use. Replens labeling should reflect this as a caution statement.**

   The mfr stated that the data provided demonstrate that the subject lubricant is condom compatible because (1) following exposure, the condom properties met the requirements outlined in ISO and ASTM standards, and (2) the subject

lubricant performed equivalently to KY Jelly, which is labeled condom compatible.

However, please note that FDA evaluates the condom compatibility of all personal lubricants based on percent drop in condom properties (typically tensile and airburst) to determine the physical effect of the lubricant on the condom membrane. Furthermore, KY Jelly is known to be condom compatible and is often used as a negative control in condom compatibility studies. It is possible that the specific test method you used to evaluate condom compatibility may have led to negative results, (e.g., brushing the lubricant onto the condom).

Therefore, please revise the Indications for Use form, 510(k) Summary, and labeling for the subject lubricant to state that it is not condom compatible, and please provide revised copies of these documents for review.

Alternatively, you may provide the results of additional condom compatibility testing to support the condom compatibility of the subject lubricant. However, please note that if the results do not demonstrate that the subject lubricant is condom compatible, you will need to revise your labeling accordingly.

As noted in the agency's question, Lil' Drug Store initially submitted the results of condom compatibility testing of Replens conducted by ARDL, Inc. that showed similar declines in condom properties for Replens and K-Y Jelly In a phone conversation on June 10, 2010, the agency questioned the protocol used in these studies, as: (1) K-Y Jelly is known to be condom compatible and should not show a decline in condom properties; and (2) based upon a review of the ingredients in Replens, the product would not be expected to cause a significant decline in condom properties, either. The agency also noted that, without a positive control, the results of these tests were difficult to interpret.

Lil' Drug Store agrees that Replens is not expected to cause significant declines in condom properties, and noted that the product has performed equivalently to K-Y Jelly, which labeled as condom compatible, on all testing conducted to date. Therefore, the company chose to conduct further testing to better assess the condom compatibility of Replens.

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Based upon concerns with the test protocol used, and inconsistent implementation of quality control measures at the initial testing laboratory, Lil' Drug Store chose to work with Nelson Laboratories to develop a protocol that would accurately assess the condom compatibility of Replens, and that would incorporate all necessary controls (both positive and negative) and quality control measures to ensure that the tests results are reliable.

The protocol for this additional testing was developed based on the ASTM condom/lubricant test standard under development, a review of condom compatibility protocols available from various labs, and a review of protocols in published studies. Improvements to the protocol at the new lab included: 1) use of both positive and negative controls; 2) testing all variations on the same day; 3) implementation of more precise cleaning and handling procedures—e.g. changing of gloves between lubricants; 4) hand rubbing the lubricant on the condoms instead of brushing; 5) replacement of Durex lubricated latex condoms with Durex non-lubricated latex condoms; 6) drying the condoms before testing them; 7) testing lubricants in order of expected performance (untreated, KY, Replens, Mineral Oil) as an additional control to avoid any possible effect of the positive control on other condoms; and 8) subjecting untreated condoms to the same humidity conditions as treated condoms prior to testing. The amount of lubricant applied and time/storage conditions in the humidity chamber did not change. Additionally, the lab exercised tighter controls over the protocol and processes.

Importantly, this study at the new laboratory yielded expected results for both the negative control (KY Jelly) and the positive control (Mineral Oil), confirming the reliability of the protocol and the study results. Please note that the Durex Avanti polyurethane condoms are labeled as compatible with oil based lubricants, so it is an expected result that the positive control did not affect them. The results demonstrate that Replens is compatible with both latex and synthetic condoms. Specifically, out of 50 measures tested (across two Replens formulas (with and without methylparaben) on five brands of condoms, two Air Burst measures and three Tensile measures), ***no performance declines greater than 20%*** were observed for Replens-treated condoms, and only five performance declines between 10-20% were observed (3 on latex condoms and 2 on synthetic condoms). These were not observed consistently (*i.e.,* none of them were seen on both Replens formulas (3 were on the formula with methylparaben and two were on the formula without methylparaben) and none were seen in prior tensile testing of Replens) and are likely

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due to variability of condom performance within a lot or occasional impact incurred during the application of the lubricant. It is concluded from this testing that Replens (both with and without methylparaben) is condom compatible. Complete test results are attached. In summary, the new test results, conducted using a more reliable protocol, procedure, and test lab, demonstrate that Replens is compatible with both latex and synthetic condoms. Unlike in prior testing, negative and positive controls performed as expected, confirming the appropriateness of the study protocol. In Air Burst testing, Replens performed as well as or better than the negative control. In Tensile testing, Replens generally had performance declines less than 10%. Therefore, Lil' Drug Store believes that Replens should be labeled as condom compatible.

Human Use Data

2. **In response to questions 9 and 10 for both 510(k)s that we sent you earlier, the mfr referred to published clinical studies of the proposed Replens gel. However, it is unclear whether the published studies used versions of the device with or without methylparaben. For each published study referenced, please identify the formulation used (with or without methylparaben), the number and frequency of applications, and negative reports following device use (e.g., irritation, allergic response, adverse events, etc). Sufficient data on the methylparaben version of the device should be provided to support safe use in humans as this version would be expected to have the greater potential for toxic effects based on the results of the acute systemic toxicity studies.**

   In addition, please provide information from complaint files or MDRs regarding any negative effects associated with use of both versions of the device (please provide results separately). Please also confirm how many samples have been sold and information on where devices have been shipped (e.g., one million in US, two million in Canada, etc.).

   If the information provided is not sufficient to demonstrate that use of both versions of the device is safe following use by humans, additional testing as described in question 10 from our previous comments (i.e., combined vaginal irritation/systemic toxicity) will be requested.

   Please see attached response to this question.

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Lil' Drug Store Products

Shelf-Life

3. **In response to question 5 for K101241, the mfr provided the results of shelf-life. In addition, you state that based on a phone conversation April 30, 2010, there was agreement that the device could be labeled with an initial shelf-life of 17 months that could be extended to one year upon completion of the shelf-life study.**

   Our review of the data showed that real-time test data is available from one lot for 6 months, and additional lots at 3 months. In addition, accelerated shelf-life testing has been conducted for 6 months on one lot, and multiple lots out to 2 months. However, the protocol does not discuss how the environmental conditions used were developed (e.g., no standards identified), or how long 2 or 6 months at these conditions relates to real-time use. Please provide a detailed discussion how the accelerated conditions were developed, and if a published standard method was not used, please provide data validating the accelerated methods used. In addition, please limit the shelf-life to a duration that is supported by data from three lots of device (accelerated or real-time). All accelerated results will need to be confirmed with real-time results.

   This question is only applicable to the Replens in Pre-filled applicators 510(k) submission, K101241.

Please do not hesitate to contact me at (319) 294-3745 or by email at tmiller@lildrugstore.com should you require any clarification regarding this response.

Sincerely,

Patricia L. Miller
Lil' Drug Store Products, Inc.
Director of Regulatory

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Lil' Drug Store Products

Attachments:

Human Use Data

Condom Compatibility Test Results Summary

Condom Compatibility Test Reports

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Human Use Data

2. In response to questions 9 and 10 for both 510(k)s that we sent you earlier, the mfr referred to published clinical studies of the proposed Replens gel. However, it is unclear whether the published studies used versions of the device with or without methylparaben. For each published study referenced, please identify the formulation used (with or without methylparaben), the number and frequency of applications, and negative reports following device use (e.g., irritation, allergic response, adverse events, etc). Sufficient data on the methylparaben version of the device should be provided to support safe use in humans as this version would be expected to have the greater potential for toxic effects based on the results of the acute systemic toxicity studies.

In addition, please provide information from complaint files or MDRs regarding any negative effects associated with use of both versions of the device (please provide results separately). Please also confirm how many samples have been sold and information on where devices have been shipped (e.g., one million in US, two million in Canada, etc.).

If the information provided is not sufficient to demonstrate that use of both versions of the device is safe following use by humans, additional testing as described in question 10 from our previous comments (i.e., combined vaginal irritation/systemic toxicity) will be requested.

Response:

Introduction

As described in the 510(k) notice, Replens has a 20 year history of safe use in the U.S. as a cosmetic. Seven clinical trials were conducted as part of the development program for Replens, described in detail below. No serious adverse events were reported in these studies. Some of the studies reported non-serious gynecological symptoms such as soreness, irritation, itching or burning; however, these symptoms were frequently observed in patients in the study at baseline. All of the studies concluded that Replens was safe and well-tolerated.

In addition, Lil' Drug Store has detailed customer complaint data from 1993-2009, also described in detail below. Overall, there have been no serious adverse events related to the product recorded during this time period. There have been 1,217 non-serious adverse events, including possible allergic reactions and infections, irritation, and applicator discomfort, reported globally during this time period for over 151million patient exposures to the product. One serious adverse event was reported (congenital anomaly), but was not related to the product. This represents an extremely low percentage (0.0008%) of patient exposures.

In reviewing this information, it is important to note that the intended users of the Replens device are patients suffering from vaginal dryness and its associated

symptoms. These symptoms can include soreness, irritation, itching or burning. Therefore, some level of these types of symptoms would be expected in this population, independent of the use of any vaginally-applied product.

In summary, Lil' Drug Store believes that the extensive clinical data on the product, including data from seven clinical studies and over 151 million doses sold, demonstrate that Replens, both with and without methylparaben, is safe and is well-tolerated in humans. Therefore, the company believes that additional biocompatibility testing of the product would not contribute any meaningful additional information to the safety profile of the device.

Replens Clinical Development Program

Overview

As described in the company's response to the agency's May 5, 2010, deficiency letter, seven clinical studies were performed as part of the development program for Replens. These studies are summarized below in **Table 1** and are described in detail in this section. As requested by the agency, information with regard to the formulation used (with or without methylparaben), the number and frequency of applications, and any negative reports following device use are described below for each of these studies.

Table 1: Overview of Replens Clinical Development Program

Protocol No.	Citation	No. Patients Enrolled (Replens)	Study Design*	Dosage Regimen	Duration
01	Bachmann et al (1)	89	D-B, X-over	2.5 g per day	5 days
01 ext.	Bachmann et al (2)	54	Open	2.5 g, 3 x weekly	12 months
02	Zinny and Lee (3)	26	D-B, parallel	2.5 g alternate nights	4 weeks
03	Young et al (4)	30	Open	2.5 g, 3 x weekly, plus option of additional application prior to intercourse.	12 months
04	Nakamura (5)	10	Open, X-over btwn treatment durations	2.5 g daily	1-5 days

1 Bachmann GA, Notelovitz M, Gonzalez SJ, Thompson C, Morecraft BA. (1991) Vaginal Dryness in Menopausal Women: Clinical Characteristics and Nonhormonal Treatment. Clinical Practice in Sexuality, 7(9): 1-8.
2 Bachmann GA, Notelovitz M, Kelly SJ, Owens A, Thompson C. (1992) Long Term Nonhormonal Treatment of Vaginal Dryness. Clinical Practice in Sexuality, 8(8/9): 3-8.
3 Zinny MA, Lee S. (1991) Double-Blind Study of the Comparative Effects of Two Gels on Vaginal pH in Postmenopausal Women. Today's Therapeutic Trends, 8(4): 65-72.
4 Young R, Goldzieher J, Kaufman R. (1991) A Study of the Effects of Col-1003 In Postmenopausal Women. Unpublished.

Protocol No.	Citation	No. Patients Enrolled (Replens)	Study Design*	Dosage Regimen	Duration
90/10	Whitehead (6)	32	D-B, X-over	2.5 g, 3 x weekly plus option of additional application prior to intercourse.	8 weeks
05	Nachtigall (7)	15	Open, parallel	2.5 g, 3 x weekly	3 months
06	Gelfand and Wendman (8)	25	Open	2.5 g, 3 x weekly, plus option of additional application prior to intercourse.	3 months

* D-B = double-blind; X-over = cross-over design

In all seven studies, a single 2.5 g application of Replens has been the standard dosage. The gel has been inserted at bed-time with a frequency ranging from alternate days (study 02) to three times weekly as long-term maintenance. Studies 01 (short-term) and 04 involved daily application of the gel ranging from one to five days.

The clinical development program was conducted with the initial formulation of Replens, which contained 0.18% methylparaben as a preservative. Therefore, all seven studies used this formulation.

The parameters employed in the studies included the influence of Replens on vaginal pH and the vaginal mucosa, the relief of the patient's symptoms, the vaginal dryness index, determination of vaginal pH at varying time intervals after single or multiple applications of the gel, PAP smears and the completion of diary cards by the patient.

Study Design and Results

Table 2 below summarizes the study design and safety and efficacy results for each of the studies. In response to the agency's questions, a detailed discussion of adverse reactions reported in these studies follows the table.

5 Nakamura R. (1991) Evaluation of Col-1003 in the treatment of vaginal dryness in postmenopausal women. Unpublished.
6 Whitehead M. (1991) A Randomised Double Blind Evaluation of Col-1003, a bioadhesive polymer system vaginal moisturizing gel and, KY Brand Lubricating Jelly in the treatment of vaginal dryness in postmenopausal women receiving concomitant oral hormone replacement therapy. Unpublished
7 Nachtigall LE. (1994) Comparative study: Replens versus local estrogen in menopausal women. Fertility and Sterility, 61(1): 178-180.
8 Gelfand MM, Wendman E. (1994) Treating Vaginal Dryness in Breast Cancer Patients: Results of Applying a Polycarbophil Moisturizing Gel. J. Women's Health, 3(6): 427-433.

Table 2: Summary of Replens Clinical Studies: Study Design and Results

Study Investigator Coordinating Center(s) Report #	**Design**	**Number of subjects with age and sex**	**Diagnosis + criteria for inclusion**	**Duration of Treatment**	**Test product Dosage Regimen Route of Administration**	**Criteria for Evaluation**	**Results (efficacy)**	**Adverse Reactions**
Bachmann RW Johnson Med Sc New Brunswick, NJ Notelovitz Women's Med & Diag Center Gainsville, FL Protocol 01 + extension	Phase I D-B, randomized crossover comparison. Replens vs. KY Jelly Phase II Open label. Replens	Phase I Enrolled: 89 women aged 40-78 yrs. Phase II Enrolled: 54 women Completed: 46	Peri and post menopausal women with symptoms of vaginal dryness	Phase I 5 days Phase II 12 months long term	Phase I Replens or KY Jelly, 2.5g/day for 5 days Phase II Replens 2.5g intravaginally x 3 per week	Vaginal dryness index, vaginal pH cytology, patient diary card.	Replens both short and long term significantly reduced vaginal pH and increased the dryness index score.	No serious events. Mainly gynecological symptoms (see discussion).
Zinny and Lee Med & Tec Res Assoc Inc Boston, MA 012309 Protocol 02	D-B, randomized parallel, controlled. Replens vs. KY Jelly	Enrolled: 51 women R=26, KY=25 R=56.0 yr KY=56.4 yr Completed: R=25, KY=25	Postmenopausal women with symptoms of vaginal dryness	4 wks	Replens or KY Jelly (2.5g) intravaginally every second night	Vaginal pH and lactobacillus counts	Replens reduced vaginal pH significantly at end of wks 1, 2, 3 and 4. No effect on lactobacillus counts.	No serious adverse events (see discussion).
Young, Goldzieher, Kaufman Baylor Coll of Med Houston, TX Protocol 03	Open label	Enrolled: 30 women aged 31-66 yrs, Mean 51 yrs. Completed: 22	Postmenopausal women with symptoms of vaginal dryness	12 months	Replens 2.5g intravaginally at night x 3 applications per week, plus option of additional application prior to intercourse.	Symptomatic relief, vaginal pH, CUE ovulation test.	Marked and sustained symptomatic relief. Small reduction in pH (NS).	No serious events. Mainly gynecological symptoms (see discussion).

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Study Investigator Coordinating Center(s) Report #	Design	Number of subjects with age and sex	Diagnosis + criteria for inclusion	Duration of Treatment	Test product Dosage Regimen Route of Administration	Criteria for Evaluation	Results (efficacy)	Adverse Reactions
Nakamura, March Univ Southern California Med Sch Los Angeles Protocol 04	Open label, Crossover between different treatment durations	Enrolled: 10 women Completed: 10	Postmenopausal women with symptoms of vaginal dryness	1, 2, 3 then 5 consecutive days	Replens 2.5g intravaginally each night.	Vaginal pH, vaginal dryness index, patient diary.	Vaginal dryness index significantly increased after 3 applications and pH significantly reduced after 2 or more applications.	Leakage of Replens or a residue in 3 patients (see discussion).
Whitehead Dept Gynaecology Kings Coll Hosp. London Protocol 90/10	D-B, randomized crossover comparison. Replens vs. KY Jelly	Enrolled: 32 women aged 41-63 yrs Completed: 30	Postmenopausal women with symptoms of vaginal dryness receiving HRT.	8 wks	Replens or KY Jelly, 2.5g intravaginally at night 3 applications per week, plus option of additional application prior to intercourse.	Vaginal pH and dryness index. Patients Diary card.	Both treatments produced a similar response for vaginal dryness. For vaginal elasticity and turgor, Replens was significantly better than KY Jelly applications.	No serious events. Mainly gynecological symptoms (see discussion).

Study Investigator Coordinating Center(s) Report #	Design	Number of subjects with age and sex	Diagnosis + criteria for inclusion	Duration of Treatment	Test product Dosage Regimen Route of Administration	Criteria for Evaluation	Results (efficacy)	Adverse Reactions
Nachtigall NY Univ Med Center New York Protocol 05	Open label, single center, randomized, controlled, parallel group. Replens vs. Premarin	Enrolled: 30 women (15 per group)	Postmenopausal women with symptoms of vaginal dryness	3 months	Replens, 2.5g intravaginally at night x 3 applications per week. Premarin, 2.0g intravaginally every day.	Onset of action with symptom improvement, vaginal dryness, vaginal pH.	Significant decrease in vaginal pH and increase in vaginal dryness index for both treatments.	No serious events reported for either treatment.
Gelfand Dept Ob/Gyn McGill Univ Montreal Protocol 06	Single center open label.	Enrolled: 25 women aged 43-78 yrs, Mean 60.1 yrs. Completed: 25	Women with a history of breast cancer in whom hormone replacement therapy is contraindicated. All were menopausal (natural, surgical or chemical)	3 months	Replens 2.5g intravaginally at night x 3 applications per week. Plus option of additional application prior to intercourse.	Vaginal pH, vaginal dryness index score.	Significant improvement in objective and subjective parameters of vaginal dryness over 3 month period.	No serious events. Mainly gynecological symptoms (see discussion).

Adverse Reactions, Tolerance and Interactions Reported

There were no serious adverse events reported in these seven studies. In some cases, non-serious events such as irritation, burning, and itching have been reported in patients while using Replens. However, conclusions regarding the relationship to the device are difficult to make, as many of these symptoms were also present in subjects at baseline, and the relationship of the reported event to the treatment as determined by the investigator was either missing or reported as unknown for a majority of the clinical studies. There were also several reports of discharge or leakage of Replens in these studies, which is not an unexpected occurrence. As described in the published articles and clinical study reports, the clinical investigators universally found Replens to be safe and well-tolerated.

A detailed description of the specific adverse events reported in the seven individual clinical studies is presented below:

Bachmann et al. (Study 01): In the short-term phase of the study, there was no difference between the treatments with respect to urethral irritation, vaginal burning, and product residue side effects (13.8% for Replens, 10.8% for K-Y Jelly; p=0.112). Except for two women on Replens and one woman on K-Y Jelly, patients reporting these problems had the symptoms present at baseline and they persisted independent of the study group (Replens or K-Y Jelly) the patient was in during the cross-over design.

Two patients were withdrawn from the study while on Replens because of urethral irritation. Urine cultures were negative in these patients. In one patient, the reason for withdrawal was not considered to be treatment related and, in the second case, an allergic reaction presenting as vaginal irritation was reported to be the reason for withdrawal. While receiving Replens, 43 patients reported a total of 77 adverse events of all types (29 K-Y Jelly patients reported 54 adverse events). The most commonly reported events while receiving Replens were discharge, leakage, burning and irritation. In the K-Y Jelly group, leakage and itching were most commonly reported.

During the twelve month extended treatment period, there were no patients who dropped out due to adverse effects. One patient withdrew due to itching which was considered as possibly related to Replens. None of the women reported serious side effects and all women reported continued improvement in their original symptoms, including irritation, burning, and itching. During the twelve months, 74 patients reported a total of 341 adverse events. Of the adverse events reported, 123 were gynecological in nature. The most commonly reported gynecological adverse events were residue and leakage. The most commonly reported non-gynecological adverse events were headache and back problems. Ten reported irritation as an adverse event, but six of these reported irritation at baseline. Twelve reported itching as an adverse event, but nine of these reported itching at baseline. The authors conclude that Replens was effective and well-tolerated.

Zinny and Lee (Study 02): No serious adverse effects were reported in either treatment group. 9 patients (36%) who received Replens and 4 who received K-Y Jelly (16%) reported 17 adverse experiences, none of which were serious or required withdrawal from the study. The most frequently reported occurrences were slight itching (2 in each group) and a trace of blood on the applicator (3 Replens, 1 K-Y Jelly). The authors note this is most likely due to localized irritation of the atrophic, friable vaginal wall by insertion of the applicator. Of those reported in the Replens group, there was only one adverse event which was considered 'probably related' to the product; one patient complained of leakage.

Young et al. (Study 03): In this long-term study (12 months duration), no patients were withdrawn due to an adverse event. There were no serious adverse events recorded throughout the study. Although mild symptoms such as itching, dryness, burning and a discharge were frequently recorded, none of them was stated as being possibly or definitely treatment related. However, in many instances the relationship between the event and the treatment was not completed on the record form. The majority of the instances of dryness (5/7 patients) or itching (8/14 patients) were considered by the investigators to be a continuation of the underlying symptoms.

Nakamura and March (Study 04): No serious adverse events were reported in the study. 3 patients reported leakage or discharge of Replens. One patient reported increased urination on one day during the study, but this patient had reported increased urination prior to the study. One patient reported exterior dryness after 5 applications of Replens. The relationship of the event to the treatment was not established. No patients were withdrawn.

Whitehead (Study 90/10): Two patients on K-Y Jelly were withdrawn due to adverse events (vaginal irritation and soreness, vaginal irritation). No patients on Replens were withdrawn for adverse events. No serious adverse events were reported throughout the study period. Vaginal dryness and irritation/soreness were the most frequently reported events. Vaginal irritation or soreness was reported by 3 patients on Replens and 2 patients on K-Y Jelly. Vaginal dryness was reported in 2 patients on Replens, but these patients had reported dryness at baseline. Candidal infection was reported in both treatment groups (Replens, 4; K-Y Jelly, 2), however, all patients were also receiving hormone replacement therapy, which is often associated with candidal vaginitis. The relationship of the events to the treatment was not established.

Nachtigall (Study 05): In this study, no serious adverse events were reported in either group. One patient withdrew from each treatment group related to itching and irritation. Itching and irritation were present in 50% of the Replens and 60% of the Premarin group at baseline and most patients had relief of these symptoms at week 12. The author concludes that Replens is a safe and effective alternative to estrogen cream.

Gelfand and Wendman (Study 06): No patients withdrew from the study due to adverse events. One patient reported continuing minor vaginal irritation at months

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