

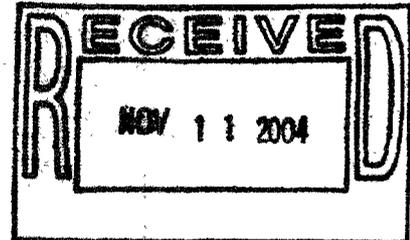


DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 20-832/S-008

Medi-Flex, Inc.
Attention: Linda McBride, R.Ph.
Director, Regulatory Affairs
11400 Tomahawk Creek Parkway, Suite 310
Leawood, Kansas 66211



Dear Ms. McBride:

Please refer to your supplemental new drug application dated July 6, 2004, received July 7, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ChloraPrep with Tint 26-mL Applicator (2% chlorhexidine gluconate w/v and 70% isopropyl alcohol v/v solution).

We acknowledge receipt of your submissions dated July 22 and September 9, 2004.

This supplemental new drug application proposes a newly-designed applicator with a sponge tip (pledget) impregnated with FD&C Green #3 dye for preoperative skin preparation.

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies are summarized as follows:

1. Conduct the Patient Pre-operative Skin Preparation (efficacy) study using the tinted formulation versus the clear formulation that was described for you in our September 3, 2004 facsimile on this subject.
2. Conduct a skin coverage study to assure that the product may be used safely according to the labeled directions. Follow the advice we provided in facsimiles sent to you on September 3 and September 23, 2004.

We recommend that you submit your protocol for the Patient Pre-operative Skin Preparation study to the IND for review and feedback before you initiate the study.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change before approval of this supplemental application.

NDA 20-832/S-008

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If you have any questions, call Tia Frazier, Regulatory Project Manager, at (301) 827-2271.

Sincerely,

{See appended electronic signature page}

Curtis Rosebraugh, M.D., M.P.H.
Deputy Director
Division of Over-the-Counter Drug Products
Center for Drug Evaluation and Research

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/s/

Curtis Rosebraugh
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The Fax begins on the next page.



Food and Drug Administration
 Center for Drug Evaluation and Research
 Office of Drug Evaluation ODE V

FACSIMILE TRANSMITTAL SHEET**DATE:** September 3, 2004

To: Linda McBride, R.Ph. Director, Regulatory Affairs	From: Tia Frazier Project Manager
Company: Medi-Flex	Division of Over-the-Counter Drug Products
Fax number: 913-451-8509	Fax number: 301-827-2315
Phone number: 913-451-0880	Phone number: 301-827-2271
Subject: Discipline Review Completed for NDA 20-832/S-008 Clinical studies	
Total no. of pages including cover: 3	

Comments:

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

Document to be mailed: YES NO

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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Message: Please refer to the clinical studies submitted on July 6, 2004 to NDA 20-832, Supplement 008, for ChloroPrep with Tint 26-mL Applicator. We wish to provide the following comments and requests for clinical information to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified.

Conduct the following two clinical studies:

Skin Coverage Study:

The study submitted in support of this supplemental application ("Evaluation of the Area Covered by a Preoperative skin Preparation") is deficient in that the product was applied for a 30 second period rather than the maximum 2 minute application period recommended in the approved labeling. Since it is the intent of this study to determine the potential for product runoff and pooling when used for the longest possible time, you need to conduct another skin coverage study to support approval of the larger applicator.

1. We presume that the preferred additional applicator size is 26-mL. Therefore, all test subjects should be tested using this size. Skin area coverage should be determined using a total of at least 20 applicators on adult volunteers of varying heights and weights. The average amount (weight/volume) of product used in the applications should be recorded.
2. The protocol should specifically instruct that the directions for application for a two-minute prep as presented in the approved labeling will be used. The report should specifically state whether product runoff and/or pooling occurred for each test subject. You can use the same format for the skin coverage report that you used for the July 6, 2004 submission.

Patient Pre-operative Skin Preparation Study:

1. Bacterial reductions in a representative number of test subjects should be determined. We recommend that the following outline be utilized:
 - A. Data from 20 evaluable subjects should be available. Ten subjects should have been prepped with the "new" (tinted) formulation, and ten should have been prepped with the "old" (untinted) formulation.
 - B. The procedure should approximate that recommended in the Tentative Final Monograph for Health-Care Antiseptic Drug Products for "dry" surgical sites. That is, the abdomen should be used for testing, the subjects should have at least a 3 log baseline bacterial count, and bacterial reductions should be determined at 10 minutes and 6 hours after prepping. A 30-second prep as recommended in the approved labeling should be used.
2. We strongly recommended that you submit the protocol for testing to the IND for review and feedback before you initiate the study.

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/s/

Tia Frazier
9/3/04 11:24:55 AM
CSO



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 Center for Drug Evaluation and Research
 Office of Drug Evaluation ODE V

FACSIMILE TRANSMITTAL SHEET

DATE: September 23, 2004

To: Linda McBride	From: Tia Frazier
Company: Medi-Flex	Division of Over-the-Counter Drug Products
Fax number: 913-451-8509	Fax number: 301-827-2315
Phone number: 913-451-0880	Phone number: 301-827-2271
Subject: Skin Coverage Protocol comments	

Total no. of pages including cover: 2

Comments:

Document to be mailed: YES NO

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FDA comments on Skin Coverage Study

Submission date: September 15, 2004

IND 46,243

September 23, 2004

1

We have received the new skin coverage protocol (submission of Sept. 15, 2004 to IND 46,243). The new protocol is satisfactory with one addition: Presently, drying time is estimated by one individual. It is recommended that drying time be estimated (separately) by 3 qualified persons, including at least one person with operating room experience, if possible. The estimated drying times should then be averaged.

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/s/

Tia Frazier
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CSO