CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

73416

CORRESPONDENCE

ANDA 73-416

SEP 18 1989

Deseret Medical, Inc.
Attention: Mr. Charles J. Welle
9450 South State Street
Sandy, UT 84070

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME OF DRUG: 4% Chlorhexidine Gluconate Surgical Brush/Sponge

DATE OF APPLICATION: August 28, 1989

DATE OF RECEIPT: September 1, 1989

We will correspond with you further after we have had the opportunity to review the application.

However, in the interim, please submit three additional copies of the analytical methods and descriptive information needed to perform the tests on the samples (both the bulk active ingredient(s) and finished dosage form) and validate the analytical methods. Please do not send samples unless specifically requested to do so. If samples are required for validation we will inform you where to send them in a separate communication.

If the above methodology is not submitted, the review of the application will be delayed.

If you wish to request a waiver of in vivo bioequivalence study requirements, a formal request citing the appropriate section of the regulations at 320.22 is required.

The Approved Drug Products with Therapeutic Equivalence Evaluations identifies a patent on this drug product. You must make an appropriate patent certification under 505(j)(2)(A)(vii).

Please identify any communications concerning this application with the ANDA number shown above.

Sincerely yours,

/S/ for 9-18-89

Acting Director
Division of Generic Drugs
Center for Drug Evaluation and Research

cc:
DUP HFN-230
Rosen/Harrison
mlb/9-15-89
Ack 2609b

/S/ 9/18/89

/S/ 9/14/89

ANDA 73-416

Deseret Medical, Inc.
Attention: Mr. Charles J. Welle
9450 South State Street
Sandy, Utah 84070

DEC 2[illegible]

Dear Sir:

Reference is made to your Abbreviated New Drug Application (ANDA) submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Chlorhexidine Gluconate Scrub Brush-Sponge, 4%.

Reference is also made to the request for waiver of in vivo bioequivalency requirements for this product, dated September 25, 1989. This request has been reviewed by the Division of Anti-Infective Drug Products, HFD-520, and they have the following comments:

The in vivo bioequivalency requirement is designed to demonstrate that a generic version of a product performs in a manner that is considered to be statistically equivalent to the innovators product. Thus, the study is not only an examination of the finished dosage form, but, by design is an examination of the generic companies manufacturing expertise in reproducing an equivalent form of the innovators product.

If the generic firm was to obtain the finished dosage form (i.e. sponges containing 4% CHG packaged in identical packaging material) from the innovator and the innovator was placing the generic firms proprietary name on the product, it would not be necessary to perform the in vivo bioequivalency study provided the product had the same indications. However, in this case Deseret Medical, Inc. is purchasing bulk 4% chlorhexidine gluconate solution as a starting material for the manufacture of their finished dosage form. The 4% CHG is injected (volume unknown relative to the innovators product) into a sponge (characteristics unknown relative to innovators product) and the package sealed to produce the finished dosage form. In addition it is not known whether the instructors for use are identical for the generic version and the innovators product.

In conclusion, the sponsor must conduct the in vivo bioequivalency study in order to demonstrate that they are capable of manufacturing a product that is equivalent to the innovators product as measured by the surgical handscrub study.

Therefore, the request for waiver of in vivo bioequivalence requirements under 21 CFR 320.22 is denied. It is recommended that you contact Mr. Albert Sheldon, of the Division of Anti-Infective Drug Products, HFD-520, at the telephone number 301-443-4290 to discuss study requirements to establish the bioequivalency of this product.

Sincerely yours,

/S/

Acting Director
Division of Generic Drugs
Center for Drug Evaluation and Research

cc:
HFD-232
PRickman
bb/12-14-89
2718b/p. 9-10

BSheldon 12/22/89

FEB 28 1991

ANDA 73-416

Deseret Medical
Attention: Charles J. Welle
9450 South State Street
Sandy, Utah 84070

Dear Mr. Welle:

Reference is made to your January 13, 1991 correspondence regarding the status of your application for Chlorhexidine Gluconate, 4% Surgical Brush/Sponge.

Please be advised that although a significant time has elapsed since your last submission that the review of your submission is nearing completion. We fully anticipate that the Office will correspond with you within the next 30 days regarding our findings.

As you are probably aware, the Office of Generic Drugs is experiencing a significant backlog in processing ANDA submissions due in part to the generic drug scandal. While we are working towards the reduction of the backlog, applications are still handled in a first-in, first reviewed queue. I apologize for the delay in Agency response and anticipate that you should be hearing from us in the near future regarding the above referenced application.

Sincerely Yours,

/S/ 2/28/91

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-416
DUP/Division File
HFD-632/RPollock/2-22-91 RPollock 2/28/91
HFD-600/Reading File
R/D initialed by RPollock
c:\wp51\bob\73416.ltr/jmk/2-22-91
F/T by jmk/2-27-91
status letter

ANDA 73-416

AUG 2 1991

Deseret Medical, Inc.
Attention: Mr. Charles J. Welle
9450 South State Street
Sandy, Utah 84070

Dear Sir:

Please refer to your abbreviated new drug application dated August 28, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for E-Z Scrub (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%.

We also acknowledge your communications of March 5, 22, and 25, 1991.

The application is not approvable under Section 505 of the Act for the following reasons:

Approval of an application is not given until it has passed both scientific and administrative scrutiny at the Branch, Division, and Office levels. In the review of your ANDA 73-416 for E-Z Scrub (Chlorhexidine Gluconate Scrub - Brush/Sponge) is was noted that it does not comply with 21 CFR 314.101(e)(1) which prohibits the filing of a submission for a drug product that is already covered by an approved application. Since your submission represents the exact same product already approved under Stuart's NDA 18-423, and relies on the Stuart data it cannot, in its present form, be approved as an NDA or ANDA. In order for your application to be considered as an ANDA you must generate your own stability data and bioequivalence studies. You may not rely on the material in the Stuart NDA.

Although this ANDA cannot be approved for the reason cited above, it would be acceptable to market the product as a distributor under Stuart's NDA. If this is not a satisfactory course of action for your firm then your present ANDA could only be approved if you conduct your own bioequivalence studies and generate new stability data so that the application stands on its own and does not reference the data of an already approved application.

Should you wish to pursue this course of action, the following revisions in product labeling will be required:

CONTAINER: Not Satisfactory

A. Main Panel

1. Revise the lines beneath "E-Z Scrub" to read:

   Antimicrobial Surgical Scrub Brush/Sponge
   with HIBICLENS*
   *Filled with...

2. We note you have included the word "antiseptic" on the main panel. Please explain why you believe the antiseptic claim for Hibiclens Topical Solution is applicable to your Scrub Brush/Sponge.

3. Chlorhexidine gluconate (rather than E-Z Scrub sponge/brush) provides rapid bactericidal action...

4. Add "Discard After Use". It should appear after "For Single Use Only".

5. Add the temperature in degrees Celsius to the storage recommendations. ...40°C (104°F).

6. We encourage you to include the words "FOR SURGICAL HAND SCRUB" on the label.

B. WARNINGS

Revise this statement to read:

WARNINGS: FOR EXTERNAL USE ONLY. KEEP OUT OF EYES, EARS AND MOUTH. CHLORHEXIDINE CONTAINING PRODUCTS SHOULD NOT BE USED AS A PREOPERATIVE SKIN PREPARATION OF THE FACE AND HEAD. MISUSE OF CHLORHEXIDINE CONTAINING PRODUCTS HAS BEEN REPORTED TO CAUSE SERIOUS AND PERMANENT EYE INJURY WHEN PERMITTED TO ENTER AND REMAIN IN THE EYE DURING SURGICAL PROCEDURES. IF HIBICLENS SHOULD CONTACT THESE AREAS, RINSE OUT PROMPTLY AND THOROUGHLY WITH WATER. Avoid contact with meninges. This product should not be used by persons who have a sensitivity to it or its components.

Chlorhexidine gluconate has been reported to cause deafness when instilled in the middle ear through perforated ear drums. Irritation, sensitization and generalized allergic reactions have been reported with chlorhexidine-containing products, especially in the genital areas. If adverse reactions occur, discontinue use immediately and if severe, contact a physician.

Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately.

C. Directions For Use - Please revise this section so it is in accord with the directions for use which appear on your other chlorhexidine gluconate scrub-brush/sponge [ANDA 72-525].

CARTON: Not Satisfactory

A. See comments A and B under Container.

B. Be sure the words "FOR SURGICAL HAND SCRUB" remain on the carton labeling.

C. Directions For Use
Item 4, sentence 2 - The word "Repeat" should appear in bold print.

Revise your labels and labeling, then prepare and submit draft copy for our review and comment.

The file is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a minor amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 8/2/91

Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: AADA #73-416
DUP/Division File
HFD-638/YMille 7/26/91
HFD-600/RF
HFD-635/RF
HFD-635/JHannan JHannan 7/18/91
HFD-635/JHarrison/RAdams/3/14/91
R/D initialed by JHarrison
mw/3/15/91/73-416.RV1

Revised 7/16/91
NOT APPROVABLE ANDA R.C. adams 7/16/91
7/16/91

ANDA 73-416

AUG 4 1992

Deseret Medical, Inc.
Attention: Mr. Charles Welle
9450 South State Street
Sandy, Utah 84070

Dear Sir:

Please refer to your abbreviated new drug application dated August 28, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for E-Z Scrub (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%.

Reference is made to your protocol submitted May 19, 1992.

The correspondence has been reviewed by the Division of Anti-infective Drug Products (HFD-520) and they have the following comments:

The protocol has been reviewed and found to be generally satisfactory. However, before you proceed with your study the following changes should be made.

1. The positive control, Hibiclens, must be used according to the directions approved for surgical handscrub use. This includes volume of product, duration of scrub and frequency of scrub.

2. The number of subjects to be enumerated as presented in Table II (Exhibit B) for each time point could be improved to maximize the statistical significance of the results. Instead of performing "Test Week" enumerations on 18 hands at time zero, 9 hands at time 3 hours and 9 hands at time 6 hours (for a total of 36 hands), we would recommend enumerating 12 hands at time zero, 12 hands at time 3 hours and 12 hands at time 6 hours. The equal distribution of subjects should result in better confidence intervals for the 3 and 6 hour time points.

3. The "Study Description and Informed Consent Form" (Addendum I) states in the fourth paragraph of page 1 that enumerations will be performed by
This statement should be corrected to reflect
will be used.

4. The "Study Description and Informed Consent Form" (Addendum I) states in the second paragraph of page 2 that persons having sensitivity or allergy to the test materials will not participate in the study. How will this be determined? Also, the investigator needs to determine whether the panelists have participated in previous studies of this type. If they have, we would recommend that at least a two week washout period be used before panelists are used again.

5. It is stated in section 7.7, Statistical Analysis, that two final reports will be issued. It should be noted that although a % CHG product is also being tested, our concern is only with the subject of this NDA which is the 4.0% CHG product. If the applicant is considering submission of an NDA for the % CHG product, then they must assure that a concomitant control is run with each test product. For example, 3 groups of two panelist could be run on day one, with each group of two assigned to one of the three products to be tested. In this manner, test and control product products are run concomitantly.

6. Finally, no information has been submitted regarding the demonstration of the neutralization potential of the neutralizers incorporated with the dilution blanks for this particular formulation. Therefore, the sponsor should submit a protocol designed to demonstrate that the neutralization system will function as suggested. The concentrations of CHG used to validate the neutralization system should mimic expected CHG carry over in the fluid used to obtain the primary sample for enumeration.

We look forward to reviewing your study.

Sincerely yours,

/S/

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-416
DUP/Division File
HFC-130/JAllen
HFD-520
HFD-630/RPollock
HFD-600/Reading File
R/D initialed by GJohnston
73416.ltr(reviews)jkg/7-22-92

GJohnston 8/3/92

Review by 520!

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

ANDA 73-416

Deseret Medical, Inc.
Attention: Charles Welle
9450 South State Street
Sandy, Utah 84070

MAR 24 1993

Dear Sir:

The subject of this letter is an Abbreviated New Drug Application dated August 28, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for E-Z Scrub (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%.

Reference is made to your correspondence dated May 19, 1992, and our letters dated February 18 and August 4, 1992. Our letters cited the reasons we could not approve your application. We are unaware of any subsequent correspondence from you that sought to resolve the pending issues.

Absent evidence of interest on the part of an applicant over such a prolonged time can be considered as a request for withdrawal pursuant to the authority cited in Section 314.120 of the regulations.

Alternatively, if you do not intend to immediately pursue approval of this application you may request withdrawal in accord with Section 314.65 of the regulations. If you do elect to request withdrawal, it will not preclude a future refiling.

If we do not receive a definitive reply from you within 30 days of the date of this letter, in which you request withdrawal or provide an explanation to resolve the pending issues we will initiate action to withdraw the application.

Additionally, you are required to inform the Agency of any change in corporate name or transfer of ownership of the application.

Sincerely yours,

/S/ for 3-24-93

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA # 73-416
DUP/Division File
HFC-130/Allen
HFD-632/Johnston/Vashio
HFD-600/Reading File
R/D initialed by GJ

Washup 3/23/93
3/24/93

30 DAY LETTER!

ANDA: 73-416

NOV 2 1993

Becton Dickinson AcuteCare
Attention: George Nolan
9450 South State Street
Sandy, Utah 84070-3234

Dear Sir:

This is in reference to your abbreviated new drug application dated August 28, 1989, submitted pursuant to Section 505(j) of the Food, Drug, and Cosmetic Act, for Chlorhexidine Gluconate, Scrub Brush Sponge, 4% (E-Z Scrub 106).

Reference is also made to your amendments dated September 10, 1991 and May 7, 1993.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies

B. Labeling Deficiencies

General Comment:

Please revise your labels and labeling to include the established name with your tradename, as follows:

E-Z Scrub® 106 Antimicrobial Surgical Scrub Brush/Sponge with Hibiclens® (Chlorhexidine Gluconate 4% w/v)

Container:

1. Warnings Statement

   a. Line 4 - Revise to read: ...**WHEN PERMITTED...** (Delete

   b. Delete the storage recommendations from this section.

   c. Line 10 - ...and, if severe, contact... (add comma)

2. Directions for use - Revise as follows:

   DIRECTIONS FOR USE - 6 MINUTE SCRUB.

   1. Wet hands and forearms with warm water.
   2. Use nail cleaner and then apply chlorhexidine gluconate from sponge side. Work up lather.
   3. Scrub difficult areas thoroughly for 3 minutes with brush side and the hands and forearms with the sponge side.
   4. Rinse with warm water.
   5. **REPEAT** scrub for 3 more minutes, use sponge side only.
   6. Rinse hands and arms thoroughly.
   7. Dry thoroughly.

Carton: 30's

1. Warnings statement

   a. Line 6 - Revise to read:

      ... **WHEN PERMITTED** ... (Delete

   b. Delete the storage recommendations from this section.

   c. Line 14 -

      ... and, if severe, contact ... (add comma)

2. Directions for Use - Revise to read:

   DIRECTIONS FOR USE:
   Six Minute Scrub Procedure

   1. Wet hands and forearms to the elbows with warm water. Avoid using very cold or very hot water.
   2. Open the package. Use nail cleaner to clean under fingernails. Apply scrub solution from the sponge side and work up an adequate lather on the skin.
   3. Scrub for 3 minutes as follows: With the brush side of the product scrub nails, cuticles and interdigital spaces. With sponge side, scrub the hands and forearms.
   4. Rinse thoroughly with warm water. **Repeat** the scrub using the sponge side only, for an additional 3 minutes. Add water as necessary to product eh desired level of suds.
   5. Discard the used product and rinse hands and arms thoroughly.
   6. Dry thoroughly.

3. See comment (3) under Container.

Please revise your labels and labeling, then prepare and submit twelve final printed container labels and carton labeling. Should further information become available relating to the safety and efficacy of this product, you may be asked to further revise your labeling prior to approval.

In addition to responding to these deficiencies, please note and acknowledge the following in your response:

A. We will request the FDA district laboratory to confirm the validity of your methods for analysis of the active ingredient and the finished product.

B. Approval of this application is contingent upon satisfactory Establishment Evaluation Reports for all referenced firms.

C. Please be advised that your bioequivalence study is currently under review. You will be informed of any deficiencies in a separate letter.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a major amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 10/21/97

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-416
ANDA #73-416/DUP/Division File
HFC-130/JAllen
HFD-600/Reading File

Chlorhexidine Gluconate Scrub Brush/Sponge 4%
ANDA 73-416

JUL 24 1995

Becton Dickinson Acute Care
Attention: George E. Nolan
9450 South State Street
Sandy UT 84070

Dear Mr. Nolan:

Reference is made to the our correspondence dated July 14, 1995, which referenced the bioequivalence study submitted on April 4, and May 7, 1993, for Chlorhexidine Gluconate Scrub Brush-Sponge 4%.

Please note that the April 4, 1993, date referenced in the July 14, 1995 letter was incorrect, the correct date should have been April 13, 1995.

If you have any questions, please call Jason A. Gross, Pharm.D., at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

/S/

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation
and Research

Chlorhexidine Gluconate Scrub Brush/Sponge 4%
ANDA 73-416

No Space Capitalized

Becton Dickinson AcuteCare

JUL 14 1995

~~Deseret Medical Inc.~~
Attention: ~~Charles J. Welle~~ George E Nolan
9450 South State Street
Sandy UT 84070

Dear Mr. Welle:

Reference is made to the bioequivalence study submitted on April ~~4~~ 13, and May 7, 1993, for Chlorhexidine Gluconate Scrub Brush-Sponge 4%.

The Office of Generic Drugs in consultation with the Division of Anti-Infective Drug Product, HFD-520, is in the process of reviewing the bioequivalence study and is unable to complete the review without the following information:

1. All treatment raw data records and calculations generated during the conduct of this study for the test and reference listed drug is required.

2. The raw data for validation of the neutralization studies that were performed for the test and control products used in this study is required. The data should include an analysis of the validation test results.

3. A list of all persons involved in performing or taking part in this study; copies of their resume; and a description of their function, is required. Also include the Institutional Review Board members, and their function at

4. The screening information records including the raw data used to screen subjects for inclusion in the study is required.

5. The Informed Consent records of all participants taking part in this study is required.

6. Please submit all records for test and reference listed drug tracking, this documentation should contain and quantify all relevant data, including but not limited to; the time products were shipped; administration to study subjects; and lost or contaminated samples: from the time the manufacturer shipped the product to the study facility to the current status of remaining samples. Also include a description regarding assurances that the correct products are tested, and the drug accountability SOP.

7. Please state whether the copies provided are actual copies of raw data sheets or are copies of other photocopies. If they are copies of other photocopies, then we will need to know why photocopies of original raw data sheets are not being provided.

As described under 21 CFR 314.96 an action which will amend this application is required, if you have any questions, please call Jason A. Gross, Pharm.D., at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

/S/

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation
and Research

ANDA 73-416

Becton Dickinson AcuteCare
Attention: George Nolan
9450 South State Street
Sandy, UT 84070

FEB 13 1996

Dear Sir:

This is in reference to your abbreviated new drug application dated August 28, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for E-Z Scrub (Chlorhexidine Gluconate, Scrub Brush/Sponge, 4%).

Reference is also made to your amendments dated May 30, and June 28, 1995.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies

B. Labeling Deficiencies

Container:

We note that there are discrepancies between your container label and carton labeling in the description of your product and in the WARNINGS section. Except for the revision to carton labeling requested below, please revise your container label to be consistent with your carton labeling.

Carton:

Revise to include the word "antiseptic" in your product labeling as seen in labeling of the listed drug.

Please revise your container labels and carton labeling, then prepare and submit final printed labeling. Should further information become available relating to the safety and efficacy of this product, you may be asked to further revise your labeling prior to approval.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. Your response to this letter will be considered a MINOR AMENDMENT and should be plainly marked as such in your cover letter. Please note that if the pending bioequivalence review is not received prior to completion of the chemistry and/or labeling review of your amendment, issuance of our subsequent action letter may be delayed. Further, if a major deficiency is cited in the bioequivalence review, the subsequent Not Approvable letter will request that the reply be declared a MAJOR AMENDMENT. You will

be notified in a separate letter of any deficiencies identified in the bioequivalence portion of your application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 11/12/96

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-416
ANDA #73-416/DUP/Division File
Field Copy
HFD-600/Reading File

Endorsements:

Not Approvable - Major

ANDA 73-416

MAY 28 1997

Becton Dickinson AcuteCare
Attention: George E. Nolan
9450 South State Street
Sandy UT 84070-3234

Dear Sir:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Chlorhexidine Gluconate Scrub-Brush/Sponge 4%.

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

/S/

for Nicholas Fleischer, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 73-416

U.S. Food and Drug Administration
Attention: Bill Sherer
HFR-SW250
6th and Kipling St.
Denver, CO 80225-0087

Dear Sir:

ANDA 73-416 has been submitted by Becton Dickinson AcuteCare for Chlorhexidine Gluconate, Scrub Brush/Sponge, 4%. The firm has submitted their regulatory methods. These proposed regulatory analytical methods should be validated by your laboratory as this subject drug product does not have a USP monograph.

As instructed under the PRE-APPROVAL INSPECTION/INVESTIGATIONS program (7346.832), you are requested to collect samples of the subject drug product including impurity reference standards (if any) from the applicant's laboratory at the address given below:

Becton Dickinson AcuteCare
9450 South State St.
Sandy, UT 84070

In addition, included is a copy of the methods validation package for this drug product as instructed in Part IV of the compliance program.

Upon completion of the District's portion of the methods validation, please send work sheets, all attachments, conclusions, and recommendations directly to the review chemist, Dr. Al Mueller at the Office of Generic Drugs, HFD-627, 7500 Standish Place, Rockville, MD 20855, within five days of completion.

Sincerely yours,

/S/ 2/22/96

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

Enclosure: Methods Validation Package

ANDA 73-416

Deseret Medical, Inc.
Attention: Mr. Charles Welle
9450 South State Street
Sandy, Utah 84070

FEB 18 1992

Dear Sir:

Please refer to your abbreviated new drug application dated August 28, 1989, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for E-Z Scrub (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%.

We also acknowledge your communications of March 5, 22, and 25, 1991 and September 10, 1991.

The application is deficient and not approvable under Section 505 of the Act for the following reasons:

You have failed to submit information which shows that the proposed drug is bioequivalent to the listed drug upon which the application relies. Each ANDA must be supported by its own bioequivalence study.

As stated in our letter of August 2, 1991, the regulations (21 CFR 314.101(e)(1) prohibit the filing of a submission for a drug product that is already the subject of an approved application. Your suggestion of referencing data contained in another application clearly supports the Agency's determination that the proposed product is the subject of a separate approved application.

Therefore, we ask that you withdraw this ANDA or provide the data based upon a product manufactured uniquely under this proposed ANDA, to include on your own bioequivalence studies and relevant stability data.

Please let us have your response promptly.

Sincerely yours,

/S/ for 2-18-92

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA #73-416
DUP/Division File
HFD-638/KShah
HFD-650/Dighe
HFD-320/Vogel
HFD-635/JHarrison/RAdams/2-8-92
HFD-632/RPollock/2-8-92
R/D initialed by GJohnston
bcw/2-7-92/73416not.app

GJohnston 2/17/92

not approvable

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070
801 565 2300
801 565 2351 Fax

BECTON DICKINSON

May 30, 1995

Also Refer to submission dated June 29, 1995 (Vol 4.1)

Food and Drug Administration
Division of Chemistry I
Office of Generic Drugs
Center for Drugs Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

RE: ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate 4% Scrub-Brush/Sponge)

Dear Gentlemen:

This letter is in response to the deficiencies listed in your November 2, 1993 letter (copy attached) concerning ANDA 73-416. It was noted that this response will be considered a major amendment.

The deficiencies will be answered as listed:

A. Chemistry Deficiencies

Redacted 1

pages of trade

secret and/or

confidential

commercial

information

Chem Deficiencies

B. Labeling Deficiencies

Questions about some of the listed deficiencies were discussed with the Agency and clarified. Letter and notes of these discussion are attached as Exhibit B-1.

Labels and labeling have been revised to read as suggested.
has requested changes; therefore copies of the print cards are attached as Exhibit B-2. Our supplies require orders in the impressions and lcng lead times to print unit labels (label on packaging film) and dispensers. Actual labels can be furnished when available.

In addition acknowledgement was requested for the following:

A. We will request the FDA district laboratory to confirm the validity of your methods for analysis of the active ingredient and the finished product.

We acknowledge that this will be requested. Methods for analysis of the active ingredient and the finished product are those required by NDA 18-423.
methods have been recommended for the USP Monograph and will be used when it is issued. Exhibit C.

B. Approval of this application is contingent upon Satisfactory Establishment Evaluation Reports for all referenced firms.

We acknowledge this requirement.

C. Please be advised that your bioequivalence study is currently under review. You will be informed of any deficiencies in a separate letter.

We acknowledge this and inform you that no letter has been received. What is the status of the study review?

As stated in the submissions and amendments the purpose of this ANDA is to let operate its packaging and testing without oversight, making us responsible for our own operation. has been manufacturing and marketing this product for many years with oversight.

Sincerely,
BECTON DICKINSON ACUTCARE, SANDY

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager

/gn

cc: ANDA 73-416
Bill Russell (FDA)

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070
(801) 565-2300
FAX (801) 565-2316

BECTON DICKINSON

30 May 1995

William A. Russell Jr.
Office of Generic Drugs
Metro Park North 2
7550 Standish Place
Room 150
Rockville, Maryland 20855-2773

RE: ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%

Dear Bill:

In response your telephone message of 30 May 1995 I'm sending the ANDA 73-416 response directly to you.

Enclosed are three copies of the response and three copies of the Methods/Validation that were requested.

We trust this will fulfill all requirements; please address any correspondence to the undersigned.

/gn

Sincerely,
BECTON DICKINSON ACUTECARE, SANDY

George E Nolan

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager
Scrub Operations

/gn

RECEIVED
JUN 02 1995
GENERIC DRUGS

cc: ANDA 73-416

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2318 (Fax)

BECTON DICKINSON

August 28, 1995

Food and Drug Administration
Keith K. Chan, Ph.D.
Division of Bioequivalence
Office of Generic Drugs
Center for Drugs Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

RE: ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate 4% Scrub-Brush/Sponge)

Dear Dr. Chan:

This is in response to your letter of 14 July 1995 requesting additional information to complete the review of the bioequivalence study for Chlorhexidine Gluconate Scrub Brush-Sponge 4%.

The items requested are as follows:

1. All treatment raw data records and calculation generated during the conduct of this study for the test and reference listed drug is required.

   This information had previously been submitted and is attached (Attachment #1) for review.

2. The raw data for validation of the neutralization studies that were performed for the test and control products used in this study is required. The data should include an analysis of the validation test results.

   In Attachment #2 are copies of the raw data for the neutralization study validation and pages 7, 8, 23,24, and 25 of the report previously sent that gives the analysis. The report and data were reviewed by Becton Dickinson microbiologists and found to be reasonable and effective.

3. A list of all person involved in performing or taking part is this study; copies of their resume; and a description of their function, is required. Also include the Institutional Review Board members, and their function at

   Attachment #3 contains the list of persons involved and copies of their resume as requested. Institutional Review Board information also included.

4. The screening information records including the raw data used to screen subjects for inclusion in the study is required.

   Attachment #4 is copies of the Baseline evaluation testing data.

5. The Informed Consent records of all participants taking part in this study is required.

   Attachment #5 has copies of the Informed Consent records.

6. Please submit all records for test and reference listed drug, this documentation should contain and quantify all relevant data, including but not limited to; the time products were shipped; administration to study subject; and lost or contaminated samples; from the time the manufacturer shipped the product to the study facility to the current status of remaining samples. Also include a description regarding assurance that the correct products are tested, and the drug accountability SOP.

One case (10 dispensers of 30 units; total 300) each of Test Product No. 1, Test Product No. 2 and Control Product were shipped on 10/16/92 to for use with Protocol 920402. Units not used in the study have been returned to and are in retain sample storage. did not provide a drug accountability SOP. The OTC drug product used in this study is 4% CHG (Hibiclens®). Records are in Attachment #6.

7. Please state whether the copies provided are actual copies of raw data sheets or are copies of other photocopies. If they are copies of other photocopies, then we will need to know why photocopies of original raw data sheets are not being provided.

Copies provided are actual copies of the raw data sheets.

As stated in the submissions and amendments the purpose of this ANDA is to let operate its packaging and testing without oversight, making us responsible for our own operation. has been manufacturing and marketing this product for many years with oversight.

This information should provide what is required to complete the review of ANDA 73-416.

Sincerely,
BECTON DICKINSON ACUTECARE, SANDY

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager

/gn

cc: ANDA 73-416
Bill Russell (FDA)
Jason A. Gross, Pharm.D (FDA)
FDA, Denver Office

Becton Dickinson Surgical Systems
9450 South State Street
Sandy, Utah 84070-3224
(801) 565-2300
(801) 565-2430 Fax

BECTON DICKINSON

9 February 1999

Joseph M. Buccine
Senior Regulatory Manager
Office of Generic Drugs
Center for Drug Evaluation and Research
HFD-570 Room 10B45
Parklawn
5600 Fishers Lane
Rockville, MD 20857

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4% PHONE AMENDMENT**

Dear Mr. Buccine:

This AMENDMENT is in response to our telephone conversation of 9 February 1999. You indicated that this PHONE AMENDMENT should be faxed to 301-594-0180.

Becton Dickinson requests withdrawal for the sites from the application ANADA 73-416. The two sites for the application are:

Becton Dickinson
9450 South State Street
Sandy, Utah 84070

Please allow us the opportunity to meet with you to clarify any questions or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan

George Nolan
QA/RA Manager
BDD, Sandy

Becton Dickinson Surgical Systems
9450 South State Street
Sandy, Utah 84070-3224
(801) 565-2300
(801) 565-2430 Fax

BIOAVAILABILITY

BECTON DICKINSON

25 January 1999

Robert D. Tollefsen
US Food & Drug Administration
22201 – 23rd Dr SE
Bothell, WA 98021

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%** **UNSOLICITED AMENDMENT**

Dear Mr. Tollefsen:

This AMENDMENT is in response to the request for samples dated 13 January 1999 (copy attached). You indicated that if a batch not in the ANDA is used, the batch record and Certificate of Analysis must be submitted as an UNSOLICITED AMENDMENT to the application; this is the route being taken.

You requested:

* Sufficient units of sample (drug substance and dosage form) for all tests requested on the attached form 2871, plus some additional units for reserve.

90 units of bioequivalence test product (E-Z SCRUB® 106 lot # 02122234E Expiration date: 8/94) are being sent. The retained/reserve sample of the bulk solution [Part Number P0021 Lot # 170686 (Supplier Lot # 0981M)] to manufacture these units is no longer available as they were packaged August 1992. THIS PRODUCT EXPIRED 8/94.

90 units of bioequivalence control product (E-Z SCRUB® 106 lot # 02122227H Expiration date: 8/94) are being sent. The retained/reserve sample of the bulk solution [Part Number P0021] to manufacture these units is no longer available as they were packaged August 1992. THIS PRODUCT EXPIRED 8/94.

90 units of 371065 E-Z SCRUB® 106 lot # 981204 Expiration date: 2000-12. Certificate of Analysis and the batch record are enclosed as Attachment #1.

mls of the bulk solution (Lot # 2919A) to used in 371065 E-Z SCRUB® 106 lot # 981204.

RECEIVED

JUL 27 1999

GENERIC DRUGS

1-29-99

* A copy of the test methods and specifications.

Copies of each of the methods to do methods validation are enclosed as Attachment #2. These are the Specifications/Methods for New Drug Substance(s) and for Finished Dosage Form(s) requested.

Copy of EZ SCRUB® 106-5 Acceptance Form and Task document E-Z SCRUB® 106 WITH HIBICLENS® RELEASE REQURIEMENTS which is our Statement of Composition of Finished Dosage Form(s) requested. Attachment #3.

Supporting Data for Accuracy, Specificity, etc. is the methods validation in Attachment #4.

* A copy of your worksheet for the analysis of the same lot with calculations, results and associated spectra and chromatograms.

Applicant's Test Results on NDS and Dosage Forms are in Attachment #5.

* Non-compendial reference standards that are needed to test the sample, including impurity and related compound standards. A non-compendial reference standard is one that is not available from the USP.

The non-compendial reference standards needed to test the sample are enclosed. These are for CHG and PCA.

One 5 gram bottle of Chlorhexidine diacetate standard 98%, lot# 11121

One 5 gram bottle of standard 98%, lot# 12312

* For new or unusual chemical compounds, safety or handling information that would be important in their laboratory use.

No new or unusual chemical compounds.

* In addition, in connection with other work that needs to be completed regarding your application, please include in your sample package a letter indicating whether an in-vivo or in-vitro bioequivalence study was performed. If so please provide the facility name and address. If no study was done, include a letter so stating nevertheless.

The Division of Bioequivalence reviewed the in-vivo bioequivalence study that was done and a copy of their response is in Attachment #6. This study was done at

This is the letter indicating status of the study.

Please allow us the opportunity to meet with you to clarify any questions or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan

George Nolan
QA/RA Manager
BDD, Sandy

Cc: M. Halladay – BD
J. Buccine – FDA HFD-570
Document and Records Section

CELEBRATING THE FIRST ONE HUNDRED: 1897-1997

BECTON DICKINSON

Becton Dickinson Division
9450 South State Street
Sandy, Utah 84070 3234
Telephone: (801) 565-2300
Fax: (801) 565-2430

22 December 1998

Joseph M. Buccine
Senior Regulatory Manager
Office of Generic Drugs
Center for Drug Evaluation and Research
HFD-570 Room 10B45
Parklawn
5600 Fishers Lane
Rockville, MD 20857

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%** **TELEPHONE AMENDMENT**

Dear Joe:

This TELEPHONE AMENDMENT is in response to the inquiries identified during telephone conversation of 22 December 1998, for ANDA 73-416 dated August 28, 1989. You indicated that this response would be considered a PHONE AMENDMENT.

This product has been on the market for over ten years and it is not being changed, what is changing is a business relationship. This is the product approved under Zeneca NDA 18-423.

You requested clarification on procedures and with procedures We are reviewing and revising, as needed, laboratory procedures; this has occurred with these documents.

Analysis of % Isopropyl Alcohol in Hibiclens Bulk Solution
Analysis of % Isopropyl Alcohol in Hibiclens Sponge-Brush by

Microbiological Evaluation of Hibiclens Bulk Solution and Sponge Brushes
Microbial Limit Analysis of Chlorhexidine Gluconate (CHG) E-Z SCRUB®

were combined into one document – % Isopropyl Alcohol in Hibiclens® Bulk Solution and Sponge/Brush was deleted from the system.)

were combined into one document – Microbial Limit Analysis of Chlorhexidine Gluconate (CHG) E-Z SCRUB®. was deleted from the system.)

You also inquired about lot sizes for the following lots:

02122234E normal production lot size of Cat. No. 371065 with Hibiclens® units packaged August 1992.

M7BX021 experimental lot size of Cat. No. 377479 3900 units packaged February 1987 as an extension of lot M7AS036 production lot size units.

M7BL880 normal production lot size of Cat. No. 371063 with Hibiclens® units packaged February 1987.

ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Bursh\Sponge, is for a product packaged and controlled by Becton Dickinson Division (BDD) [formerly Becton Dickinson AcuteCare Division and before that Deseret Medical] using the bulk HIBICLENS® solution obtained from It is the same product marketed for well over 10 years under NDA 18-423. When this application is approved it will let BDD operate its packaging and testing, making us responsible for our own operation and provide a vehicle for communicating any future changes, stability data, distribution data and so forth to the Agency.

Please allow us the opportunity to meet with you to clarify any questions or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan
QA/RA Manager
BDD, Sandy

Cc: M. Halladay – BD

CELEBRATING THE FIRST ONE HUNDRED: 1897-1997

BECTON DICKINSON

Becton Dickinson Division
9450 South State Street
Sandy, Utah 84070-3234
Telephone: (801) 565-2300
Fax: (801) 565-2430

5 October 1998

ORIG AMENDMENT
N/A

Rashmikant M. Patel, Ph.D.
Director / Supervisory Chemist
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
HFD-620 Room 204
Metro Park North 2
7500 Standish Place
Rockville, MD 20855-2773

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%** **MINOR AMENDMENT**

Dear Dr. Patel:

This MINOR AMENDMENT is in response to the deficiencies identified in the not approvable faxed document (copy attached) of March 13, 1998, for ANDA 73-416 dated August 28, 1989. It was indicated that this response will be considered a MINOR AMENDMENT unless a major deficiency was cited in the bioequivalence review. The letter (copy attached) received May 28, 1997 from the Division of Bioequivalence stated; "The Division of Bioequivalence has completed its review and has no further questions at this time."

The response to the minor deficiencies is as follows:

A. Chemistry Deficiencies:

OCT 13 1998

GENERIC DRUGS

Redacted 3

pages of trade

secret and/or

confidential

commercial

information

Chem Deficiencies

B. Labeling Deficiencies:

1. CONTAINER (Unit)

a. General Comment

Revise to include the established name, in alphabetical order, of **EACH** inactive ingredient contained in your product. (Please see Section 412 of Title IV of the FDA Modernization Act of 1997).

Revision has been made. (See attachment 5).

b. Principal display panel

i. "Antiseptic" rather than 'antispectic" (spelling)

ii. Revise the storage temperature range to read, "...15-30° C (59-86°F)." (Delete "[See USP]")

Revision has been made. (See attachment 5).

c. Directions for Use

Revise to combine the first two sentences of Direction #2 so that it appears as: Use nail cleaner and then apply...

Revision has been made. (See attachment 5).

2. CARTON (Dispenser)

a. See CONTAINER comments.

Revision has been made. (See attachment 5).

b. WARNINGS

Revise the fifth sentence to read,
IF THIS PRODUCT SHOULD...

Revision has been made. (See attachment 5).

Please revise your labels and labeling, as instructed above, and submit in final print.

Revision has been made. (See attachment 5).

ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Bursh\Sponge, is for a product packaged and controlled by Becton Dickinson Division (BDD) [formerly Becton Dickinson AcuteCare Division and before that Deseret Medical] using the bulk HIBICLENS® solution obtained from It is the same product marketed for years under NDA 18-423. When this application is approved it will let BDD operate its packaging and testing without oversight, making us responsible for our own operation and provide a vehicle for communicating any future changes, stability data, distribution data and so forth to the Agency. What is changing is a business relationship, not the product. Becton Dickinson had thought that approval would quickly be granted because it is exactly the same product approved under NDA 18-423 [it may be clearer to state that it is the product approved under NDA 18-423].

Please allow us the opportunity to meet with you to clarify any questions or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan
QA/RA Manager
BDD, Sandy

Cc: M. Halladay - BD
J. Buccine – FDA HFD-570

Becton Dickinson Surgical Systems
9450 South State Street
Sandy, Utah 84070-3224
(801) 565-2300
(801) 565-2430 Fax

BECTON DICKINSON

19 April 1999

Janet Burke
US Food & Drug Administration
22201 – 23rd Dr SE
Bothell, WA 98021

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%** **TELEPHONE AMENDMENT**

Dear Dr. Burke:

This TELEPHONE AMENDMENT is in response to the deficiencies identified during telephone conversation with you, Janet Burke, FDA Chemist, on 15 April 1999, for ANDA 73-416 UNSOLICITED AMENDMENT of 25 January 1999.

The response to the minor deficiencies is as follows:

Chemistry Deficiencies:

This section is clarified to indicate the consideration for specific gravity.

Thank you for allowing us the opportunity to clarify these questions and vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan
QA/RA Manager
BDD, Sandy

Cc: M. Halladay – BD
J. Buccine – FDA HFD-570
P. Schwartz, Ph.D.
Document Center

BD Medical Systems
9450 South State Street
Sandy, Utah 84070
tel: 801.565.2300
fax: 801.565.2740
www.bd.com

BD

Indispensable to human health

13 January 2000

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA ORIG AMENDMENT
N/A 1

Bonnie McNeal
Project Manager

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4% MINOR AMENDMENT**

Dear Ms McNeal:

This AMENDMENT is in response to the your facsimile of October 22, 1999 [copy attached], which indicated a CMC deficiency only. The designation for this response is that it is a MINOR AMENDMENT.

The deficiency identified by Rashmikant M. Patel, Ph.D. is as follows:

A. Deficiency:

DMF for Chlorhexidine Gluconate 20% solution, as referenced in NDA 18-423 for Chlorhexidine Gluconate 4% w/v is inadequate. The DMF holder has been notified of the deficiencies. Please do not respond to this letter until you have obtained a letter from the DMF holder stating that the DMF deficiencies have been satisfactorily resolved.

Attached is a letter from indicating that the DMF amendment addressing the deficiencies was submitted to the agency December 20, 1999.

B. In addition to responding to the deficiency presented above, please note and acknowledge the following comment in your response.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JAN 18 2000
OGD

Firms referenced in this ANDA and
manufacturer of Chlorhexidine Gluconate 20% solution, should be in compliance with current good manufacturing practices at the time of approval.

Attached is a letter from indicating the current good manufacturing practices compliance of Becton Dickinson Surgical Systems, Sandy, Utah has corrected observations identified by the agency and is in compliance with current good manufacturing practices.

Please allow us the opportunity to meet with you to clarify any questions or vague areas as to aid in the rapid review and approval of this ANDA.

Please note in your files that the Becton Dickinson contact person for ANDA 73-416 is now Jane Stickel, Director,Regulatory Affairs, BD Medical Systems, Sandy Utah as Mr. George Nolan has retired.

Sincerely,

Jane Stickel

Jane Stickel
Director, Regulatory Affairs

R. Beck – BD
J. Buccine – FDA HFD-570
B. McNeal – FDA HFD-623
Rashmikant M. Patel, Ph.D. - FDA HFD-620 Room 204

Becton Dickinson Surgical Systems
9450 South State Street
Sandy, Utah 84070-3224
(801) 565-2300
(801) 565-2430 Fax

BECTON DICKINSON

25 June 1999

FDA ORIG AMENDMENT
N/AM

Paul Schwartz, Ph.D.
Team Leader
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
HFD-629 Room 204
Metro Park North 2
7500 Standish Place
Rockville, MD 20855-2773

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%**
TELEPHONE AMENDMENT

Dear Dr. Schwartz:

This TELEPHONE AMENDMENT is in response to the deficiencies discussed during telephone conversations with you 6/12/99 and Joe Buccine 6/23/99.

This information was previously sent 4/19/99:

> This TELEPHONE AMENDMENT is in response to the deficiencies identified during telephone conversation with, Janet Burke, FDA Chemist, on 15 April 1999, for ANDA 73-416 UNSOLICITED AMENDMENT of 25 January 1999.
>
> "The response to the minor deficiencies is as follows:
>
> **A. Chemistry Deficiencies:**
>
> **Chemists agree; they will test and validate the change than revise this section of the procedure."**

After receiving your phone call I discussed this with the chemists and was told that testing results confirm that either methods works. The current method has been used for some years now and they wanted to generate more data before changing a method that works.

The procedure has been revised [copy attached] to make the pH adjust for DI water (section 8.1) rather in the organic phase as recommended by Janet Burke, FDA Chemist.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUL 02 1999
OGD

Sincerely,

George Nolan

George Nolan
QA/RA Manager
BDD, Sandy

Cc: M. Halladay – BD
J. Buccine – FDA HFD-570

BD Medical Systems
9450 South State Street
Sandy, Utah 84070
tel: 801.565.2300
fax: 801.565.2740
www.bd.com

NEW CORRESP
NC

8 March 2000

BD
Indispensable to human health

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Pat M. Beers Block
Supervisor Consumer Safety

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%**

Dear Ms Beers Block:

This is in response to the your telephone request of March 3, 2000 and March 6, 2000 which indicated the need for Form FDA 356h for June 25, 1999, January 13, 2000 and February 22, 2000 submissions for ANDA 73-416. The request to has been made for an updated Authorization Letter for access to their NDA 18-423 and DMF

Sincerely,

Jane Stickel
Director, Regulatory Affairs
Becton Dickinson, Sandy, Utah

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAR 09 2000
OGD

BD Medical Systems
9450 South State Street
Sandy, Utah 84070
tel: 801.565.2300
fax: 801.565.2740
www.bd.com

NDA ORIG AMENDMENT
N/Am

BD
Indispensable to human health

22 February, 2000

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Elaine J. Hu
Assistant Regulator

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4% TELEPHONE AMENDMENT**

Dear Ms Hu:

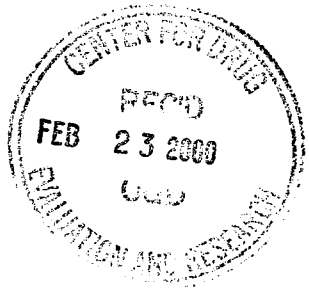
This TELEPHONE AMENDMENT is in response to the request for Debarment Certification during the telephone conversation of 22 February 2000, for ANDA 73-416 dated August 28, 1989. This response is a PHONE AMENDMENT.

This product has been on the market for over ten years and it is not being changed, what is changing is a business relationship. This is the product approved under Zeneca NDA 18-423. The application was submitted August 28, 1989 before the Generic Drug Enforcement Act of 1992 (GDEA) became effective; therefore, the Debarment Certification had not previously been sent.

Sincerely,

Jane Stickel

Jane Stickel
Director Regulatory Affairs
Becton Dickinson, Sandy, Utah



AstraZeneca

COPY 1

SENT VIA UNITED PARCEL SERVICE

MAR 13 2000

NEW CORRESP
NC

Ms. Patricia Beers-Block
Supervisor, Consumer Safety
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 640, Room No. E-260
1Metro Park North II
7500 Standish Place
Rockville, MD 20855

73-416

Dear Ms. Beers-Block:

Re: HIBICLENS® (chlorhexidine gluconate) Sponge Brush
NDA 18-423

We hereby authorize the Food and Drug Administration to refer to NDA 18-423, for HIBICLENS® (chlorhexidine gluconate) Sponge Brush, in support of Abbreviated New Drug Application 73-416 submitted by or on behalf of:

Becton Dickinson Surgical Systems
9450 South State St.
Sandy, Utah 84070-3224

We hereby certify that the methods used in, and the facilities used for, the mixing, processing, and packaging of HIBICLENS Sponge Brush, NDA 18-423, conform with the Good Manufacturing Practices and are in accordance with the 21 CFR, Parts 210 and 211, of the regulation.

The information submitted herein is considered confidential and is provided for exclusive reference use by your Agency, with respect to Becton Dickinson Surgical Systems' application only.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAR 14 2000
OGD

AstraZeneca A Business Unit of Zeneca Inc.
1800 Concord Pike PO Box 15437 Wilmington DE 19850-5437
Tel 302 886 3000
www.astrazeneca-us.com

Please do not hesitate to contact me if further information or clarification is necessary.

Sincerely,

Carol Stinson Fisher

Carol Stinson-Fisher
Technical Regulatory Associate
Regulatory Affairs Department
(302) 886-8074
(302) 886-2822 (fax)

CSF/jr

cc: Mr. George Nolan
Quality Assurance/Regulatory Affairs Manager
Beckton Dickinson Surgical Systems
9450 South State St.
Sandy, UT 84070-3224

Becton Dickinson Surgical Systems
9450 South State Street
Sandy, Utah 84070-3224
(801) 565-2300
(801) 565-2430 Fax

BECTON DICKINSON

15 January 1998

Rashmikant M. Patel, Ph.D.
Director / Supervisory Chemist
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
HFD-620 Room 204
Metro Park North 2
7500 Standish Place
Rockville, MD 20855-2773

RE: **ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%** **MINOR AMENDMENT**

Dear Dr. Patel:

This MINOR AMENDMENT is in response to the deficiencies identified in the not approvable letter (copy attached) of February 13, 1996, for ANDA 73-416 dated August 28, 1989. Your letter indicated that this response will be considered a MINOR AMENDMENT unless a major deficiency was cited in the bioequivalence review. The letter (copy attached) received May 28, 1997 from the Division of Bioequivalence stated; "The Division of Bioequivalence has completed its review and has no further questions at this time."

The response to the deficiencies are as follows:

A. Chemistry Deficiencies:

Redacted 1

pages of trade

secret and/or

confidential

commercial

information

Chem. Deficiencies

B. Labeling Deficiencies

Container: (Unit)

We note that there are discrepancies between container your label and carton labeling in the description of your product and in the WARNINGS section. Except for the revision to carton labeling requested below, please revise your container label to be consistent with your carton.

Print card for the revised label to make it consistent with the carton label is attached for your review and comment. Attachment #6.

Carton: (Dispenser)

Revise to include the word "antiseptic" in your product labeling as seen in labeling of the listed drug.

Print card for the revised label is attached for your review and comment. Attachment #7.

ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Bursh\Sponge, is for a product packaged and controlled by Becton Dickinson Division (BDD) [formerly Becton Dickinson AcuteCare Division and before that Deseret Medical] using the bulk HIBICLENS® solution obtained from It is the same product marketed for years under NDA 18-423. When this application is approved it will let BDD operate its packaging and testing without oversight, making us responsible for our own operation and provide a vehicle for communicating any future changes, stability data, distribution data and so forth to the Agency. What is changing is a business relationship, not the product. BDD had thought that approval would quickly be granted because it is exactly the same product approved under NDA 18-423 [it may be clearer to state that it is the product approved under NDA 18-423].

Please allow us the opportunity to meet with you to clarify any questions or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan
QA/RA Manager
BDD, Sandy

cc: ANDA73-416
M. Halladay

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070
(801) 565-2300
(801) 565-2740 Fax

ORIG NEW CORR

BECTON DICKINSON

Patel / Nai - AMW
4/1/96

27 March 1996

RECEIVED

APR 0 1 1996

GENERIC DRUGS

Rashmikant M. Patel, PhD
Office of Generic Drugs
Metro Park North 2
7550 Standish Place
Room 204 HFD-620
Rockville, Maryland 20855-2773

RE: ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%

Dear Dr. Patel:

Your letter of Feb 13, 1996 in reference to ANDA 73-416 indicates '...pending bioequivalence...', this is of concern to us. The bioequivalence study for AND 73-416 was sent to the agency in May, 1993 and additional information as requested in August, 1995 (Referred question to Mark Cinderella - AMW)

Item C. on the last page of the Nov 2, 1993 letter from the agency stated - ["Please be advised that your bioequivalence study is currently under review. You will be informed of any deficiencies in a separate letter."] What is the status of the review? No letter has been received about the review of the bioequivalence study. (Recommended firm contact John Grace on this issue - AMW)

August 2, 1991 letter from Robert A. Jerussi, Division of Chemistry II, Office of Generic Drugs, questioned the use of the "antiseptic" in the label and we thought our revisions had been as directed by the agency.

ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Brush/Sponge, is for a product packaged and controlled by Becton Dickinson Division

[BDD] (formerly Becton Dickinson AcuteCare Division and before that Deseret Medical before) using the Bulk HIBICLENS solution obtained from It is the same product marketed for years under NDA 18-423 by permission of Zeneca (Stuart) Pharmaceutical. When approved this application would do two things: (1) let BDD (Deseret) operate its packaging and testing without oversight, making us responsible for our own operation and (2) provide a vehicle for communicating any future changes, stability data, distribution data and so forth to Generic Drugs. What is changing is a business relationship, not the product.

/gn

Sincerely,
BECTON DICKINSON DIVISION, SANDY

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager

/gn

cc: ANDA 73-416
A. Weikel (FDA)
M. Halladay
T. Hutchinson

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070
(801) 565-2300
(801) 565-2740 Fax

BECTON DICKINSON

27 November 1995

NEW CORRESP
NC

William A. Russell Jr.
Office of Generic Drugs
Metro Park North 2
7550 Standish Place
Room 150
Rockville, Maryland 20855-2773

RE: ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%

Dear Mr. Russell:

What is the status of ANDA 73-416? Our last response was sent the end of August 1995 and we would like to know the status of the review.

/gn

Sincerely,
BECTON DICKINSON ACUTECARE, SANDY

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager
Scrub Operations

/gn

cc: ANDA 73-416

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070
(801) 565-2300
(801) 565-2740 Fax

4/24/95

BECTON DICKINSON

24 April 1995

Noted - Am Waited
5/5/95

William A. Russell Jr.
Office of Generic Drugs
Metro Park North 2
7550 Standish Place
Room 150
Rockville, Maryland 20855-2773

NEW CORRES

RE: ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%

Dear Bill:

In response to our telephone conversation of 20 April 1995 this letter to indicate that Becton Dickinson AcuteCare will respond to the Nov 2, 1993 letter concerning ANDA 73-416 by May 31, 1995.

The loss of personnel here at BDAC has contributed to the delay in the response.

Item C. on the last page of the Nov 2, 1993 letter ["Please be advised that your bioequivalence study is currently under review. You will be informed of any deficiencies in a separate letter."] also contributed to the delay in the response.

/gn

Sincerely,
BECTON DICKINSON ACUTECARE, SANDY

George Nolan

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager
Scrub Operations

/gn

RECEIVED
APR 25 1995
GENERIC DRUGS

cc: ANDA 73-416

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2818 (Fax)

BECTON DICKINSON

May 18, 1993

NEW CORRESP

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

BIOAVAILABILITY

RE: **ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%**

Dear Dr. Williams:

In response to a telephone conversation with Margo L Bennett on 18 May 1993 this dupiculate copy of bioequivalence studies and stability data for the referenced application is being submitted.

This abbreviated new drug application dated August 28, 1989, ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Brush/Sponge, will do two things: (1) let BDAC operate its packaging and testing without oversight, making us responsible for our own operation and (2) provide a vehicle for communicating any future changes, stability data, distribution data and so forth to Generic Drugs. What is changing is a business relationship, not the product.

Enclosed is the Final Report #920402 **"Single Blind Surgical Handscrub Evaluation (Glove Juice) of Two Test Products and One Standard Control Product"** and a five month stability study.

We would like the opportunity to clarify any question or areas thought to be vague as to aid in the rapid review and approval of this ANDA.

Sincerely,

RECEIVED
MAY 20 1993
GENERIC DRUGS

RECEIVED
MAY 13 1993
GENERIC DRUGS

George E. Nolan
Manager
Quality Assurance/Regulatory Affairs
Becton Dickinson AcuteCare, Sandy

DUPLICATE

3.1

Noted
9P 9-8-94
Copy sent to HFD-82

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2818 (Fax)

BECTON DICKINSON

July 28, 1993

Department of Health and Human Services
Food and Drug Administration
Center for Drugs and Biologics
Document Control Section
Room 17B30
5600 Fishers Lane
Rockville, MD 20857

NEW CORRESP

RE: ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%

Gentlemen:

Herewith we are forwarding in duplicate the orginal FORM FDA 356h as requested. An updated copy showing NAME OF APPLICANT change is also enclosed.

We take this opportunity to inform you that Deseret Medical, Inc., has changed its name to Becton Dickinson Vascular Access. And the name of the sponsor for ANDA 73-416 from Deseret Medical, Inc. to Becton Dickinson AcuteCare.

Becton Dickinson Vascular Access and Becton Dickinson AcuteCare are both divisions of Becton Dickinson and Company and are both located at:

9450 South State Street
Sandy, Utah 84070

We trust report will satisfy all the requirements.

Sincerely,
BECTON DICKINSON ACUTCARE, SANDY

George Nolan

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager
Scrub Operations

/gn

RECEIVED
AUG 05 1993
GENERIC DRUGS

Sept 94
Pending

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2818 (Fax)

Branch Chief Notified of this NC JP 9-8-94

BECTON DICKINSON

NEW CORRESP
NC

August 29, 1994

Doug Sporn, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

RE: **ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%**

Dear Dr. Sporn:

Becton Dickinson AcuteCare (BDAC) has ANDA 73-416 for a surgical scrub rush/sponge that is impregnated with 4% Chlorhexidine Gluconate (CHG).

BDAC is considering putting the same 4% CHG into a bottle dispenser. Can a supplement to ANDA 73-416, using the Glove Juice and other testing in it, be used to market this product? If not what would the requirements be?

/gn

Sincerely,

George E. Nolan

George E. Nolan
Manager
Quality Assurance/Regulatory Affairs
Becton Dickinson AcuteCare, Sandy

/gn

cc: ANDA 73-416
John Dawson (FDA)

RECEIVED
SEP 2 1994
GENERIC DRUGS

ORIGINAL

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070
(801) 565-2300
(801) 565-2740 Fax

BECTON DICKINSON

June 28, 1995

Food and Drug Administration
Division of Chemistry I
Office of Generic Drugs
Center for Drugs Evaluation and Research
5600 Fishers Lane
Rockville, MD 20857

NEW CORRESP
N/C

To be reviewed in association with firm's 5/30/95 Major amendment
Russell 7/6/95

RE: ANDA 73-416, E-Z SCRUB® (Chlorhexidine Gluconate 4% Scrub-Brush/Sponge)

Dear Gentlemen:

I apologize for the inconvenience that this may cause but it was recently discovered that incorrect print cards were sent to you with the June 1, 1995, letter that was in response to the deficiencies listed in your November 2, 1993 letter (copy attached) concerning ANDA 73-416. It was noted that response would be considered a major amendment.

Copies of the correct print cards are enclosed.

B. Labeling Deficiencies

Labels and labeling have been revised to read as suggested. has requested changes; therefore copies of the print cards are attached as Exhibit B-2. Our supplies require orders in the impressions and long lead times to print unit labels (label on packaging film) and dispensers. Actual labels can be furnished when available.

As stated in the submissions and amendments the purpose of this ANDA is to let BDAC operate its packaging and testing without oversight, making us responsible for our own operation. BDAC has been manufacturing and marketing this product for many years with oversight.

Sincerely,
BECTON DICKINSON ACUTECARE, SANDY

George E. Nolan

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager

/gn

cc: ANDA 73-416

RECEIVED
JUN 29 1995
GENERIC DRUGS

Bill Russell (FDA)

cc Final 6/6

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2818 (Fax)

BECTON DICKINSON

April 13, 1993

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

MAR 10 4 20 93
NEW CORRESP

BIOAVAILABILITY

RE: **ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%**

Dear Dr. Williams:

In response to your letter of March 24, 1993, (copy attached) we are pursuing this Abbreviated New Drug Application. You did not list our correspondence of October 22, 1992; therefore, a copy is being sent.

A five month stability study has been completed and the report is being written. This data will be sent to you.

Sincerely,

George E. Nolan

George E. Nolan
Manager
Quality ASsurance/Regulatory Affairs
Becton Dickinson AcuteCare, Sandy

/gn

cc: ANDA 73-416
Kent Johnson (FDA)

RECEIVED
APR 16 1993
GENERIC DRUGS

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2818 (Fax)

BECTON DICKINSON

N-000/Ac
NDA ORIG AMENDMENT

May 7, 1993

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

BIOAVAILABILITY

RECEIVED
MAY 1 3 1993
GENERIC DRUGS

RE: **ANDA 73-416, E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush/Sponge) 4%**

Dear Dr. Williams:

In response to your letter of February 18, 1992, (copy attached) we are providing the data based upon a product manufactured uniquely under this proposed ANDA, to include our own bioequivalence studies and stability data.

This abbreviated new drug application dated August 28, 1989, was submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for E-Z SCRUB (Chlorhexidine Gluconate Scrub-Brush / Sponge) 4%.

ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Brush/Sponge, is for a product packaged and controlled by Becton Dickinson AcuteCare (BDAC) using the Bulk HIBICLENS solution obtained from It is the same product marketed for several years under NDA 18-423 by permission of When approved this application would do two things: (1) let BDAC operate its packaging and testing without oversight, making us responsible for our own operation and (2) provide a vehicle for communicating any future changes, stability data, distribution data and so forth to Generic Drugs. What is changing is a business relationship, not the product.

Enclosed is the Final Report #920402 **"Single Blind Surgical Handscrub Evaluation (Glove Juice) of Two Test Products and One Standard Control Product".** Each of the product configurations, 106 Test, 106 (Test Product #2 - packaged with a E-Z SCRUB 160 label and overlabeled as a 106), and 106 Control, demonstrated

effective antimicrobial activity. In comparison, the 106 Test and the 106 products achieved equivalent efficacy to the 106 Control Product.

A five month stability study has been completed and the report is included. This study indicates that no significant difference exists between the Control Hibiclens (Foil Film package) samples, Lot #02233337H, and the Test Hibiclens (Foil Film package) samples, lot #02122234E, with respect to percent Chlorhexidine Gluconate (CHG), pH values and concentrations.

The Test Hibiclens package samples exhibits similar results to Control for pH and values. The values for percent CHG for room temperature test are not significantly different. Accelerated aging indicate an increase in percent CHG for the package, due to moisture loss.

We would like the opportunity to clarify any question or areas thought to be vague as to aid in the rapid review and approval of this ANDA.

Sincerely,

George E. Nolan

George E. Nolan
Manager
Quality Assurance/Regulatory Affairs
Becton Dickinson AcuteCare, Sandy

/gn

cc: ANDA 73-416
Desk copy to:
Al Sheldon (FDA)
Kent Johnson (FDA)

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2818 (Fax)

BECTON DICKINSON

March 31, 1992

Kent T. Johnson
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville, MD 20857

RE: ANDA 73-416

Dear Mr. Johnson:

I tried telephoning you (301-443-4080) but was unable to reach anyone. Chuck Welle, Dr. M. Khan, Dennis Lamb and I spoke with you on a conference called March 5, 1992, about what Becton Dickinson AcuteCare can do to make ANDA 73-416 approveable.

You gave us suggestions on bioequivalence and stability that we are formulated in a proposal to you. An additional issue here has delayed that letter.

What effect would changing the packaging from
have on the ANDA 73-416? Should we included it in the proposal or would it be better to wait and make that change as a supplement once approval is received?

Sincerely,

George E. Nolan

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager
BDAC, Sandy

/gn

consult ORIGINAL 3.1

Becton Dickinson and Company
One Becton Drive
Franklin Lakes, New Jersey 07417-1880

(201) 848-6800

BECTON DICKINSON

May 19, 1992

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

ORIG NEW CORRES 1

RE: ANDA 73-416, 4% CHLORHEXIDINE GLUCONATE SURGICAL BRUSH/SPONGE

Dear Dr. Williams:

With this response to your letter of February 18, 1992, we are forwarding a protocol to collect the data to show bioequivalence and relevant stability in support of approval of this ANDA 73-416.

The protocol describes the usual glove juice study and the work has been contracted to
is the principle investigator.

was selected to conduct study based on his recognized expertise in the evaluation of topical antimicrobials. He has conducted glove juice studies for Becton Dickinson in connection with other NDA's and is well known to industry and the Administration. He is the President of
. Please refer to the attached curriculum vitae for our monitor (exhibit A).

The planned investigation is outlined in the attached (exhibit B) glove juice protocol, #920402, Single Blind Surgical Handscrub Evaluation (Glove Juice) of Two Test Products and One Standard Control Product. The protocol for stability testing is attached (exhibit C).

In view of the safety and history of the related solution approved under Stuart Pharmaceutical's NDA 18-423 HIBICLENS [4% w/v HIBITANE {Chlorhexidine gluconate}] we ask that approval be granted to begin the study immediately.

RECEIVED

MAY 27 1992

GENERIC DRUGS

Sincerely,

Russell J. Arnsberger
Assistant Director
Regulatory Affairs

/gn

cc: ANDA 73-416
Desk copy to Kent T. Johnson (FDA)

Becton Dickinson AcuteCare
9450 South State Street
Sandy, Utah 84070-3234
(801) 565-2300
(801) 565-2740 (Fax)

BECTON DICKINSON

May 19, 1992

Kent T. Johnson
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville, MD 20857

RE: ANDA 73-416, 4% CHLORHEXIDINE GLUCONATE SURGICAL BRUSH/SPONGE PROTOCOL FOR BIOEQUIVALENCE AND STABILITY (DESK COPY)

Dear Mr. Johnson:

With this letter we are forwarding a protocol for collection of data to show bioequivalence and relevant stability in support of approval of this ANDA 73-416. As you will notice, the protocol describes the usual glove juice study and the work has been contracted to is the principle investigator.

Chuck Welle, Dr. M. Khan, Dennis Lamb and I spoke with you via a conference call March 5, 1992, about what Becton Dickinson AcuteCare can do to make ANDA 73-416 approveable.

You gave us suggestions on bioequivalence and stability that we have formulated into this proposal. A contract has been signed and arrangements made so the study can begin upon Agency approval of the protocol. You were kind enough to offer an answer within three weeks.

In view of the safety and history of the related solution approved under Stuart Pharmaceutical's NDA 18-423 HIBICLENS [4% w/v HIBITANE {Chlorhexidine gluconate}] we ask that approval be granted to begin the study immediately.

We have sent this protocol in triplicate to:

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

Sincerely,

George E. Nolan

George E. Nolan
Quality Assurance/
Regulatory Affairs
Manager
BDAC, Sandy

/gn

cc: ANDA 73-416

Deseret Medical
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

March 22, 1991

Mr. Richard C. Adams
Office of Generic Drugs
Center for Drug Evaluation & Research
Food & Drug Administration (HFD-635)
Metro Park North II
Room 223
7500 Standish Place
Rockville, MD 20857

Dear Mr. Adams:

Thank you for your call of March 22, I believe we can resolve any labeling issues very quickly.

As promised herewith, I am sending copy of Section 4 as it appears in my copy of NDA 73-416. We have annotated the labeling on "proposed" being the draft labeling for ANDA 73-416. "Current" being the labeling on the currently marketed product covered by Stuart's NDA 18-423.

Please call me if this fails to answer your reviewer's concerns.

Sincerely,

DESERET MEDICAL, INC.

Charles J. Welle
Manager, Regulatory Affairs

/ca

DESERET

Deseret Medical
9450 South State Street
Sandy. Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

March 25, 1991

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20857

RE: **ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Dear Dr. Williams:

In recent conversations with Mr. Richard Adams we have learned that there has been raised a question regarding the labeling submitted in Section 4 of the above-cited application.

As we have indicated in our submission, under the current business arrangement prepares the solution, controls the packaging performed by Becton Dickinson, and controls the testing and release for distribution as described in the Stuart NDA 18-423. is a contract packager and a distributor only. Under the new contract prepares the solution. All subsequent testing of the bulk solution, approval for use, packaging, in-process control, testing of the finished pharmaceutical, release for distribution, and marketing is performed by Becton Dickinson as described in ANDA 73-416. Becton Dickinson exercises control of the bulk drug and control of the finished product.

The labeling clearly states that the sponge brush is, "Filled with 22ml of HIBICLENS [4% w/v HIBITANE (Chlorhexidine gluconate)] ...." and correctly attributes this solution, "HIBICLENS is a product of Stuart Pharmaceuticals Division of ICI Americas, Inc." The labeling correctly identifies Becton Dickinson as the party responsible for the E-Z SCRUB 106 product.

In the event of problem, the company to be contacted is Becton Dickinson. In this regard too, the proposed label is clear and truthful.

DESERET

Your concurrence will be appreciated.

Sincerely,

Charles J. Welle, Manager
Regulatory Affairs

/tlc

cc: Mr. Richard Adams

Deseret Medical
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

March 25, 1991

Document Control Center
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20857

RE: **ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Document Control Center:

The copy of the above cited applications in use by the reviewer reportedly is no longer complete. To assure that all pages are available, herewith I am forwarding duplicate copies of Section 4. Labeling.

Please use your discretion as to distribution of these copies.

Sincerely,

C J Welle

Charles J. Welle, Manager
Regulatory Affairs

/tlc

cc: Richard Adams, FDA

DESERET

3.1

Deseret Medical
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

noted JD 9-5-94

June 20, 1991

DRUG NEW COPIES

Mr. David Doleski
Division of Generic Drugs
Office of Generic Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: **ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Dear Mr. Doleski:

As promised in my letter of June 11, 1991, herewith I am forwarding the manufacturing site addresses as provided by It is our assumption that these correspond to the addresses contained in the Stuart Pharmaceuticals NDA 18-423 for Hibiclens brand Chlorhexidine Gluconate Brush/Sponge.

Please call me if other questions arise.

Sincerely,

Charles J. Welle
Manager, Regulatory Affairs

/tlc

RECEIVED
JUL 3 19
GENERIC DRUGS

DESERET

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2740

BECTON DICKINSON

May 3, 1990

File

Mr. R. W. Pollock
Division of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-230)
Room 17B45
5600 Fishers Lane
Rockville, MD 20857

RE: ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE AND ANDA 72-525, CHLORHEXIDINE GLUCONATE TOPICAL SOLUTION

Dear Mr. Pollock:

Two letters have surfaced in my follow-up file. I am sending along copies of these and a couple of letters to Mr. Al Sheldon which may be of interest.

In addition, I have a new inquiry. HIBICLENS brand chlorhexidine gluconate, the pioneer product used to show bioequivalence in ANDA 72-525, is also approved for patient preoperative skin preparation. Can we submit an ANDA for a 4% chlorhexidine gluconate gel product for patient prepping comparing its effect to the 4% HIBICLENS brand product? If so, is the patient prep test currently used to show bacterial flora reduction an acceptable demonstration of bioequivalence? Further, do you have a rule of thumb as to the number of volunteers to be included in the study assuming that we would randomly apply HIBICLENS or the new gel to left/right sides of each volunteer.

Thank you for your help.

Sincerely,

Charles J. Welle
Director
Regulatory Affairs

/dp

cc: ANDA 72-525
ANDA 73-416
CHG Gel

DESERET

31

Becton Dickinson
Deseret Division
9450 South State Street
Sandy, Utah 84070
(801) 565-2300
(801) 565-2740 Fax

BECTON DICKINSON

June 11, 1991

Mr. David Doleski
Division of Generic Drugs
Office of Generic Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE

Dear Mr. Doleski:

This letter is to acknowledge your request for additional information regarding the source of the active ingredient used by in their preparation of the Chlorhexidine Gluconate Topical Solution supplied to us under Stuart's NDA 18-423.

I have been promised street addresses and will forward these to you via FAX as quickly as I can obtain them.

Sincerely,

Charles J. Welle
Manager, Regulatory Affairs

/dp

ORIG

dup = 2

Becton Dickinson and Company
One Becton Drive
Franklin Lakes, New Jersey 07417-1880

BIOAVAILABILITY MATERIAL

BECTON DICKINSON

September 10, 1991

Robert A. Jerussi
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
Room 17B-45
Food and Drug Administration (HFD-631)
5600 Fishers Lane
Rockville, MD 20857

RECEIVED
SEP 19 1991
GENERIC DRUGS
NDA ORIG AMENDMENT
N/AM

RE: ANDA 73-416, 4% CHLORHEXIDINE GLUCONATE SURGICAL BRUSH/SPONGE

Dear Mr. Jerussi:

This response to your letter of August 2, 1991, provides the required information for approval of ANDA 73-416. You asked that we indicate that this is a minor amendment.

Our understanding is that bioequivalence studies are conducted to furnish proof of equivalence between an innovator drug and a generic drug, but not the innovator drug and itself. The drug in ANDA 73-416 (HIBICLENS [4% w/v HIBITANE {Chlorhexidine gluconate}]) is identical to that contained in Stuart Pharmaceutical's NDA 18-423 (HIBICLENS [4% w/v HIBITANE {Chlorhexidine gluconate}]); it is the same drug. We mold the brush, assemble the sponge/brush, package the product, do the testing (such as for by a method developed here) and we desire to release finished product. The drug is identical; therefore, studies of bioequivalence maybe interpreted as deceptive.

We are forwarding our study, Glove Juice Evaluation of Two Deseret Medical Test Products and Standard Control Product, Report 8704-09-001D. This independent study we sponsored shows the effectiveness of the product while not comparing the proposed product and innovator product because they are one and the same.

ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Brush/Sponge, is for a product packaged and controlled by Deseret Medical [BDAC] using the Bulk HIBICLENS solution obtained from It is the same product marketed for several years under NDA 18-423 by permission of Stuart Pharmaceutical. When approved this application would do two things:

(1) let Deseret [BDAC] operate its packaging and testing without oversight, making us responsible for our own operation (a postition supports, indicating in the last contract that they would support this ANDA) and (2) provide a vehicle for communicating any future changes, stability data, distribution data and so forth to Generic Drugs. What is changing is a business relationship, not the product.

In Section 13. STABILITY PROFILE of ANDA 73-416 there is provided stability data independently determined for the product; this has been up-dated (Data Attached). The 24 month expiry period used for this product is appropriate. Stability studies will be conducted and reported annually to the Administration and appropriate action based on those results taken.

REVISIONS IN PRODUCT LABELING

Container:

A. Main Panel

1. Lines beneath "E-Z Scrub" revised to read:

   Antimicrobial surgical Scrub Brush/Sponge with HIBICLENS*
   *Filled with...

2. The word removed.

3. Label changed to indicate the Chlorhexidine gluconate (rather than E-Z Scrub sponge/brush) provides rapid bactericidal action...

4. "Discard After Use" added after "For Single Use Only".

5. Temperature in degrees Celsius added to storage recommendations. ...(ABOVE 104°F/40°C).

6. "FOR SURGICAL HAND SCRUB" is include on label.

B. WARNINGS

Statement revised to read as recommended.

C. Directions For Use - revised so that it is in accord with directions for use which appear on our other chlorhexidine gluconate scrub-brush/sponge [ANDA 72-525].

CARTON:

A. Comments revised for A and B under Container were also revised for Carton.

B. "FOR SURGICAL HAND SCRUB" will remain on the carton labeling.

C. The word "Repeat" Item 5 in Directions For Use will be in bold print.

Print cards for the revised labels and labeling are attached for your review and comment.

We would like the opportunity to meet with you to clarify any question or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

Russell J. Arnsberger
Assistant Director
Regulatory Affairs

/gn

cc: ANDA 73-416

noted
9P 9-8-94

Becton Dickinson and Company
One Becton Drive
Franklin Lakes, New Jersey 07417-1880

(201) 848-6800

BECTON DICKINSON

November 18, 1991 3.1

Robert A. Jerussi
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
Room 17B-45
Food and Drug Administration (HFD-631)
5600 Fishers Lane
Rockville, MD 20857

NEW CORRESP.

RE: ANDA 73-416

Dear Mr. Jerussi:

In our response (attached) to your letter of August 2, 1991, providing the required information for approval of ANDA 73-416 we mentioned that this business relationship is of mutual interest to Stuart Pharmaceutical and Becton Dickinson AcuteCare.

Stuart Pharmaceutical supports this ANDA and have asked to have you call concerning their support or if there are any questions that they may be able to answer. Please contact:

Robert Castor
Manager
ICI Pharmaceuticials Group
Stuart Pharmaceuticals
Technical Regulatory Affairs and Compliance
Drug Regulatory Affairs Department
Wilmington, Delaware 19897
(302) 886-2594

We would like the opportunity to clarify any question or vague areas as to aid in the rapid review and approval of this ANDA.

Sincerely,

George Nolan for

Russell J. Arnsberger
Assistant Director
Regulatory Affairs

ORIGINAL

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NOV 25 1991
GENERIC DRUGS

1 Sep 94
Phillips

NOTED JHannan 3/25/91
GIVE TO John Harrison

ORIGINAL

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Deseret Medical
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

March 5, 1991

ORIG NEW CORRES

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

RE: **ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Dear Mr. Williams:

The above application was submitted August 28, 1989. As you know from our previous correspondence, the purpose of this application is to make responsible for bulk drug solution compounding only and would make Deseret Medical responsible for the packaging, testing, release, and distribution of the finished form. This involves a change of authority and responsibility, but does not change any aspect of the product or its manufacture.

If a meeting to clarify this matter would be helpful, we would appreciate the opportunity to meet with you as soon as possible.

Sincerely,

C J Welle

Charles J. Welle, Manager
Regulatory Affairs

/tlc

cc: R. Pollock

RECEIVED

MAR 13 1991

DESERET **GENERIC DRUGS**

3-20-90

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2740

BECTON DICKINSON

March 5, 1990

Mr. R. W. Pollock
Division of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-230)
Room 17B45
5600 Fishers Lane
Rockville, MD 20857

ORIG NEW CORRES

RE: ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE

Dear Mr. Pollock:

In our letter of January 2, 1990 we responded to a letter dated December 26, 1989 from Mr. Terselic. In the letter we attempted to clarify the relationship of the subject scrub to the Hibiclens brand product. Our subsequent discussion led to your questioning whether, if filing was denied under 21 CFR 314.101, the contract with would be affected. Our Law Department has indicated that such denial would not nullify our agreement.

Aside from the precedent set for similar products, we need a vehicle for stability data, packaging changes, labeling changes, and so forth as the product may evolve. Somehow we have to establish a communication line. It would seem that ANDA 73-416 would describe where we are today, as approved via Stuart's NDA 18-423, would acknowledge that Deseret Medical is responsible for the packaged product, and would set a baseline from which any changes would be made.

I would appreciate knowing the status of our application.

Sincerely,

Charles J. Welle
Director, Regulatory Affairs

/dp

cc: ANDA 73-416

RECEIVED
MAR 16 1990
GENERIC DRUGS

DESERET

Deseret Medical
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

January 31, 1991

Roger Williams, M.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-600)
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

RE: **ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Dear Dr. Williams:

The above application was submitted August 28, 1989 and assigned number 73-416 in the Administration's letter of September 18, 1989. Since that time we have provided additional copies of analytical procedures and copies of a glove juice study, previously reviewed, to facilitate your handling of the application.

This application would allow Deseret Medical to purchase Chlorhexidine Gluconate Solution from and to package this bulk drug into unit packages; that is, solution impregnated surgical brush/sponges for distribution as E-Z SCRUB 106. As explained in the application, essentially this same arrangement has been in place under NDA 18-423 for several years. The ANDA, when approved, would make responsible for bulk drug solution compounding only and would make Deseret responsible for the packaging, testing, release, and distribution.

We are anxious to establish this new business relationship and, quite honestly, feel that approval is overdue. We would appreciate your determining the actual status of the application and providing us with the anticipated date when your review will be completed.

Thank you for your attention to this matter.

Sincerely,

Charles J. Welle
Manager, Regulatory Affairs

/tlc

cc: R. Pollock

DESERET

ORIGINAL

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Deseret Medical
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2378

BECTON DICKINSON

73-416

January 14, 1991

Office of Generic Drugs
CDER
Food and Drug Administration
Attention: Mr. Pollock
MPN II, HFD-600
5600 Fishers Lane
Rockville, MD 20857

RE: **ANDA 73-46, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Dear Mr. Pollock:

It has been some little while since the approval of the above-cited application was discussed. In-as-much as this application was submitted in August, 1989 and in-as-much as we are asking only for transfer of certain authority from one company to another, approval is overdue. That we can successfully produce the product has been long since established by our having done so for about eight years.

We would appreciate your determining the actual status and the anticipated approval date so our business relationship with can be amended as both parties wish.

Sincerely,

C. J. Welle
Manager
Regulatory Affairs

/tlc

DESERET

ORIGINAL

Dup to Bio

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2740

BECTON DICKINSON

January 2, 1990

ORIG NEW CORRES

Acting Director
Division of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration (HFD-230)
Room 17B25
5600 Fishers Lane
Rockville, MD 20857

RE: **ANDA 73-416, CHLORHEXIDINE GLUCONATE BRUSH/SPONGE**

Dear Sir:

This is in response to your letter dated December 26, 1989 regarding the above-cited application and, more specifically, section 16 of that application.

The implied questions make it apparent that whomever in the Anti-Infective Drug Division reviewed the request for a waiver of in vivo bioequivalence did not have access to our submission in its entirety. The attached pages taken from ANDA 73-416 will clarify the relationship of the proposed product to the currently marketed product.

Nonetheless, so that more time is not lost, we are forwarding the study, Glove Juice Evaluation of Two Deseret Medical Test Products and Standard Control Product, Report 8704-09-001D. While this shows the effectiveness of the product, it cannot compare the proposed product and innovator product because these are one and the same product. All the Hibiclens®brand product available to anyone has been compounded in bulk by and packaged by As has been explained, what is changing is a business relationship; not the product.

We are asking that our ANDA 73-416, which describes the product and processes already approved under Stuart Pharmaeuticals' NDA 18-423, also be approved to establish that Deseret Medical is responsible for the product bearing our name and that it is under our control.

DESERET

ORIGINAL

We trust that this matter has been made clear and understandable. However, we are prepared to meet with you and Dr. Gavrilovich if such a meeting would be helpful.

Sincerely,

Charles J. Welle
Director, Regulatory Affairs

CJW/tlc

cc: D. L. Rosen
A. T. Sheldon
ANDA 73-416

505(b)(2)(A)
info in suppl
for 10/4/89

Becton Dickinson and Company
One Becton Drive
Franklin Lakes, New Jersey 07417-1880

(201) 848-6800

(201) 848-7107

Drug

BECTON DICKINSON

September 27, 1989

73-416

Division of Generic Drugs
Food and Drug Administration (HFN-230)
5600 Fishers Lane
Rockville, MD 20857

Re: ALL INFORMATION REGARDING TO CHLORHEXIDINE GLUCONATE 4% TOPICAL SOLUTION

To Whom It May Concern:

In connection with the above identified application, applicant's undersigned patent attorney hereby certifies that U.S. patents 3,855,140 and 3,960,745 assigned to Imperial Chemical Industries, London, England who is listed by the FDA as the "pioneer" manufacturer also known as Stuart Pharmaceuticals Division of ICI Americas, Inc., Wilmington, Delaware 19897 are not infringed.

A review of the claims of these patents has been made and the compositions covered by the claims thereof would not be infringed by the manufacture, use or sale of the material for which application has been made.

Very truly yours,

Aaron Passman
/apf

cc: Stuart Pharmaceuticals
Attn: Director, Regulatory/Affairs
Division of ICI Americas, Inc.
Wilmington, Delaware 19897

RECEIVED
OCT 3 1989
GENERIC DRUGS

2177H

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2740

Drug

BECTON DICKINSON

September 25, 1989

ORIG NEW CORRES
BIOAVAILABILITY MATERIAL

Mr. Kent T. Johnson
Division of Generic Drugs
Attention: Document Control Room
HFN-230 Room 17B20
Food and Drug Administration
Center for Drugs and Biologics
5600 Fishers Lane
Rockville, MD 20857

Ref: ANDA 73-416,
4% Chlorhexidine Gluconate
Surgical Brush/Sponge

Dear Mr. Johnson:

As requested in your letter of September 18, 1989, herewith we are forwarding, in triplicate, additional copies of the analytical methods and descriptive information needed to perform testing of the bulk 4% chlorhexidine glyconate solution received from and the finished dosage form. The bulk 4% solution is our starting material. As indicated in our application these methods are the methods approved previously under NDA 18-423 and currently in use under that NDA.

With regard to bioequivalence study requirements, we wish to request a waiver of in vivo studies under 21 CFR 320.22(2) on the basis that the drug is a topically applied preparation intended for local therapeutic effect.

Sincerely,

Charles J. Welle
Director
Regulatory Affairs

RECEIVED
OCT 2 1989
GENERIC DRUGS

/dp

DESERET

DUPLICATE

NDA/BRG Corres

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2740

BECTON DICKINSON

March 21, 1990

Document Control
Room 12B30
Anti-Infective Drug Products
Food and Drug Administration (HFD-520)
5600 Fishers Lane
Rockville, MD 20857
Attn: Mr. A. T. Sheldon

RE: CHLORHEXIDINE GLUCONATE PRODUCTS

Dear Mr. Sheldon:

As we have discussed, it may prove worthwhile to review the relationships and status of our applications related to chlorhexidine gluconate. Briefly, we have the following documents:

1. ANDA 72-525, Chlorhexidine Gluconate Topical Solution, 4% Formula 267P Sponge

This ANDA was approved October 24, 1989 as a hand scrub. It is for the generic equivalent to Stuart Pharmaceutical's HIBICLENS brand chlorhexidine gluconate solution.

2. ANDA 73-416, 4% Chlorhexidine Gluconate Surgical Brush/Sponge

This ANDA was submitted August 28, 1989 as a hand scrub. It is for a product packaged and controlled by using the bulk HIBICLENS solution obtained from It is the same product we have marketed for several years under Stuart's NDA 18-423. When approved this application would do two things: (1) let Deseret operate its packaging and testing without oversight making us responsible for our own operation and (2) provide a vehicle for communicating any future changes, stability data, distribution data and so forth to Generic Drugs.

3. NDA

This NDA was submitted November 1, 1989 for a sterile hand scrub filled with our generic equivalent formula previously approved under ANDA 72-525.

DESERET

There is a study which ties these three applications together. Study 8704-09-001D, Glove Juice Evaluation of Two Deseret Medical Test Products and Standard Product, dated December 7, 1987, compares our generic chlorhexidine gluconate 4% solution (267P) and our generic chlorhexidine gluconate 4% solution (267P) after to HIBICLENS brand chlorhexidine gluconate 4% solution. reported in the conclusion, "In this surgical hand scrub evaluation, the two test products and the control product were equivalent in antimicrobial effectiveness (P<.05)."

Essentially, our intention was to obtain approval for our solution via an ANDA. When the Generic Drug operation fell into confusion, we were forced to contract with for another three year period. But, this was with the provision that would support an ANDA for our packaging HIBICLENS much as several companies buy and package solution. The NDA is part of our overall company goal to produce sterile products without the use of environmentally dirty ETO processes.

I hope this will facilitate future discussions. I know it helps clarify the matter for me.

Sincerely,

Charles J. Welle
Director
Regulatory Affairs

/dp

cc: D. Bostwick
C. Evans
L. Gavrilovich
NDA 20-039

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
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Fax (801) 565-2740

BECTON DICKINSON

NOV 1 ? 1989

ORIG NEW CORRES

Mr. Kent T. Johnson
Division of Generic Drugs
Attention: Document Control Room
HFN-230 Room 17B20
Food and Drug Administration
Center for Drugs and Biologics
5600 Fishers Lane
Rockville, MD 20857

Ref: ANDA 73-416
4% Chlorhexidine Gluconate
Brush/Sponge

Dear Mr. Johnson:

As requested in your letter dated September 18, 1989, herewith we are forwarding two letters. One letter is from our patent attorney, Mr. Passman, to the Division of Generic Drugs certifying that we do not infringe the patents held by ICI. The other is from our corporate senior attorney, Mr. Hector, to Stuart Pharmaceuticals informing them of our filing an ANDA with references to their NDA 18-423 for HIBICLENS® brand chlorhexidine gluconate solution.

Our use of bulk solution compounded by is in accord with the contract between the two companies which specially provides for this ANDA and the supply of bulk solution.

A copy of the certified mail receipt is attached.

Sincerely,

Charles J. Welle
Director
Regulatory Affairs

ORIGINAL

/dp

RECEIVED

NOV 21 1989

GENERIC DRUGS

DESERET

505(b)(2)(A) info is not acceptable for 9/12/89 DMR

Deseret Medical, Inc.
9450 South State Street
Sandy, Utah 84070
(801) 565-2300 Telex 499-1990 DMI UI
Fax (801) 565-2740

BECTON DICKINSON

AUG 28 1989

Mr. Richard A. Terselic
Division of Generic Drugs
Attention: Document Control Room
HFN-230, Room 17B-20
Food and Drug Administration
Center for Drugs and Biologics
5600 Fishers Lane
Rockville, MD 20857

Dear Mr. Terselic:

With this letter we are forwarding form FDA 356h, Application to Market a New Drug for Human Use as provided under 21 CFR 314. As indicated, this application is an abbreviated application for Chlorhexidine Gluconate Surgical Brush/Sponge, an antimicrobial surgical hand scrub containing 4% chlorhexidine gluconate as the active ingredient.

The bulk solution is manufactured by and the brush/sponge product is packaged and marketed by Deseret Medical, Inc., a part of Becton Dickinson and Company. This arrangement, which is covered under NDA 18-423, has existed for several years with Deseret Medical being both contract packager and distributor for the E-Z SCRUB® 106 product. The current package acknowledges the relationship of the two companies by the use of "manufactured for" above the Becton Dickinson name. In this application we propose to buy bulk solution and to package the E-Z SCRUB® 106 as our own product. The change will result in minor labeling revisions. However, the solution, the brush/sponge component, the package, the packaging operation, and quality aspects are unaffected.

All correspondence related to this application should be directed to me.

Very truly yours,

Charles J. Welle
Director
Regulatory Affairs

/dp

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SEP 1 1989
GENERIC DRUGS

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