

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*  
**NDA 19-422 / S-032**

**LABELING REVIEW(S)**



## OTC DRUG LABELING REVIEW

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Food and Drugs Administration  
Center For Drug Evaluation and Research  
Division of Over-the-Counter Drug Products (HFD-560)

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**SUBMISSION DATE:** October 31, 2003      **REVIEW DATE:** November 7, 2003

**NDA:** 19-422

**SUBMISSION TYPE:** SE8-032-AZ

**SPONSOR:** Xttrium Laboratories, Inc.  
415 West Pershing Road  
Chicago, IL 60609

**CONTACT:** Dr. Ram Charkroborty  
Vice President  
(773) 268-5800

**DRUG PRODUCT:** Dyna-Hex 2<sup>®</sup>

**ACTIVE INGREDIENT:** 2% chlorhexidine gluconate

**PHARMACOLOGICAL CATEGORY:** Healthcare Antiseptic:  
Surgical Hand Scrub,  
Healthcare Personnel Hand Antiseptic,  
Patient Preoperative Skin Preparation,  
Skin Wound and General Skin Cleansing

**LABELING SUBMITTED:** - Principle Display Panel  
- *Drug Facts* Labeling

**PROJECT MANAGER:** Tia Frazier, R.N., M.S.

**REVIEWER:** Michelle M. Jackson, Ph.D.

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**Background:** Labeling for chlorhexidine gluconate 2% solution was originally approved on December 17, 1985. On December 19, 2002, the Agency issued a "approvable" letter to the sponsor with a summarized list of deficiencies on the principle display panel (PDP) and *Drug Facts* labeling in supplement SE8-032. The December 19, 2002, letter also requested information on the sponsor's assertion that their products' inactive ingredients should be considered "trade secret" and should not be included in labeling. On February 10, 2003, the

sponsor submitted a supplement (SE8-032/AL) in response to the Agency's December 19, 2002, letter that included supportive information on their belief that the inactive ingredients for Exidine solution 2% and Dyna-Hex 2<sup>®</sup> products are considered to be a trade secret.

In an "approvable" letter dated August 11, 2003, the Agency disputed the sponsor's contention that the product's inactive ingredients can be considered "trade secret" and provided a list of labeling deficiencies. On August 22, 2003, the sponsor submitted a supplement (SE8-032/AL) for its Dyna-Hex 2<sup>®</sup> (chlorhexidine gluconate 2% solution) drug product addressing the issues raised by the Agency's August 11, 2003, letter. On September 3, 2003, the sponsor submitted another supplement that provided color drafts PDP and *Drug Facts* labeling of the following: 4 ounce, 8 ounce, 16 ounce, 30 ounce, 32 ounce, and 1 gallon container labels. In the response to the Agency's action letter dated August 11, 2003, the sponsor included a listing of the inactive ingredients on all of their labeled products.

In response to the Agency's letter dated October 27, 2003, the sponsor submitted draft copy of the labeling for the 4- and 8- ounce containers.

#### Reviewer's comments on the labeling:

The sponsor's response to the deficiencies in the Agency's letter dated October 27, 2003:

1. Agency's recommendation: Add the phrase "Peel here for *Drug Facts* ►" to the outermost surface of your 4- and 8-ounce containers, rather than on page 2 of the leaflet. The statement is located on the wrong panel. Currently, the statement appears inside the folded label, but should be located on the principal display panel (PDP) so that it is visible to the reader looking at the bottle.

*Reviewer's comment: The sponsor has clarified that the statement "Peel here for Drug Facts" is visible to the reader looking at the bottle. This has been implemented and is acceptable.*

#### Additional comments on the labeling:

1. The sponsor will need to remove the extra subheading **Warnings**, on the fourth page of the 4-ounce container and also remove the hairline just below the subheading. These changes can be made at the time of the next printing.

#### Recommendation:

- 1.) The sponsor should be issued an approval letter for the 4- and 8- ounce container labels.
- 2.) The sponsor should be informed to remove the extra subheading **Warnings**, on the fourth page of the 4-ounce container and also remove the hairline just below the subheading. These changes can be made at the time of the next printing.
- 3.) The sponsor should be requested to submit 20 copies of the final printed labeling.

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Michelle M. Jackson, Ph.D.  
IDS Reviewer

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Concurrence  
Debbie L. Lumpkins, Team Leader

**APPEARS THIS WAY  
ON ORIGINAL**

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This is a representation of an electronic record that was signed electronically and  
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/s/

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Michelle Jackson  
11/25/03 01:36:45 PM  
INTERDISCIPLINARY

Debbie Lumpkins  
11/25/03 01:50:49 PM  
INTERDISCIPLINARY



## OTC DRUG LABELING REVIEW

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Food and Drugs Administration  
Center For Drug Evaluation and Research  
Division of Over-the-Counter Drug Products (HFD-560)

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**SUBMISSION DATE:** August 22, 2003  
September 3, 2003

**REVIEW DATE:** September 24, 2003

**NDA:** 19-422

**SUBMISSION TYPE:** SE8-032 AL  
SE8-032 BZ

**SPONSOR:** Xttrium Laboratories, Inc.  
415 West Pershing Road  
Chicago, IL 60609

**CONTACT:** Dr. Ram Charkroborty  
Vice President  
(773) 268-5800

**DRUG PRODUCT:** Dyna-Hex 2<sup>®</sup>

**ACTIVE INGREDIENT:** 2% chlorhexidine gluconate

**PHARMACOLOGICAL CATEGORY:** Healthcare Antiseptic:  
Surgical Hand Scrub,  
Healthcare Personnel Hand Antiseptic,  
Patient Preoperative Skin Preparation,  
Skin Wound and General Skin Cleansing

**LABELING SUBMITTED:** - Principle Display Panel  
- *Drug Fact* Labeling

**PROJECT MANAGER:** Tia Frazier, R.N., M.S.

**REVIEWER:** Michelle M. Jackson, Ph.D.

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**Background:** Labeling for chlorhexidine gluconate 2% solution was originally approved on December 17, 1985. On December 19, 2002, the Agency issued a "approvable" letter to the sponsor with a summarized list of deficiencies on the principle display panel (PDP) and *Drug*

*Facts* labeling in supplement SE8-032. The December 19, 2002, letter also requested information on the sponsor's assertion that their products' inactive ingredients should be considered "trade secret" and should not be included in labeling. On February 10, 2003, the sponsor submitted a supplement (SE8-032/AL) in response to the Agency's December 19, 2002, letter that included supportive information on their belief that the inactive ingredients for Exidine solution 2% and Dyna-Hex 2<sup>®</sup> products are considered to be a trade secret.

In an "approvable" letter dated August 11, 2003, the Agency disputed the sponsor's contention that the product's inactive ingredients can be considered "trade secret" and provided a list of labeling deficiencies. On August 22, 2003, the sponsor submitted a supplement (SE8-032/AL) for its Dyna-Hex 2<sup>®</sup> (chlorhexidine gluconate 2% solution) drug product addressing the issues raised by the Agency's August 11, 2003, letter. On September 3, 2003, the sponsor submitted another supplement that provided color drafts PDP and *Drug Facts* labeling of the following: 4 ounce, 8 ounce, 16 ounce, 30 ounce, 32 ounce, and 1 gallon container labels. Three copies were provided for each label: an unmarked copy, a highlighted copy to demonstrate the revisions made and a call-out copy to indicate font sizes. In the response to the Agency's action letter dated August 11, 2003, the sponsor included a listing of the inactive ingredients on all of their labeled products. This reviewer will address the supplement (SE8-032 BZ) submitted September 3, 2003.

**Reviewer's comments on the labeling:**

The sponsor's response to the deficiencies in the Agency's approvable letter dated August 11, 2003:

1. **Agency's recommendation:** Place the established drug name (chlorhexidine gluconate 2% solution) in direct conjunction with the trade name, followed by the pharmacological category (antiseptic).

**Reviewer's comment:** *This has been implemented and is acceptable.*

2. **Agency's recommendation:** Revise the 16- and 30-ounce and 1-gallon container labels to retain the standard order and required flow of *Drug Facts* information onto multiple panels, as required by 21 CFR 201.66(d)(5). Relocate Net Contents, Lot Number and Expiration Date information so as not to interrupt the flow and order of the *Drug Facts* panels.

**Reviewer's comment:** *This has been implemented and is acceptable.*

3. **Agency's recommendation:** Revise the PDP's for the 30- and 32-ounce container sizes so that the net contents information is listed only once, and is contained in the lower 30% of the PDP. Refer to 21 CFR 201.62(e) for clarification.

**Reviewer's comment:** *This has been implemented and is acceptable.*

4. **Agency's recommendation:** Revise the *Drug Facts* labeling for all container sizes to incorporate barlines that surround information by a box or similar enclosure, as required by CFR 201.66(d)(8).

**Reviewer's comment:** *This has been implemented and is acceptable.*

5. **Agency's recommendation:** Revise the 4- and 8-ounce container labels so that their outermost labeling surfaces contain the title, headings, subheadings and information set forth in paragraphs (c)(1) through (c)(8) in 21 CFR 201.66. Adding the phrase "Peel here for *Drug Facts*▶" to the outermost surface of your 4- and 8-ounce containers would satisfy this requirement.

**Reviewer's comment:** *The sponsor needs to add the phrase "Peel here for Drug Facts▶" to the outermost surface of their 4- and 8-ounce containers. It appears that the statement was placed on the wrong panel and should not be part of Drug Facts. As currently placed it appears that this statement is placed inside the folded label. This is not acceptable.*

6. **Agency's recommendation:** Revise the laminate panels for the 4- and 8-ounce container to include the statement "*Drug Facts* (continued)" directly above the header *Directions* on the next adjacent panel.

**Reviewer's comment:** *The sponsor has added the requested statement. However, the hairline after the header Directions on the last page of the label on the 4-ounce container and on page 4 of the 8-ounce container label should be removed.*

7. **Agency's recommendation:** Revise the labeling for the 16-, 30-, 32-ounce, and 1-gallon container sizes so that the bulleted statements under *Directions* are vertically aligned, to ensure visual separation and adequate white space between discrete chunks of information. Bulleted statements can be only wrapped when using the modified format. See 21 CFR 201.66(d)(10).

**Reviewer's comment:** *This has been implemented and is acceptable.*

8. **Agency's recommendation:** Remove \_\_\_\_\_ from the 8-ounce container labels currently located after *Active ingredients*; at the end of the bulleted statement *patient preoperative skin preparation*, under *Uses*; after **Do not use**; and, at the end of the first bulleted statement under **When using this product**.

**Reviewer's comment:** *This has been implemented and is acceptable.*

9. **Agency's recommendation:** Under *Questions or comments?*, for the 16-ounce container size, revise your labeling to include a telephone number for consumer inquires. Specify the days of the week and the hours of operation when a person is available to respond to questions.

Reviewer's comment: *This has been implemented and is acceptable.*

10. Agency's recommendation: Revise the labeling for the 4- and 8-ounce containers so that the **Drug Facts** contents fit within the two panels inside the leaflet. Thus, place the first panel (page 2) directly behind the PDP, and the second panel (page 3) flush against the container so that it is immediately visible. The exposed Drug Facts panel should include the **Directions**, **Other information**, **Inactive ingredient**, and **Questions?** Sections.

Reviewer's comment: *This has been implemented and is acceptable.*

11. Agency's recommendation: Left justify **Active ingredient** information and right justify the corresponding **Purposes** information so that it runs continuously, on one line for the 4- and 8-ounce container labels.

Reviewer's comment: *This has been implemented and is acceptable.*

12. Agency's recommendation: Under **Active ingredient**, place the phrase "chlorhexidine gluconate 2% solution" on two separate lines, so that the phrase "chlorhexidine gluconate" lies on the first line, and "2% solution" lies on the second line followed by a succession of dots for the 4- and 8-ounce container labels.

Reviewer's comment: *This has been implemented and is acceptable.*

13. Agency's recommendation: Remove the term "continued" that follows the **Warnings** and **Directions** headers for the 4- and 8-ounce container labels, to reduce redundancy and confusion with required "**Drug Facts (continued)**" headers.

Reviewer's comment: *This has been implemented and is acceptable.*

#### Recommendations:

1. Add the phrase "Peel here for **Drug Facts**➤" to the outermost surface of their 4- and 8-ounce containers. It appears that the statement was placed on the wrong panel and should not be part of **Drug Facts**. As currently placed the statement appears inside the folded label.
2. Remove the hairline after the header **Directions** on the last page of label for the 4 ounce container and on page 4 of the 8-ounce container label.

The sponsor has made most of the required and recommended changes to the PDP and *Drug Facts* labeling and also included the listing of the inactive ingredients. Please inform the sponsor that their labeling can be approved if they make the two revisions listed above.

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Michelle M. Jackson, Ph.D.  
IDS Reviewer

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Concurrence  
Debbie L. Lumpkins, Team Leader

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/s/

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Michelle Jackson  
10/2/03 03:51:49 PM  
INTERDISCIPLINARY

Debbie Lumpkins  
10/2/03 04:44:17 PM  
INTERDISCIPLINARY



## OTC DRUG LABELING REVIEW

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Food and Drugs Administration  
Center For Drug Evaluation and Research  
Division of Over-the-Counter Drug Products (HFD-560)

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**SUBMISSION DATE:** February 10, 2003      **REVIEW DATE:** April 14, 2003

**NDA:** 19-422

**SUBMISSION TYPE:** SE8-032 AL

**SPONSOR:** Xttrium Laboratories, Inc.  
415 West Pershing Road  
Chicago, IL 60609

**CONTACT:** Dr. Ram Charkroborty  
Vice President  
(773) 268-5800

**DRUG PRODUCT:** Dyna-Hex 2<sup>®</sup>

**ACTIVE INGREDIENT:** 2% chlorhexidine gluconate

**PHARMACOLOGICAL CATEGORY:** Healthcare Antiseptic:  
Surgical Hand Scrub,  
Healthcare Personnel Hand Antiseptic,  
Patient Preoperative Skin Preparation,  
Skin Wound and General Skin Cleansing

**LABELING SUBMITTED:** - Principle Display Panel  
- *Drug Facts* labeling

**PROJECT MANAGER:** Tia Frazier, N.R., M.S.

**REVIEWER:** Michelle M. Jackson, Ph.D.

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**Background:** Labeling for chlorhexidine gluconate 2% solution was approved on December 17, 1985. On December 19, 2002, the Agency issued a "approvable" letter to the sponsor with a summarized list of deficiencies on the principle display panel (PDP) and *Drug Facts* labeling. On February 10, 2002, the sponsor submitted a supplement (SE8-032/AL) for its Dyna-Hex 2<sup>®</sup> (chlorhexidine gluconate 2% solution) drug product in *Drug Facts* format to be in

conformance with 21 CFR 201.66. This supplement provides draft PDP and *Drug Facts* labeling of the following: 4 ounce, 8 ounce, 16 ounce, 30 ounce, 32 ounce, and 1 gallon container labels. The sponsor also included in this supplement supportive information on their belief that the inactive ingredients for Exidine Solution 2% and Dyna-Hex 2% products are considered to be a trade secret and need not be listed in the labeling for these products in accordance with Section 302 (e)(1)(A)(iii) of the Federal Food, Drug, and Cosmetic Act. It is noted that the issue of listing inactive ingredients will not be addressed in this review.

**Reviewer's comments on the labeling:**

The sponsor's response to the deficiencies in the Agency's approvable letter dated December 19, 2002:

1. **Principle Display Panel (PDP):**

(i). **Agency's recommendation:** Revise the established name and the pharmacologic category on all labels to be in bold print, in accordance with 21 CFR 201.61(c).

*Reviewer's comment: This has been implemented and is acceptable.*

(ii). **Agency's recommendation:** Revise all labeling so that the established name directly follows the pharmacologic category and both statements are positioned in direct conjunction with the most prominent display of the trade name, in accordance with 21 CFR 201.61.

*Reviewer's comment: We gave the sponsor the correct advice in the prototype but stated the wrong thing in the letter. In fact, the sponsor has implemented the Agency's recommendation in the letter. We need to inform the sponsor that the established name of the drug, i.e., "chlorhexidine gluconate 2% solution," needs to be placed in direct conjunction with the tradename and followed by the pharmacologic category, i.e., "antiseptic". The sponsor must revise as follows:*

*DYNA-HEX2  
Chlorhexidine Gluconate 2% Solution  
Antiseptic*

(iii). **Agency's recommendation:** Revise the PDP for the 32 ounce and 1 gallon containers so that the same size font is used to list both the established name of the drug and the pharmacologic category, in accordance with 21 CFR 201.61.

*Reviewer's comment: This has been implemented and is acceptable.*

(iv). **Agency's recommendation:** Enlarge the font size for the statements of identity included in the labeling for the 4 and 8 ounce containers in order to increase their prominence.

**Reviewer's comment:** *This has been implemented and is acceptable.*

(v). **Agency's recommendation:** Revise all labels to have the net contents in the lower 30 percent of the PDP, as required by 21 CFR 201.62.

**Reviewer's comment:** *The declaration of net quantity of contents, lot number, and expiration date on the 16 and 30 ounce and 1 gallon container label should not interrupt the flow of the Drug Facts information. The sponsor will need to modify the labeling format to conform to the proper flow of the Drug Facts information. Section 201.66 (d)(5) indicates that the continuation of the required content and format onto multiple panels must retain the required order and flow of headings, subheadings, and information. (See prototype.)*

## 2. **Drug Facts:**

(i). **Agency's recommendation:** In order to improve the legibility of your labeling, verify that the labeling for the 4 and 8 ounce containers comply with the leading (space between two lines) requirements, as described in 21 CFR 201.66(d)(3).

**Reviewer's comment:** *This has been implemented and is acceptable.*

(ii). **Agency's recommendation:** Revise the bulleted statements under the directions for use as a surgical handscrub to comply with 21 CFR 201.66(d)(4), or justify your use of a modified format for the 16 ounce label. (Refer to prototype, attached.)

**Reviewer's comment:** *This has been implemented and is acceptable.*

(iii). **Agency's recommendation:** Realign the bulleted statements under the Directions section for surgical hand scrub to comply with 21 CFR 201.66(d)(4).

**Reviewer's comment:** *This has been implemented and is acceptable.*

(iv). **Agency's recommendation:** Revise the bulleted statements under the Directions section for patient preoperative skin preparations and surgical hand scrubs, and under the *Do not use* section for the 32 ounce label, in order to comply with 21 CFR 201.66(d)(4).

**Reviewer's comment:** *This has been implemented and is acceptable.*

(v). **Agency's recommendation:** Remove the phrase " \_\_\_\_\_ " from the bottom of the first labeling panels for the 16 ounce and 1 gallon labels.

**Reviewer's comment:** *The sponsor has removed the phrase " \_\_\_\_\_ " from the bottom of the first labeling panels for the 16 ounce and 1 gallon labels. The sponsor will also need to remove this phrase on the bottom the second and third page panel for the 8 ounce and the second, third, and fourth page for the 4 ounce container labels. The continuation of the required content and format onto multiple panels requires a visual graphic (e.g., an arrow symbol) that is used to signal the continuation of the **Drug Facts** labeling to the adjacent panel. (See prototypes.)*

(vi). **Agency's recommendation:** Increase the font size in the **Inactive ingredients** section of the labeling for the 4 and 8 ounce sizes, so that all your **Drug Facts** headings are the same size.

**Reviewer's comment:** *This has been implemented and is acceptable.*

(vii). **Agency's recommendation:** Under **Directions**, correct the spelling of the subheading "Healthcare personnel handwash" so that it reads "Healthcare personnel handwash" (1 gallon container size).

**Reviewer's comment:** *This has been implemented and is acceptable.*

(viii). **Agency's recommendation:** Identify the location of the lot number and expiration date on each package.

**Reviewer's comment:** *This has been implemented and is acceptable.*

**Sponsor's additional comments specifically to address the 30 ounce label.**

(i). **Sponsor's Additional Comments:** Widen the space between each line (leading) of text in your labeling so that it is at least 0.5-point and conforms to the requirements described in 21 CFR 201.66(d)(3).

**Reviewer's comment:** *This has been implemented and is acceptable.*

(ii). **Sponsor's Additional Comments:** Ensure that the bullets beside each bulleted statement are at least 0.5 point.

**Reviewer's comment:** *This has been implemented and is acceptable.*

(iii). **Sponsor's Additional Comments:** Bulleted first statements under **Warnings** subheadings titled, "When using this product", "**Directions**" for "Surgical Hand Scrub" and "Skin wound and general skin cleansing" need to be vertically aligned with the other bulleted statements.

**Reviewer's comment:** *This has been implemented and is acceptable.*

(iv). Sponsor's Additional Comments: Under the "Do not use" subheading under *Warnings*, correct the spelling of the word "\_\_\_\_\_ " to read "meninges".

Reviewer's comment: *This has been implemented and is acceptable.*

(v). Sponsor's Additional Comments: Increase the font size in the *Questions or Comments* heading so that it is identical to the font size of the other headings.

Reviewer's comment: *This has been implemented and is acceptable.*

### Reviewer's Additional Comments:

#### 1. PDP:

(i). The bottom the PDP for the 4 and 8 ounce container labels should include the statement "Peel here for *Drug Facts* ➔". (See prototype for 4 and 8 ounce container labels.)

(ii). The net content requirements on the 30 and 32 ounce container labels need to be only mentioned once on the PDP. Section 201.62(e) states that the net contents are required to be in the lower 30% of the PDP. (See prototype for 30 and 32 ounce container labels.)

#### 2. Drug Facts:

(i). All of the labels need to be revised to have the "*Drug Facts*" information set off in a box or similar enclosure by the use of barlines, as required by CFR 201.66(d)(8). (See Prototypes.)

(ii). It is recommended that the 4 and 8 ounce container labels be revised so that the *Drug Facts* labeling can be fitted onto the two panels inside the leaflet (first panel, page 2 located directly behind the PDP and the second panel, page 3 located flush against the container) and one panel exposed directly on the container. The panel exposed on the container should include the *Directions*, *Other information*, *Inactive ingredient*, and *Questions?* sections. (See prototype for 4 and 8 ounce container labels.)

(iii). It is recommended that the *Active ingredient* information be left justified, and the corresponding *Purposes* information be right justified on the same line for the 4 and 8 ounce container labels. (See prototype for 4 and 8 ounce container labels.)

(iv). Under the header *Active ingredient*, it is recommended that chlorhexidine gluconate 2% solution should be separated to utilize two lines, "chlorhexidine gluconate" on the first line and "2% solution" on the second line followed by a succession of dots for the 4 and 8 ounce container labels. (See prototype for 4 and 8 ounce container labels.)

(v). The 8 ounce container label contains \_\_\_\_\_ after the header *Active ingredient*, the subheader **Do not use** and end of the first bulleted statement under the subheader **When using this product** which needs to be removed from the label.

(vi). The header *Questions or comments?* should be included in the *Drug Facts* for the 16 ounce container label. A telephone number for consumer inquires, the days of the week, and the hours of operation when a person is available to respond to questions should be included.

(vii). The 4 and 8 ounce container labels have the term "\_\_\_\_\_" on the **Warnings** and **Directions** headings. Section 201.66 does not require this, however, this is redundant to "*Drug Facts* (continued)" and we recommend its removal.

(viii). The 4 and 8 ounce container labels on the outer leaflet panel should have the statement "*Drug Facts* (continued)" located directly above the header *Directions*. (See prototype for 4 and 8 ounce container labels.)

(ix). The bullets under the header *Directions*, on the 16, 30, 32 ounce, and 1 gallon container labels need to be vertically aligned, to ensure visual separation and adequate white space between discrete chunks of information. Bulleted statements can be only wrapped when using the modified format. (See prototype for 16, 30, 32 ounce and 1 gallon container labels.)

(x). The 8 ounce container label contains \_\_\_\_\_ which should be removed at the following locations on the label: after the header *Active ingredient*; at the end of the bulleted statement **patient preoperative skin preparation**, under the header *Uses*; after the subheader **Do not use**; and at the end of the first bulleted statement under the subheader **When using this product**.

### RECOMMENDATIONS:

Please inform the sponsor that the *Drug Facts* label need further revisions as follows:

#### Required changes

1. The established name of the drug, i.e., chlorhexidine gluconate 2% solution, needs to be placed in direct conjunction with the trade name and followed by the pharmacologic category, i.e., antiseptic. (see PDP prototypes).

2. The declaration of net quantity of contents, lot number, and expiration date on the 16 and 30 ounce and 1 gallon container label should not interrupt the flow of the *Drug Facts* information. The sponsor will need to modify the labeling format to conform to the proper flow of the *Drug Facts* information. Section 201.66 (d)(5) indicates that the continuation of the required content and format onto multiple panels must retain the required order and flow of headings, subheadings, and information. (See prototype.)
3. The net content requirements on the 30 and 32 ounce container labels need to be only mentioned once on the PDP. Section 201.62(e) states that the net contents are required to be in the lower 30% of the PDP. (See prototype for 30 and 32 ounce container labels.)
4. All of the packaging labels needs to be revised to have the "*Drug Facts*" information set off in a box or similar enclosure by the use of barlines, as required by CFR 201.66(d)(8). (See prototypes.)
5. The top of the PDP for the 4 and 8 ounce container labels need to include the statement "Peel here for *Drug Facts* ➔". (See prototype for 4 and 8 ounce container labels.)
6. The sponsor has removed the phrase " \_\_\_\_\_" from the bottom of the first labeling panels for the 16 ounce and 1 gallon labels. The sponsor will also need to remove this phrase on the bottom the second and third page panel for the 8 ounce and the second, third, and fourth page for the 4 ounce container labels. The continuation of the required content and format onto multiple panels requires a visual graphic (e.g., an arrow symbol) that is used to signal the continuation of the *Drug Facts* labeling be placed at the top of the adjacent panel. (See prototypes.)
7. The 4 and 8 ounce container labels on the outer leaflet panel should have the statement "*Drug Facts (continued)*" located directly above the header *Directions*. (See prototype for 4 and 8 ounce container labels.)
8. The bullets under the header *Directions*, on the 16, 30, 32 ounce, and 1 gallon container labels need to be vertically aligned, to ensure visual separation and adequate white space between discrete chunks of information. Bulleted statements can be only wrapped when using the modified format. (See prototype for 16, 30, 32 ounce and 1 gallon container labels.)
9. The 8 ounce container label contains \_\_\_\_\_ which should be removed at the following locations on the label: after the header *Active ingredient*; at the end of the bulleted statement **patient preoperative skin preparation**, under the header *Uses*; after the subheader **Do not use**; and at the end of the first bulleted statement under the subheader **When using this product**.

### Recommended changes

1. The header *Questions or comments?* should be included in the *Drug Facts* for the 16 ounce container label. A telephone number for consumer inquiries, the days of the week, and the hours of operation when a person is available to respond to questions should be included.
2. It is recommended that the 4 and 8 ounce container labels be revised so that the *Drug Facts* labeling can be fitted onto the two panels inside the leaflet (first panel, page 2 located directly behind the PDP and the second panel, page 3 located flush against the container) and one panel exposed directly on the container. The panel exposed on the container should include the *Directions*, *Other information*, *Inactive ingredient*, and *Questions?* sections. (See prototype for 4 and 8 ounce container labels.)
3. It is recommended that the *Active ingredient* information to be left justified, and the corresponding *Purposes* information to be right justified on the same line for the 4 and 8 ounce container labels. (See prototype for 4 and 8 ounce container labels.)
4. Under the header *Active ingredient*, it is recommended that chlorhexidine gluconate 2% solution should be separated to utilize two lines, "chlorhexidine gluconate" on the first line and "2% solution" on the second line followed by a succession of dots for the 4 and 8 ounce container labels. (See prototype for 4 and 8 ounce container labels.)
5. The 4 and 8 ounce container labels have the term "\_\_\_\_\_ " on the **Warnings** and **Directions** headings. Section 201.66 does not require this, however this is redundant to "*Drug Facts* (continued)" and we recommend its removal.

The sponsor should be advised to make the revisions listed above and referred to pending discussions on the listing of the inactive ingredients.

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Michelle M. Jackson, Ph.D.  
IDS Reviewer

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Concurrence  
Debbie L. Lumpkins, Team Leader

**PROTOTYPE : 4 ounce container label**  
**(Also used this prototype for 8 ounce container label.)**

Page 2

<b>Drug Facts</b>	
<b>Active ingredient</b> chlorhexidine gluconate 2% solution.....	<b>Purposes</b> surgical hand scrub healthcare personnel handwash patient preoperative skin preparation skin wound and general skin cleansing
<b>Uses</b>	
<ul style="list-style-type: none"> <li>• <b>surgical hand scrub:</b> significantly reduces the number of microorganisms on the hands and forearms prior to surgery or patient care</li> <li>• <b>healthcare personnel handwash:</b> helps reduce bacteria that potentially can cause disease</li> <li>• <b>patient preoperative skin preparation:</b> preparation of the patient's skin prior to surgery</li> <li>• <b>skin wound and general skin cleansing</b></li> </ul>	
<b>Warnings</b>	
For external use only	
Do not use • if you are allergic to chlorhexidine gluconate or any other ingredients • in contact with meninges • in the genital area • as a preoperative skin preparation of the head or face	

Page 3

<b>Drug Facts (continued)</b>
<b>When using this product</b>
<ul style="list-style-type: none"> <li>• keep out of eyes, ears, and mouth. May cause serious and permanent eye injury if placed or kept in the eye during surgical procedures or may cause deafness when instilled in the middle ear through perforated eardrums</li> <li>• if solution should contact these areas, rinse out promptly and thoroughly with water</li> <li>• wounds which involve more than the superficial layers of the skin — not be routinely treated</li> <li>• repeated general skin cleansing of large body areas should not be done except when the underlying condition makes it necessary to reduce the bacterial population of the skin</li> </ul>
Stop use and ask a doctor if irritation, sensitization or allergic reaction occurs. These may be signs of a serious condition.
Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

Page 4

Page 1

<i>Peel here for Drug Facts</i> ➔	
NDC 17187-1021-2	
<b>DYNA-HEX2<sup>®</sup></b> (Chlorhexidine Gluconate 2% Solution) <b>Antiseptic</b>	
Contains:	2% Chlorhexidine Gluconate
Manufactured By:	Xttrium Laboratories, Inc. 415 West Pershing Road Chicago, IL 60609
<b>FOR EXTERNAL USE ONLY</b>	
Net Contents:	4 fl oz (118 mL)
Lot Number:	
Exp. Date:	

**PROTOTYPE : 4 ounce container label**

(Also used this prototype for 8 ounce container label.)

<b>Drug Facts (continued)</b>		<b>Laminate Flap</b>
<p><b>Directions</b></p> <p><b>Surgical hand scrub:</b> • wet hands and forearms under running water for 30 seconds. Clean fingernails using a nailstick or similar cleaner. • scrub for 1.5 minutes with about 8 ml of product with or without a wet brush, paying close attention to the nails, cuticles, and skin between the fingers</p> <p>• rinse thoroughly under running water for 30 seconds • wash for an additional 1.5 minutes with 8 ml of product and rinse under running water for 30 seconds • dry thoroughly</p> <p><b>Healthcare personnel handwash:</b> • wet hands with water • dispense about 5 ml of product into cupped hands and wash in a vigorous manner for 15 seconds • rinse and dry thoroughly</p> <p><b>Patient preoperative skin preparation:</b> • apply product liberally to surgical site and swab for at least 2 minutes • dry with a sterile towel</p> <p>• repeat procedure for an additional 2 minutes and dry with a sterile towel</p> <p><b>Skin wound and general skin cleansing:</b> • thoroughly rinse the area to be cleaned with water • apply the minimum amount of product necessary to cover the skin or wound area and wash gently • rinse again thoroughly</p>		
<p><b>Other information</b> • store at 20-25°C (68-77°F) • avoid excessive heat above 40°C (104°F)</p>		
<p><b>Inactive ingredients</b> _____</p>		
<p><b>Questions or comments?</b> Call 1-773-268-5800 Monday through Friday 8:00 AM to 4:30 PM</p>		

**APPEARS THIS WAY  
ON ORIGINAL**

**PROTOTYPE: 16 ounce container label**  
**(Also use this prototype for 1 gallon container label.)**

NDC 17187-1021-3

**DYNA-HEX 2®**  
**(Chlorhexidine Gluconate 2% Solution)**  
**Antiseptic**

**Contains:** 2% Chlorhexidine Gluconate  
**Manufactured By:** Xttrium Laboratories, Inc.  
 415 West Pershing Road  
 Chicago, IL 60609

**FOR EXTERNAL USE ONLY**

**Lot Number:**  
**Exp. Date:**

**Net Contents: 16 fl oz (1 pt) (473 mL)**

<b>Drug Facts</b>	
<p><b>Active ingredient</b>                      chlorhexidine gluconate 2% solution.....</p>	<p><b>Purposes</b>                      .....surgical hand scrub                      healthcare personnel handwash                      patient preoperative skin preparation                      skin wound and general skin cleansing</p>
<p><b>Uses</b></p> <ul style="list-style-type: none"> <li>• <b>surgical hand scrub:</b> significantly reduces the number of microorganisms on the hands and forearms prior to surgery or patient care</li> <li>• <b>healthcare personnel handwash:</b> helps reduce bacteria that potentially can cause disease</li> <li>• <b>patient preoperative skin preparation:</b> preparation of the patient's skin prior to surgery</li> <li>• <b>skin wound and general skin cleansing</b></li> </ul>	

**PROTOTYPE: 16 ounce container label continued.**

**(Also use this prototype for 1 gallon container label.)**

<b>Drug Facts</b> (continued)
<b>Warnings</b>
<b>For external use only</b>
Do not use • if you are allergic to chlorhexidine gluconate or any other ingredients • in contact with meninges • in the genital area • as a preoperative skin preparation of the head or face
<b>When using this product</b>
• keep out of eyes, ears, and mouth. May cause serious and permanent eye injury if placed or kept in the eye during surgical procedures or may cause deafness when instilled in the middle ear through perforated eardrums • if solution should contact these areas, rinse out promptly and thoroughly with water • wounds which involve more than the superficial layers of the skin — not be routinely treated • repeated general skin cleansing of large body areas should not be done except when the underlying condition makes it necessary to reduce the bacterial population of the skin
<b>Stop use and ask a doctor if:</b> irritation, sensitization or allergic reaction occurs. These may be signs of a serious condition.
<b>Keep out of reach of children.</b> If swallowed, get medical help or contact a Poison Control Center right away.
<b>Directions</b>
<b>Surgical hand scrub:</b> • wet hands and forearms under running water for 30 seconds. Clean fingernails using a nailstick or similar cleaner. • scrub for 1.5 minutes with about 8 ml of product with or without a wet brush, paying close attention to the nails, cuticles, and skin between the fingers • rinse thoroughly under running water for 30 seconds • wash for an additional 1.5 minutes with 8 ml of product and rinse under running water for 30 seconds • dry thoroughly
<b>Healthcare personnel handwash:</b> • wet hands with water • dispense about 5 ml of product into cupped hands and wash in a vigorous manner for 15 seconds • rinse and dry thoroughly
<b>Patient preoperative skin preparation:</b> • apply product liberally to surgical site and swab for at least 2 minutes • dry with a sterile towel • repeat procedure for an additional 2 minutes and dry with a sterile towel
<b>Skin wound and general skin cleansing:</b> • thoroughly rinse the area to be cleaned with water • apply the minimum amount of product necessary to cover the skin or wound area and wash gently • rinse again thoroughly
<b>Other information</b> • store at 20-25°C (68-77°F) • avoid excessive heat above 40°C (104°F)
<b>Inactive ingredients</b>
<b>Questions or comments?</b> Call 1-773-268-5800 Monday through Friday 8:00 AM to 4:30 PM

**PROTOTYPE: 30 ounce container label**  
**(Also use this prototype for 32 ounce container label.)**

NDC 0116-4242-30

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**DYNA-HEX 2<sup>®</sup>**  
**(Chlorhexidine Gluconate 2% Solution)**  
**Antiseptic**

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Contains:	2% Chlorhexidine Gluconate
Manufactured By:	Xtrium Laboratories, Inc. 415 West Pershing Road Chicago, IL 60609

**FOR EXTERNAL USE ONLY**

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30 fl oz (887 mL)

Lot Number:  
Exp. Date:

PROTOTYPE: 30 ounce container label continued.

(Also use this prototype for 32 ounce container label.)

<b>Drug Facts</b>	
<b>Active ingredient</b> chlorhexidine gluconate 2% solution.....	<b>Purposes</b> surgical hand scrub healthcare personnel handwash patient preoperative skin preparation skin wound and general skin cleansing
<b>Uses</b>	
<ul style="list-style-type: none"> <li>• surgical hand scrub: significantly reduces the number of microorganisms on the hands and forearms prior to surgery or patient care</li> <li>• healthcare personnel handwash: helps reduce bacteria that potentially can cause disease</li> <li>• patient preoperative skin preparation: preparation of the patient's skin prior to surgery</li> <li>• skin wound and general skin cleansing</li> </ul>	
<b>Warnings</b>	
<b>For external use only</b>	
Do not use • if you are allergic to chlorhexidine gluconate or any other ingredients	
• in contact with meninges • in the genital area • as a preoperative skin preparation of the head or face	
<b>When using this product</b>	
<ul style="list-style-type: none"> <li>• keep out of eyes, ears, and mouth. May cause serious and permanent eye injury if placed or kept in the eye during surgical procedures or may cause deafness when instilled in the middle ear through perforated eardrums</li> <li>• if solution should contact these areas, rinse out promptly and thoroughly with water</li> <li>• wounds which involve more than the superficial layers of the skin — not be routinely treated</li> <li>• repeated general skin cleansing of large body areas should not be done except when the underlying condition makes it necessary to reduce the bacterial population of the skin</li> </ul>	
Stop use and ask a doctor if irritation, sensitization or allergic reaction occurs. These may be signs of a serious condition.	
Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.	
<b>Directions</b>	
Surgical hand scrub: • wet hands and forearms under running water for 30 seconds. Clean fingernails using a nailstick or similar cleaner.	
• scrub for 1.5 minutes with about 8 ml of product with or without a wet brush paying close attention to the nails, cuticles, and skin between the fingers	
• rinse thoroughly under running water for 30 seconds	
• wash for an additional 1.5 minutes with 8 ml of product and rinse under running water for 30 seconds	
• rinse and dry thoroughly	
Healthcare personnel handwash: • wet hands with water	
• dispense about 5 ml of product into cupped hands and wash in a vigorous manner for 15 seconds	
• dry thoroughly	
Patient preoperative skin preparation: • apply product liberally to surgical site and swab for at least 2 minutes	
• dry with a sterile towel	
• repeat procedure for an additional 2 minutes and dry with a sterile towel	
Skin wound and general skin cleansing: • thoroughly rinse the area to be cleaned with water	
• apply the minimum amount of product necessary to cover the skin or wound area and wash gently	
• rinse again thoroughly	
<b>Other information</b> • store at 20-25°C (68-77°F) • avoid excessive heat above 40°C (104°F)	
<b>Inactive ingredients</b> _____	
<b>Questions or comments?</b> Call 1-773-268-5800 Monday through Friday 8:00 AM to 4:30 PM	

cc:

NDA: 19-422

HFD-560:CGanley

HFD-560:CRosebraugh

HFD-560:DLumpkins

HFD-560:MJackson

HFD-560:TFrazier

R/D: MJackson: 4/14/03

Rev: DLumpkins: 6/9; 6/16/03

Rev: MJackson: 6/11; 6/17/03

19-422-SE8-032-AL.doc

Division of OTC Drug Products Labeling Review

NDA 19-422 SE8-032/BL

Submission Date: August 30, 2002

Review Date: November 20, 2002

**Applicant:** Xttrium Laboratories, Inc.  
415 West Pershing Road  
Chicago, Illinois 60609

**Applicant's Representative:** Dr. Ram Chakroborty  
Vice President  
773-268-5800

**Drug:** Exidine 2 (chlorhexidine gluconate 2% solution)

**Pharmacologic Category:** Antiseptic

**Submitted:** Container labeling for Dyna-Hex 2 in 4 oz, 8 oz, 16 oz, 32 oz, and 1 gallon, and Allegiance 2 in a 30 oz size distributed by the sponsor

**Background:** On January 10, 2002, the sponsor submitted labeling in typewritten form in an efficacy supplement revising directions for use of the product as a surgical hand scrub, providing for two 1.5 minute scrubs rather than the previously approved two 3 minute scrubs. The revised directions recommend use of 8 mL of product per scrub, rather than 5 mL, and permitted for scrubbing without use of a scrub brush. By letter dated June 20, 2002, and by telephone conversation of August 28, 2002, the Agency notified the sponsor that original labeling and font specifications were needed for evaluation. In response, the sponsor submitted this supplement of its products consisting of five labeling sizes of Dyna-Hex 2 and one distributor label for Allegiance 2.

**Reviewer's comments:** Strikethrough for deletion; redline for addition for labeling in general followed by specific recommendations for labels on each of the individual products.

13 page(s) of draft  
labeling has been  
removed from this  
portion of the review.

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This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.  
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/s/

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Michael Benson  
11/20/02 02:20:44 PM  
INTERDISCIPLINARY

Debbie Lumpkins  
11/20/02 02:39:07 PM  
INTERDISCIPLINARY