Executive CAC
Date of Meeting: July 22, 2008

Committee: David Jacobson-Kram, Ph.D., OND IO, Chair
Abby Jacobs, Ph.D., OND IO, Member
Paul Brown, Ph.D., OND IO, Member
Barbara Hill, Ph.D., DDDP, Team Leader
Jiaqin Yao, Ph.D., DDDP, Presenting Reviewer

Author of Draft: Jiaqin Yao, Ph.D.

The following information reflects a brief summary of the Committee discussion and its recommendations. Detailed study information can be found in the individual review.

b(4)

NDA: 50-819
Drug Name: Acanya ——— Gel (IDP-110 Gel)
Sponsor: Dow Pharmaceuticals

Background:

The original IND (41,733) was submitted by Glaxo Dermatology and then was transferred to the current Sponsor. The Sponsor submitted an ANDA [65,443, ——— (1/5)] using the already marketed BenzaClin (clindamycin 1% - benzoyl peroxide 5%) Gel as the reference drug. The formulation for Acanya ——— Gel (1/2.5) is different from that for ——— (1/5), which was tested in the two carcinogenicity studies. In addition to the reduced concentration of benzoyl peroxide from 5% to 2.5% and the ——— concentration of propylene glycol from ——— , Acanya ——— Gel has Carbomer 980 instead of ——— and Carbomer ——— The sponsor plans to rely on a clinical bridge with BenzaClin and ——— (1/5) and the safety data generated from the ——— (1/5) Gel to support this NDA filing [505(b)(2)] for the Acanya ——— Gel (1/2.5).

b(4)

Rat Oral Carcinogenicity Study:

Seven groups of 62 male and 62 female ——— CD(SD)IGS BR rats were treated via gavage with 0.3, 0.9, or 3.0 mL/kg/day Admixture Active Gel (——— , 0.9 or 3.0 mL/kg/day Benzoyl Peroxide 5% Gel, OR 0.9 or 3.0 mL/kg/day Clindamycin Phosphate 1% Gel for up to 97 weeks. Two additional control groups were treated with the Placebo Gel at 3.0 mL/kg/day as the test articles. The study was terminated at Week 97 due to mortality. No range finding data were available for this study and the adequacy of the study was discussed based on the toxicity.. A maximum tolerated dose appeared to have been achieved based on differences in body weights (i.e., decrease of approximately 10%) in males and females in groups treated with the high dose of Admixture Active Gel or Clindamycin Phosphate 1% Gel. Although there were some statistically significant differences in tumor incidence when control groups 1 and 2 were compared to the various treated groups, it appears that these differences were not biologically significant, due to either no trend with increasing dose or no difference from one of the placebo controls.

b(4)

Mouse Dermal Carcinogenicity Study:

Seven groups of 60 male and 60 female CD-1 mice were treated topically with 0.9, 2.7, or 15 mL/kg/day Admixture Active Gel (——— , 2.7 or 15 mL/kg/day Benzoyl Peroxide 5% Gel, or 2.7 or 15 mL/kg/day Clindamycin Phosphate 1% Gel for 2 years. Two additional control

b(4)

groups were treated with the Placebo Gel at 15 mL/kg/day as the test articles. No range finding data were available for this study and the adequacy of the study was based on dermal effects. A maximum tolerated dose appeared to have been achieved since animals in the high dose groups exhibited hyperkeratosis and epithelial hyperplasia at the treated site. Although there were some statistically significant differences in tumor incidence when control groups were compared to the various treated groups, it appears that these differences were not biologically significant, due to either no trend with increasing dose or no difference from one of the placebo controls.

Executive CAC Recommendations and Conclusions:

Rat:

- The Committee agreed that the study was acceptable, although not optimal.
- The Committee concurred that there were no drug-related neoplasms in this study

Mouse:

- The Committee agreed that the study was acceptable, although not optimal.
- The Committee concurred that there were no drug-related neoplasms in this study
- The Committee noted that another formulation by another sponsor, using the same active ingredients, caused drug-related skin neoplasms in a 2-year rat dermal carcinogenicity study.

David Jacobson-Kram, Ph.D.
Chair, Executive CAC

cc:\
/Division File, DDDP
Barbara Hill/HillB/Team leader, DDDP
Jiaqin Yao/YaoJ/Reviewer, DDDP
Tamika White/WhiteTA/CSO/PM, DDDP
Adele Seifried/ASeifried, OND IO

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/s/

David Jacobson-Kram
7/23/2008 03:00:58 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-819

Dow Pharmaceutical Sciences, Inc.
Attention: Barry M. Calvarese, M.S.
Vice President, Regulatory & Clinical Affairs
1330 Redwood Way
Petaluma, CA 94954-7121

Dear Mr. Calvarese:

Please refer to your December 21, 2007 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRADENAME /——— Gel (clindamycin phosphate 1.2%, benzoyl peroxide 2.5%). b(4)

We have reviewed your request for proposed trade name " —— and have the following comments and information requests. b(4)

We object to your proposed trade name " —— because it is vulnerable to name confusion that could lead to medication errors with Elocon, Cleocin T, and Ala-Quin. b(4)

Your proposed second choice trade name "Acanya" is currently under review. We request that you submit at least one additional new trade name for consideration as soon as possible.

We have also reviewed your label, labeling and packaging for the product and have the following requests.

1. General Comment

   Revise the active ingredients and corresponding product strengths to read as follows throughout the labels and labeling:

   TRADENAME
   (clindamycin phosphate and benzoyl peroxide gel)
   1.2 %/ 2.5 %

   or

TRADENAME

clindamycin phosphate 1.2 %
and
benzoyl peroxide 2.5 %

2. Trade Container Label and Carton Label

   a. Delete the graphic of the face to increase the available label area to increase the size of text and inclusion of other important information.

   b. Insert an area on the label and labeling that allows for inclusion of the 3 month expiration after pharmacist admixture of the product.

   c. [redacted] b(4)

3. Professional Sample Container Label

   Delete the graphic of the face from the container lid label to increase the available label area to increase the size of text and inclusion of other important information.

4. Clindamycin Vial Label

   Increase the prominence of the statements "For external use only" and "Not for separate dispensing".

5. Package Insert

   Delete all trailing zeros from numerical designations throughout the text as trailing zeros can often lead to confusion.

If you have any questions, call Tamika White, Regulatory Project Manager, at 301-796-0310.

Sincerely,

{See appended electronic signature page}

Bronwyn Collier
Acting Supervisor, Project Management Staff
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Bronwyn Collier
7/18/2008 09:22:11 AM

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: July 1, 2008

To: Barry M. Calvarese, MS, Vice President, Regulatory and Clinical Affairs	**From:** Tamika White, Regulatory Project Manager
Company: Dow Pharmaceutical Sciences, Inc.	Division of Dermatology and Dental Products
Fax number: 707-793-0145	**Fax number:** 301-796-9895
Phone number: 707-793-2600 x601	**Phone number:** 301-796-2110

Subject: NDA 50-819 Information Requests

Total no. of pages including cover: 3

Comments:

Review the attached request for information and respond no later than 3:00 p.m. on July 9, 2008.

Document to be mailed: ☐ YES ☑ NO

NDA 50-819

Please refer to your December 21, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [redacted] Jel (1.2% clindamycin phosphate, 2.5% benzoyl peroxide). b(4)

We are reviewing your submission and have the following nonclinical and clinical information requests.

1. [redacted] major degradation products of clindamycin phosphate, [redacted] have been identified and may be a potential safety concern for the drug product. Provide the amount of the [redacted] degradants in test materials tested in nonclinical and clinical studies. In addition, provide any nonclinical information available for these degradants as well as an integrated safety summary for these degradants from the literature. b(4)

2. Provide the location in the NDA for the 1% clindamycin phosphate solution/5% benzoyl peroxide gel combination formulation and batch number(s) used in contact/sensitization study Protocol No. CLN-101, Besselaar Study #9145. If this information was not included in the NDA, please provide.

3. Is the 1% clindamycin phosphate/5% BP gel combination formulation referenced above the "final-to-be-marketed" formulation for the submitted ANDA?

We request receipt of your written response no later than 3:00 p.m. on July 9, 2008.

If you have any questions, call Tamika White, Regulatory Project Manager, at 301-796-0310.

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/s/

Tamika White
7/1/2008 03:01:08 PM
CSO

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: June 9, 2008

To: Barry M. Calvarese, MS, Vice President, Regulatory and Clinical Affairs	**From:** Tamika White, Regulatory Project Manager
Company: Dow Pharmaceutical Sciences, Inc.	Division of Dermatology and Dental Products
Fax number: 707-793-0145	**Fax number:** 301-796-9895
Phone number: 707-793-2600 x601	**Phone number:** 301-796-0310

Subject: NDA 50-819 Chemistry Information Request

Total no. of pages including cover: 3

Comments:

Review the attached request for information and respond no later than 3:00 p.m. on June 23, 2008.

Document to be mailed: ☐ YES ☑ NO

NDA 50-819

Please refer to your December 21, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [redacted] Gel (1.2% clindamycin phosphate, 2.5% benzoyl peroxide). b(4)

We are reviewing your submission and have the following CMC information requests.

1. Upon the review of your Executed Batch Record, it is noted that [redacted] is used in the manufacture of benzoyl peroxide gel and clindamycin phosphate solution batches without a justification. Use of [redacted] is not appropriate. Provide justification. b(4)

2. Provide results of USP <661> testing on both the jar and bottle.

3. Provide a Letter of Authorization from [redacted] and their DMF number to review the CMC information pertaining to the [redacted]. b(4)

4. Establish acceptance criterion for microbial limit testing USP <61> for the compounded gel product.

5. Tighten the acceptance criteria for benzoyl peroxide, total clindamycin content, and clindamycin phosphate content to [redacted]. We recognize that your product may not be stable under room temperature storage conditions to meet the recommended tightened acceptance criteria; therefore, we recommend that the trade and physician's samples be stored at [redacted] In addition, limits for individual and total degradants for clindamycin should be tightened accordingly based on results of 5^0C stability studies. Propose tightened acceptance criteria for these degradants. b(4)

We request receipt of your written response no later than 3:00 p.m. on June 23, 2008.

If you have any questions, call Tamika White, Regulatory Project Manager, at 301-796-0310.

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/s/

Tamika White
6/9/2008 09:43:17 AM
CSO

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Office of Drug Evaluation ODEIII

FACSIMILE TRANSMITTAL SHEET

DATE: April 24, 2008

To: Barry M. Calvarese, MS, Vice President, Regulatory and Clinical Affairs	**From:** Tamika White, Regulatory Project Manager
Company: Dow Pharmaceutical Sciences, Inc.	Division of Dermatology and Dental Products
Fax number: 707-793-0145	**Fax number:** 301-796-9894/9895
Phone number: 707-793-2600 x601	**Phone number:** 301-796-2110

Subject: NDA 50-819 Chemistry Information Request

Total no. of pages including cover: 3

Comments:

Review the attached request for information and respond no later than 3:00 p.m. on May 8, 2008.

Document to be mailed: ☐ YES ☑ NO

NDA 50-819

Please refer to your December 21, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [redacted] Gel (1.2% clindamycin phosphate, 2.5% benzoyl peroxide). b(4)

We are reviewing your submission and have the following CMC information requests.

1. As stated in meetings dated September 18, 2006 and November 27, 2007, provide a comparative in-vitro release testing of the two products ([redacted]

2. As stated in the September 18, 2006 meeting, provide the results of photostability testing of clindamycin phosphate solution, benzoyl peroxide gel, and the combination product.

3. Update the application with any additional stability data as soon as possible.

4. Provide the following:

   a) Information on the type of samples [redacted] used in the clinical trial.
   b) Ages of the drug product samples used in the clinical trials.
   c) Storage conditions of samples prior to their use in the clinical trials.

We request receipt of your written response no later than 3:00 p.m. on May 8, 2008.

If you have any questions, call Tamika White, Regulatory Project Manager, at 301-796-2110.

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/s/

Tamika White
4/24/2008 04:00:14 PM
CSO