US Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmacoepidemiology and Statistical Science
Office of Biostatistics

Statistical Review and Evaluation Addendum

New Drug Application

Clinical Studies

NDA/Serial Number:	50-819
Drug Name:	IDP-110
Indication(s):	Acne vulgaris
Applicant:	Dow Pharmaceutical Sciences
Dates:	Submitted: December 26, 2007
	PDUFA: October 24, 2008
Review Priority:	Standard
Biometrics Division:	Division of Biometrics III
Statistics Reviewer:	Mat Soukup, Ph.D.
Concurring Reviewer:	Mohamed Alosh, Ph.D.
Medical Division:	Division of Dermatology and Dental Products
Clinical Team:	Brenda Vaughan, M.D./Markham Luke, M.D., Ph.D.
Project Manager:	Tamika White
Keywords:	Acne vulgaris, combination product

Background and Revisions

The original statistical review of NDA 50-819 by Dr. Clara Kim was signed and archived in DFS on July 29, 2008. In the original review there were some typographical errors in Table 13 (page 20 of the original review) in which the table stated that the numbers in the table corresponded to the absolute change when in fact they corresponded to percent changes with the standard deviation included in parentheses.

The following table is intended to replace Table 13 of the original review.

Table 1: Secondary Endpoint Analysis - Mean Percent Change in Lesion Count (ITT)

	Study 012			
	IDP-110 n=399	Clindamycin n=408	BPO n=406	Vehicle n=201
Inflammatory lesions				
Mean percent change (SD)	55.0 (39.9)	47.1 (39.1)	49.3 (36.5)	34.5 (43.8)
p-value†	NA	0.001	0.013	<0.001
Non-inflammatory lesions				
Mean percent change (SD)	45.3 (38.8)	38.0 (37.3)	40.2 (37.9)	43.8 (41.7)
p-value†	NA	0.002	0.037	<0.001

	Study 017			
	IDP-110 n=398	Clindamycin n=404	BPO n=403	Vehicle n=194
Inflammatory lesions				
Mean percent change (SD)	54.2 (39.1)	45.3 (44.0)	45.7 (43.8)	23.3 (52.2)
p-value†	NA	0.002	0.002	<0.001
Non-inflammatory lesions				
Mean percent change (SD)	41.2 (37.8)	34.3 (41.4)	34.5 (42.0)	19.2 (44.6)
p-value†	NA	0.013	0.019	<0.001

† P-values were calculated using ANCOVA with the respective baseline lesion count as covariate and treatment, analysis center, dichotomized skin type, and baseline severity as factors. Each arm was tested against IDP-110.

Missing values were imputed using LOCF.

Source: Study Report DPSI-06-22-2006-012, pg. 194-195; Study Report DPSI-06-22-2006-017, pg. 193-194; and Reviewer analysis.

Signatures/Distribution List

Primary Statistical Reviewer: Mat Soukup, Ph.D.
Date: October 7, 2008

Statistical Team Leader: Mohamed Alosh, Ph.D.

cc:
Archival NDA
DDDP/Walker
DDDP/Kukich
DDDP/Luke
DDDP/Vaughan
DDDP/White
OBIO/Patrician
DBIII/Wilson
DBIII/Alosh
DBIII/Soukup
October 7, 2008

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/s/

Matt Soukup
10/7/2008 10:16:31 AM
BIOMETRICS

Mohamed Alosh
10/7/2008 10:32:29 AM
BIOMETRICS

Statistical Review and Evaluation
Fileability Review

NDA:	50-819	b(4)
Name of Drug:	[redacted] Gel	
Applicant:	Dow Pharmaceutical Sciences, Inc.	
Indication:	Treatment of [redacted] acne vulgaris	b(4)
Filing Date:	February 22, 2008	
Fileability Meeting Date:	February 13, 2008	
User Fee Date:	October 26, 2008	
Statistical Reviewer:	Clara Y. Kim, Ph.D., DB3	
Clinical Reviewer:	Brenda Vaughan, M.D., DDDP	

Clinical Studies: DPSI-06-22-2006-012
DPSI-06-22-2006-017

I. ORGANIZATION AND DATA PRESENTATION	YES/NO/NA
A. Is there a comprehensive table of contents with adequate indexing and pagination?	Yes
B. Are the original protocols, protocol amendments, and proposed label provided?	Yes
C. Are the following tables/listings provided in each study report?	Yes
1. Patient profile listings by center, for all enrolled patients.	Yes
2. Discontinued subject tables by center (includes reason and time of loss).	Yes
3. Subgroup analysis summary tables (gender, age, race, etc.)	Yes
4. Adverse event listings by center and time of occurrence.	Yes
D. Have the data been submitted electronically?	Yes
1. Has adequate documentation of the data sets been provided?	Yes
2. Do the data appear to accurately represent the data described in the study reports?	Yes
3. Can the data be easily merged across studies and indications?	No (Information requested)

II. STATISTICAL METHODOLOGY	YES/NO/NA
A. Are all primary efficacy studies of appropriate design to meet basic approvability requirements within current Division policy, or to the extent agreed upon previously with the sponsor by the Division?	Yes
B. For each study, is there a comprehensive statistical summary of the efficacy analyses which covers the intent-to-treat population and per protocol population?	Yes
C. Based on the summary analyses of each study,	
1. Are the analyses appropriate for the type of data collected, the study design, and the study objectives (based on protocol objectives and proposed labeling claims?)	Yes
2. Are the intent-to-treat and per protocol patient analyses properly performed?	Yes
3. Has missing data been appropriately handled?	Yes
4. Have multiplicity issues (regarding endpoints, timepoints, or dose groups) been adequately addressed?	NA
5. If interim analyses were performed, were they planned in the protocol and appropriate significance level adjustments made?	NA
D. Were sufficient and appropriate references included for novel statistical approaches?	NA
E. Are all of the pivotal studies complete?	Yes
F. Has the safety data been comprehensively and adequately summarized?	Yes

III. FILEABILITY CONCLUSIONS

From a statistical perspective this submission, or indications therein, **is** reviewable with only minor further input from the sponsor.

IV. 74-DAY LETTER COMMENTS

The following Information Request was faxed to the sponsor on February 7, 2008. The sponsor submitted adequate information regarding this request on February 12, 2008.

Request for Information:

You submitted dataset titled "Analysis Dataset Subject Level" (ADSL.xpt) for both studies: DPSI-06-22-2006-012 and DPSI-06-22-2006-017. However, these datasets do not include a unique subjects ID number for each subject. It appears that the last digit in Variable USUBJID is missing. This is shown in the following example of the identification numbers that were included in ADSP.xpt (Study DPSI-06-22-2006-012).

Obs	INVID	SUBJID	USUBJID
1	11	2	01100
2	11	3	01100
3	11	5	01100
4	11	7	01100
5	11	11	01101
6	11	15	01101
7	11	16	01101
8	11	18	01101
9	11	19	01101
10	11	21	01102
11	11	22	01102

The Division requests that you provide datasets that include the full USUBJID variable.

Clara Kim, Ph.D.
Mathematical Statistician, Biometrics III

Concur: Mohamed Alosh, Ph.D.
Team Leader, Biometrics III

cc:
Archival NDA 50-819
DDDP/Walker
DDDP/Kukich
DDDP/Luke
DDDP/Vaughan
DDDP/White
OBIO/Patrician
DBIII/Wilson
DBIII /Alosh
DBIII /Kim

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/s/

Clara Kim
2/13/2008 10:26:19 AM
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Mohamed Alosh
3/24/2008 04:39:54 PM
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