

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

50-802

**ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS**

14.0 PATENT CERTIFICATION

Paragraph II Certification

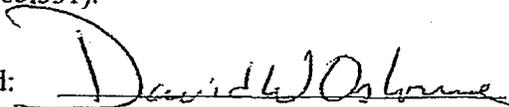
The sponsor, Dow Pharmaceutical Sciences, Inc., seeks marketing approval of Ziana in the treatment of acne vulgaris via a 505(b)(2) application.

Ziana is protected under two issued and effective US patents. The first is patent No. 6,387,383 B1 issued May 14, 2002. Since the patent was filed on August 3, 2000 and does not claim priority from any earlier filed application, the expiration date will be August 3, 2020. Ziana is further protected under US Patent No. 5,721,275 issued February 24, 1998. The expiration date of this second patent will be February 24, 2015.

To the best of DPSI knowledge, any other patents relating to clindamycin gel or tretinoin gel have expired and Ziana does not infringe on any existing patents.

Pursuant to 21 CFR 314.108, Ziana also qualifies for three (3) years of exclusivity, since a clinical investigation was essential in showing the effectiveness of Ziana in a once-a-day application for the treatment of acne vulgaris and the clinical investigation was conducted by the Sponsor (as per IND #65,531).

Signed:



Date:

10/18/06

David Osborne, Ph.D.
Vice President
Product Development

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On Original**

14.0 PATENT CERTIFICATION

The sponsor, Dow Pharmaceutical Sciences, Inc., seeks marketing approval of Clin RA gel in the treatment of acne vulgaris via a 505(b)(2) application.

Clin RA gel is protected under two issued and effective US patents. The first is patent No. 6,387,383 B1 issued May 14, 2002. Since the patent was filed on August 3, 2000 and does not claim priority from any earlier filed application, the expiration date will be August 3, 2020. Clin RA is further protected under US Patent No. 5,721,275 issued February 24, 1998. The expiration date of this second patent will be February 24, 2015.

In the opinion and to the best knowledge of Dow Pharmaceutical Sciences, Inc. with the exception of the two aforementioned patents, there are no patents that claim the drug or drugs on which the investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

Pursuant to 21 CFR 314.108, Clin RA also qualifies for three (3) years of exclusivity, since a clinical investigation was essential in showing the effectiveness of Clin RA in a once-a-day application for the treatment of acne vulgaris and the clinical investigation was conducted by the Sponsor (as per IND #65,531).

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Department of Health and Human Services Food and Drug Administration		Form Approved: OMB No. 0910-0513 Expiration Date: 07/31/06 See OMB Statement on Page 3.	
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT <i>For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use</i>		NDA NUMBER 050802	
		NAME OF APPLICANT / NDA HOLDER Dow Pharmaceutical Sciences, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME) Clin RA			
ACTIVE INGREDIENT(S) Clindamycin Tretinoin		STRENGTH(S) 1 w/w% 0.025 w/w%	
DOSAGE FORM Topical Gel			
<p>This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.</p>			
<p>For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.</p>			
<p>FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.</p>			
<p>For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.</p>			
1. GENERAL			
a. United States Patent Number 6,387,383B1		b. Issue Date of Patent 5/14/2002	c. Expiration Date of Patent 8/3/2020
d. Name of Patent Owner Dow Pharmaceutical Sciences, Inc.		Address (of Patent Owner) 1330 Redwood Way	
		City/State Petaluma, CA	
		ZIP Code 94954	FAX Number (if available) 707-793-0145
		Telephone Number 707-793-2600	E-Mail Address (if available)
e. <u>Name of agent or representative</u> who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) 		Address (of agent or representative named in 1.e.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No 			
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No 			

<p><i>For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.</i></p>	
<p>2. Drug Substance (Active Ingredient)</p>	
2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	<input type="checkbox"/> Yes <input type="checkbox"/> No
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.	
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
2.6 Does the patent claim only an intermediate?	
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	
<input type="checkbox"/> Yes <input type="checkbox"/> No	
<p>3. Drug Product (Composition/Formulation)</p>	
3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
3.2 Does the patent claim only an intermediate?	
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	
<input type="checkbox"/> Yes <input type="checkbox"/> No	
<p>4. Method of Use</p> <p><i>Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:</i></p>	
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
4.2 Patent Claim Number (as listed in the patent) 18-23, 30, 31	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?
	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.) Indication: Acne Vulgaris Directions: Apply to affected areas once daily at bedtime.
<p>5. No Relevant Patents</p> <p>For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.</p>	
<input type="checkbox"/> Yes	

6. Declaration Certification

6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed



5-4-06

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Barry Calvarese, VP Clinical and Regulatory Affairs	
Address 1330 Redwood Way	City/State Petaluma, CA
ZIP Code 94954	Telephone Number 707-793-2600
FAX Number (if available) 707-793-0145	E-Mail Address (if available)

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
 CDER (HFD-007)
 5600 Fishers Lane
 Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

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Department of Health and Human Services Food and Drug Administration		Form Approved: OMB No. 0910-0513 Expiration Date: 07/31/06 See OMB Statement on Page 3.	
PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT <i>For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use</i>		NDA NUMBER 050802	
		NAME OF APPLICANT / NDA HOLDER Dow Pharmaceutical Sciences, Inc.	
<i>The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.</i>			
TRADE NAME (OR PROPOSED TRADE NAME) ClinRA			
ACTIVE INGREDIENT(S) Clindamycin Tretinoin		STRENGTH(S) 1 w/w% 0.025 w/w%	
DOSAGE FORM Topical Gel			
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.			
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For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.			
1. GENERAL			
a. United States Patent Number 5,721,275		b. Issue Date of Patent 2/24/1998	c. Expiration Date of Patent 2/24/2015
d. Name of Patent Owner Gail Bazzano		Address (of Patent Owner) 4506 Avron Blvd.	
		City/State Metairie, LA	
		ZIP Code 70006	FAX Number (if available)
		Telephone Number 504-296-6618	E-Mail Address (if available) gailbazz@aol.com
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)		Address (of agent or representative named in 1.a.)	
		City/State	
		ZIP Code	FAX Number (if available)
		Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?		<input type="checkbox"/> Yes <input type="checkbox"/> No	

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.	
2. Drug Substance (Active Ingredient)	
2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	<input type="checkbox"/> Yes <input type="checkbox"/> No
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2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
2.6 Does the patent claim only an intermediate?	
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	
<input type="checkbox"/> Yes <input type="checkbox"/> No	
3. Drug Product (Composition/Formulation)	
3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	
<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	
3.2 Does the patent claim only an intermediate?	
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3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	
<input type="checkbox"/> Yes <input type="checkbox"/> No	
4. Method of Use	
<i>Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:</i>	
4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	
<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	
4.2 Patent Claim Number (as listed in the patent)	Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?
	<input type="checkbox"/> Yes <input type="checkbox"/> No
4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
5. No Relevant Patents	
For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.	
<input type="checkbox"/> Yes	

6. Declaration Certification	
<p>6.1 <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i></p> <p>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</p>	
<p>6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)</p> 	<p>Date Signed</p> <p>5-4-06</p>
<p>NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</p>	
<p>Check applicable box and provide information below.</p>	
<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
<p>Name Barry Calvarese, VP Clinical and Regulatory Affairs</p>	
<p>Address 1330 Redwood Way</p>	<p>City/State Petaluma, CA</p>
<p>ZIP Code 94954</p>	<p>Telephone Number 707-793-2600</p>
<p>FAX Number (if available) 707-793-0145</p>	<p>E-Mail Address (if available)</p>
<p>The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:</p> <p style="text-align: center;">Food and Drug Administration CDER (HFD-007) 5600 Fishers Lane Rockville, MD 20857</p> <p style="text-align: center;"><i>An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.</i></p>	
<p>Appears This Way On Original</p>	

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

21,739

NAME OF APPLICANT / NDA HOLDER

Dow Pharmaceutical Sciences

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

ClinRA

ACTIVE INGREDIENT(S)

Clindamycin
Tretinoin

STRENGTH(S)

1 w/w%
0.025 w/w%

DOSAGE FORM

Topical Gel

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

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FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

6,387,383B1

b. Issue Date of Patent

5/14/2002

c. Expiration Date of Patent

8/3/2020

d. Name of Patent Owner

Dow Pharmaceutical Sciences

Address (of Patent Owner)

1330A Redwood Way

City/State

Petaluma, CA

ZIP Code

94954

FAX Number (if available)

707.793.0145

Telephone Number

707.793.2600

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

Address (of agent or representative named in 1.e.)

City/State

ZIP Code

FAX Number (if available)

Telephone Number

E-Mail Address (if available)

Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

Drug Substance (Active Ingredient)

- 1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

Drug Product (Composition/Formulation)

- 1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
- 3.2 Does the patent claim only an intermediate? Yes No
- 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

- 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2 Patent Claim Number (as listed in the patent) 18-23, 30, 31 Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.

Use: (Submit indication or method of use information as identified specifically in the approved labeling.)
 Indication: Acne Vulgaris
 Directions: Apply to affected areas once daily at bedtime.

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in manufacture, use, or sale of the drug product. Yes

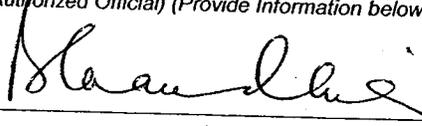
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6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed
2/5/2004



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Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Dow Pharmaceutical Sciences

Address

1330A Redwood Way

City/State

Petaluma, CA

ZIP Code

94954

Telephone Number

707.793.2600

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INFORMATION AND INSTRUCTIONS FOR FORM 3542a
PATENT INFORMATION SUBMITTED WITH THE FILING
OF AN NDA, AMENDMENT OR SUPPLEMENT

General Information

- To submit patent information to the agency the appropriate patent declaration form must be used. Two forms are available for patent submissions. The approval status of your New Drug Application will determine which form you should use.
- Form 3542a should be used when submitting patent information with original NDA submissions, NDA amendments and NDA supplements prior to approval.
- Form 3542 should be used after NDA or supplemental approval. This form is to be submitted within 30 days after approval of an application. This form should also be used to submit patent information relating to an approved supplement under 21 CFR 314.53(d) to change the formulation, add a new indication or other condition of use, change the strength, or to make any other patented change regarding the drug, drug product, or any method of use.
- Form 3542 is also to be used for patents issued after drug approval. Patents issued after drug approval are required to be submitted within 30 days of patent issuance for the patent to be considered "timely filed."
- Only information from form 3542 will be used for Orange Book Publication purposes.
- Forms should be submitted as described in 21 CFR 314.53. An additional copy of form 3542 to the Orange Book Staff will expedite patent publication in the Orange Book. The Orange Book Staff address (as of July 2003) is: Orange Book Staff, Office of Generic Drugs OGD/HFD-610, 7500 Standish Place, Rockville, MD 20855.
- The receipt date is the date that the patent information is date stamped in the central document room. Patents are considered listed on the date received.
- Additional copies of these forms may be downloaded from the Internet at: <http://forms.psc.gov/forms/fdahtm/fdahtm.html>.

First Section

Complete all items in this section.

1. General Section

Complete all items in this section with reference to the patent itself.

- 1c) Include patent expiration date, including any Hatch-Waxman patent extension already granted. Do not include any applicable pediatric exclusivity. The agency will include pediatric exclusivities where applicable upon publication.
- 1d) Include full address of patent owner. If patent owner resides outside the U.S. indicate the country in the zip code block.

- 1e) Answer this question if applicable. If patent owner and NDA applicant/holder reside in the United States, leave space blank.

2. Drug Substance (Active Ingredient)

Complete all items in this section if the patent claims the drug substance that is the subject of the pending NDA, amendment, or supplement.

- 2.4) Name the polymorphic form of the drug identified by the patent.
- 2.5) A patent for a metabolite of the approved active ingredient may not be submitted. If the patent claims an approved method of using the approved drug product to administer the metabolite, the patent may be submitted as a method of use patent depending on the responses to section 4 of this form.
- 2.7) Answer this question only if the patent is a product-by-process patent.

3. Drug Product (Composition/Formulation)

Complete all items in this section if the patent claims the drug product that is the subject of the pending NDA, amendment, or supplement.

- 3.3) An answer to this question is required only if the referenced patent is a product-by-process patent.

4. Method of Use

Complete all items in this section if the patent claims a method of use of the drug product that is the subject of the pending NDA, amendment, or supplement.

- 4.2) Identify by number each claim in the patent that claims the use(s) of the drug for which approval is being sought. Indicate whether or not each individual claim is a claim for a method(s) of use of the drug for which approval is being sought.
- 4.2a) Specify the part of the proposed drug labeling that is claimed by the patent.

5. No Relevant Patents

Complete this section only if applicable.

6. Declaration Certification

Complete all items in this section.

- 6.2) Authorized signature. Check one of the four boxes that best describes the authorized signature.

14.0 PATENT CERTIFICATION

The sponsor, Dow Pharmaceutical Sciences, seeks marketing approval of Clin-RA gel in the treatment of acne vulgaris via a 505(b)(2) application.

Clin-RA gel is protected under US Patent No. 6,387,383 B1, issued May 14, 2002. Since the patent was filed on August 3, 2000 and does not claim priority from any earlier filed application, the expiration date of the patent will be August 3, 2020. Pursuant to 21CFR 314.108, Clin-RA also qualifies for three (3) years of exclusivity, since a clinical investigation was essential in showing effectiveness of Clin-RA in a once-a-day application for the treatment of acne vulgaris and the clinical investigation was conducted by the sponsor (as per IND # 65,531).

Appears This Way
On Original

EXCLUSIVITY SUMMARY

NDA # 50802

SUPPL # N/A

HFD # 540

Trade Name ZIANA Gel

Generic Name clindamycin 1.2% and tretinoin 0.025%

Applicant Name Medicis, The Dermatology Company

Approval Date, If Known 11/07/06

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

three

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

Appears This Way
On Original

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 017579

Retin A Gel

NDA# 50615

Cleocin T Gel

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of

summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

MP-1501-02, phase 3 pivotal trial

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

Investigation #1

YES

Explain:

!
!

! NO

! Explain:

Investigation #2

YES

Explain:

!
!

! NO

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

Name of person completing form: Shalini Jain, PA-C

Title: Regulatory Project Manager

Date: 10/31/06

Name of Office/Division Director signing form: Susan Walker, M.D.

Title: Director, Division of Dermatology and Dental Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

EXCLUSIVITY SUMMARY FOR NDA # 50-802

SUPPL # _____

Trade Name TRADENAME Gel Generic Name clindamycin 1%, tretinoin 0.025%

Applicant Name Dow Pharmaceutical Sciences HFD # 540

Approval Date If Known _____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES / X / NO / ___ /

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES / X / NO / ___ /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES / X / NO / ___ /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3

e) Has pediatric exclusivity been granted for this Active Moiety?

YES / ___ / NO / X /

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES / ___ / NO / X /

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/
If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____

NDA# _____

NDA# _____

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES / X / NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 17-579 Retin A Gel

NDA# 20-475 Retin A Micro Gel

NDA# 50-537 Cleocin T Gel

NDA# 50-600 Cleocin T Gel

NDA# 50-615 Cleocin T Gel

NDA# 20-400 Avita Cream

NDA# 20-404 Avita Cream

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered ``NO'' for original approvals of new molecular entities.) IF ``YES'' GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES / X / NO / /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / X / NO / /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES / X / NO / ___ /

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES / ___ / NO / X /

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES / ___ / NO / X /

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

7001-G2HP-06-02

7001-G2HP-07-02

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied

on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 7001-G2HP-06-02 YES /___/ NO /X/

Investigation #2 7001-G2HP-07-02 YES /___/ NO /X/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /X/

Investigation #2 YES /___/ NO /X/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

7001-G2HP-06-02

7001-G2HP-07-02

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
IND # 65,531 _____ YES / X / ! NO / ___ / Explain: _____
!
!
Investigation #2 !
IND # 65,531 _____ YES / X / ! NO / ___ / Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study? N/A

Investigation #1 !
YES / ___ / Explain _____ ! NO / ___ / Explain _____
!
!
Investigation #2 !
YES / ___ / Explain _____ ! NO / ___ / Explain _____
!

!
!
!

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_X_/

If yes, explain: _____

Signature
Title:

Date

Signature of Office/
Division Director

Date

Form OGD-011347 Revised 05/10/2004

cc:

Archival NDA

HFD- /Division File

HFD- /RPM

HFD-610/Mary Ann Holovac

HFD-104/PEDS/T.Crescenzi

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

DA #: 50-802 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: May 6, 2006 PDUFA Goal Date: November 6, 2006

HFD 540 Trade and generic names/dosage form: ZIANA GEL (proposed)/ clindamycin phosphate 1.2% and
and tretinoin 0.025%

Applicant: Medicis Therapeutic Class: 3S

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- Yes. Please proceed to the next section. (Submission provides for new dosage form)
 No. PREA does not apply. Skip to signature block.

* SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.

Indication(s) previously approved (please complete this section for supplements only): N/A

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): one

Indication #1: acne vulgaris

Is this an orphan indication?

- Yes. PREA does not apply. Skip to signature block.
 No. Please proceed to the next question.

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
 No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
 Disease/condition does not exist in children
 Too few children with disease to study
 There are safety concerns
 Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min 0 kg _____ mo. _____ yr. 11 Tanner Stage _____

Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- X Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies (fill in applicable criteria below): 12 years and older

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Shalini Jain

Regulatory Project Manager

cc: NDA 50-802

HFD-960/ Rosemary Addy or Grace Carmouze

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG
DEVELOPMENT, HFD-960, 301-594-7337.
(revised 6-23-2005)**

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 21-739 Supplement Type (e.g. SE5): _____ Supplement Number: _____

HFD-540 Trade and generic names/dosage form: Clin-RA Gel (clindamycin/tretinoin)

Applicant: Dow Pharmaceuticals, Inc. Therapeutic Class: 3S

Indication(s) previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Treatment of Acne Vulgaris

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. 0 yr. 0 Tanner Stage _____
Max _____ kg _____ mo. 0 yr. 10 Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other:

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. 0 yr. 11 Tanner Stage _____
Max _____ kg _____ mo. 0 yr. 17 Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Jacquelyn Smith, M.A.
Regulatory Project Manager

cc: NDA

HFD-960/Grace Carmouze
(revised 12-22-03)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

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/s/

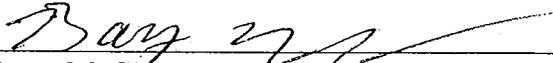
Brenda Carr
4/12/04 07:33:54 AM

Jonathan Wilkin
5/19/04 04:30:11 PM

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16.0 DEBARMENT CERTIFICATION

Dow Pharmaceutical Sciences herewith certifies that the services of any persons debarred under Section 306 (a) or (b) were not and will not be used in any capacity in conjunction with this application.

Signed: 
Barry M. Calvarese
Vice President
Regulatory and Clinical Affairs

Date: February 5, 2004

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Form 3454 Certification-Financial Interests and Arrangements of Clinical Investigators

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS	Form Approved: OMB No. 0910-0396 Expiration Date: February 28, 2006.
--	---

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

- (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	_____	

- (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

- (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME Barry Calvarese	TITLE VP, Regulatory and Clinical Affairs
FIRM / ORGANIZATION Dow Pharmaceutical Sciences, Inc.	
SIGNATURE 	DATE 4-27-06

Paperwork Reduction Act Statement

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Department of Health and Human Services
 Food and Drug Administration
 5600 Fishers Lane, Room 14C-03
 Rockville, MD 20857

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 Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

✓ Privacy (b6)

NDA 50-802
Ziana for Acne Vulgaris
Interdisciplinary Summary Memorandum

October 23, 2006

The Dermatology Clinical Team Leader (TL) concurs with the Primary Medical Officer clinical reviewer, Dr. Brenda Carr in recommending that Ziana (clindamycin phosphate 1.2% and tretinoin 0.025%) Gel for topical use only be approved for treatment of acne vulgaris.

The NDA submission dated May 6, 2006 is a Complete Response to a Not Approvable (NA) letter dated December 7, 2004 and adequately addresses the NA issues, namely "The contribution to efficacy of each component of your combination product was not adequately demonstrated. Specifically, the contribution of tretinoin to efficacy was not adequately demonstrated."

Efficacy

The original NDA submission of February 6, 2004 included information from two Phase 3 studies. Both of those studies demonstrated that Ziana Gel was superior in efficacy to the vehicle. As Ziana Gel is a combination product (containing both clindamycin and tretinoin active ingredients), a demonstration of the contribution of each of these components is required per 21 CFR 300.50. The two pivotal studies from the original NDA submission only demonstrated the contribution of clindamycin, but not tretinoin. Hence, the prior non-approval action.

In the submission of May 6, 2006, data from one additional study, Study MPI-02, with two arms, Ziana Gel and clindamycin in the gel vehicle, was provided. This trial enrolled 2010 subjects, 1008 were randomized to Ziana Gel and 1002 were randomized to clindamycin gel. The basic study design for this trial was discussed with the Agency and agreed upon via a Special Protocol Assessment reviewed in May of 2005.

In Study MPI-02, Ziana Gel achieved superiority over clindamycin gel in the primary efficacy endpoints of Investigator's Global Assessment (IGA), and both inflammatory and non-inflammatory lesion counts. The p-values for each of these assessments was <0.001. Please see the review by Dr. Mat Soukop, FDA Biostatistician for further details.

Safety

As is expected from a topical product containing tretinoin, local skin reactions are expected. These are evidenced in the clinical trial monitoring data for Ziana. The potential for teratogenicity with tretinoin is described in the labeling. However, systemic exposure of tretinoin is considered to be minimal due to the topical dosage form. In this regard, the labeling for Ziana is to be similar to other topical products that contain tretinoin.

Systemic adverse events that may correlate possibly to the use of an antibiotic such as clindamycin were few and are described in the labeling. These are considered for all topical clindamycin products, and as such, are not specific to this product.

Even though the review by Dr. Brenda Carr states that the applicant's proposed wording for the pregnancy category labeling is based on the Avita label, and the annotated labeling provided in the original 2004 submission references the Avita package insert for class labeling, that reliance is actually based on our previous finding of safety and efficacy for Retin-A Gel. Avita was actually a 505(b)(2) application that relied upon the Agency's previous finding of safety and efficacy for Retin-A Gel.

Labeling

Ziana Gel is the Division of Dermatology and Dental Products' first label using the Physician's Labeling Rule. It may also be the first topical product to be labeled using the Physician's Labeling Rule. Coordination between the various Agency divisions involved in labeling was achieved through consultations and internal meetings.

New to this labeling is the name format for a fixed combination topical product and the location (Dosage and Administration section) for notation indicating Ziana Gel is a topical product that is not intended for oral, ophthalmic or intravaginal use.

Chemistry, Manufacturing and Controls

Various issues regarding specifications for the drug substance and product are discussed in the December 7, 2004 action letter. The sponsor addressed many of these concerns during the review cycle in NDA amendments dated August and September, 2006. Please see CMC review, pages 11 thru 22, for a list of seventeen concerns and the sponsor's responses. None of these concerns were deemed to be sufficient to withhold approval for Ziana Gel.

Pharmacology Toxicology, Clinical Microbiology, Clinical Pharmacology

No new issues were raised and no post-marketing studies are requested from any of these disciplines.

Specific labeling issues are raised by the Clinical Microbiology reviewer. These are included after revisions into the new labeling format.

Conclusion

In conclusion, the Dermatology Clinical Team Leader (TL) recommends that Ziana Gel be approved with the labeling as revised by the team.

Markham C. Luke, M.D., Ph.D.
Lead Medical Officer, Dermatology

Cc: Susan Walker, Director, DDDP
Brenda Carr, MO, Dermatology

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/s/

Markham Luke
10/24/2006 10:21:19 AM
MEDICAL OFFICER
TL Division Summary Memo

Susan Walker
11/7/2006 04:00:49 PM
DIRECTOR

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/s/

Jane Chang
10/18/2006 03:49:27 PM
CHEMIST

Moo-Jhong Rhee
10/19/2006 09:47:33 AM
CHEMIST
Chief, Branch III

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MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: October 18, 2006

TO: Susan Walker, M.D., Director
Division of Dermatologic and Dental Products

VIA: Shalini Jain, Regulatory Project Manager
Division of Dermatologic and Dental Products

FROM: Jeanine Best, M.S.N., R.N., P.N.P.
Patient Product Information Specialist
Division of Surveillance, Research, and Communication Support

THROUGH: Toni Piazza-Hepp, Pharm.D., Deputy Director
Division of Surveillance, Research, and Communication Support

SUBJECT: DSRCS Review of Patient Labeling for Ziana (clindamycin phosphate, 1.2% and tretinoin, 0.025%) Gel, NDA 50-802

Background and Summary

The sponsor submitted a Complete Response May 5, 2006, for Ziana (clindamycin phosphate, 1.2% and tretinoin, 0.025%) Gel, NDA 50-802 in response to a December 7, 2004 Non-Approval Action Letter. Patient Labeling in the form of a patient package insert (PPI) was submitted for review.

The sponsor submitted patient labeling in a non patient-friendly format and written at 9.9 grade level (Flesh-Kincaid). To enhance comprehension, patient information should be written at a 6th to 8th grade reading level. We have simplified the wording, made it consistent with the Prescribing information (PI), removed unnecessary information, and put it in a Medication Guide question and answer-type format as described in 21 CFR 208.20. Although not required for Patient Information, we recommend that the Medication Guide format be used for Ziana. Research and experience support the communication effectiveness of the Medication Guide format. All of our recommended changes are consistent with current research to improve risk communication to a broad audience of varying educational backgrounds including those with lower literacy. Our revised PPI is written at a 6.6 grade level (Flesh-Kincaid)

We also have the following comment:

The submitted PPI mentions acne improvement at Weeks 2 and 4, which is inconsistent with the PI. Information cannot be presented to patients that is not derived from the prescribing

information.

Attached are the marked and clean copies containing our revisions of the submitted PPI. Please call us if you have any questions.

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 Draft Labeling (b4)

✓ Draft Labeling (b5)

 Deliberative Process (b5)

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/s/

Jeanine Best
10/18/2006 12:55:17 PM
DRUG SAFETY OFFICE REVIEWER

Toni Piazza Hepp
10/18/2006 02:08:43 PM
DRUG SAFETY OFFICE REVIEWER

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1 **Memo to the File**

2
3 Date: October 11, 2006

4
5 To: Jain Shalini
6 Regulatory Project Manager, Division of Dermatology and Dental
7 Products (DDDP)

8
9 Subject: Established Pharmacologic Classification for the Highlights of Labeling
10 NDA 50-802 (Ziana)

11
12 This memo provides guidance to the Ziana review team on how to address the
13 pharmacologic classification requirement [21 CFR 201.57(a)(6)] for the Highlights of
14 labeling.

15
16 **Established Pharmacologic Classification of Ziana:**

17
18 Although the Office of New Drugs has determined that establishing pharmacologic
19 classification is optimally accomplished with consideration of drugs on a class-by-class
20 basis rather than on a drug-by-drug basis as new labeling is reviewed, we have
21 inadequate time to invoke that process for Ziana. Additionally, Ziana (Clindamycin
22 Phosphate and Tretinoin Gel) is comprised of two drugs that are well established in
23 clinical practice. Thus, we propose the following pharmacologic classification to be
24 included in Highlights under the Indications and Usage subheading:

b(5)

25
26
27

28 Clindamycin is a **lincosamide antibiotic**. Lincosamides (e.g. lincomycin, clindamycin)
29 are a class of drugs which bind to 50S subunit of bacterial ribosomes and suppress
30 protein synthesis. Lincosamide refers to the amide chemical structure of the clindamycin
31 and lincomycin compounds. In this case, including the term lincosamide adds clinically
32 important information as it relates to the spectrum of activity, resistance patterns, and the
33 evaluation of drug regimens. The term lincosamide antibiotic is widely use in the
34 medical community, including resources such as Drug Facts and Comparisons, Drug
35 Information Handbook, FDA approved labeling, and PubMed articles. The term
36 lincosamide antibiotic is thus considered scientifically valid and clinically meaningful for
37 the description of the clindamycin component of Ziana.

38 Tretinoin is a **retinoid**. Retinoids are a class of chemical compounds that are related
39 chemically to vitamin A. Thus, retinoid is a scientifically valid and clinically meaningful
40 term to describe the tretinoin component of Ziana.

41 Please do not hesitate to contact the SEALD-Labeling team if you require further
42 assistance.

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/s/

Lilliam Rosario
10/11/2006 03:32:39 PM
PHARMACOLOGIST

Laurie Burke
10/11/2006 07:48:27 PM
INTERDISCIPLINARY

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MEMORANDUM

To: Shalini Jain
DDDP

From: Iris Masucci, DDMAC
for Study Endpoints and Label Development (SEALD) Team, OND

Date: October 5, 2006

Re: Comments on draft labeling for Ziana (clindamycin and tretinoin) gel
NDA 50-802

We have reviewed the proposed label for Ziana (FDA's 10-02-06 version) and offer the following comments. These comments are based on Title 21 of the Code of Federal Regulations (201.56 and 201.57), the preamble to the Final Rule, labeling Guidances, and FDA recommendations to provide for labeling quality and consistency across review divisions. We recognize that final labeling decisions rest with the review division after a full review of the submitted data.

HIGHLIGHTS

General

- The proprietary and established name should be presented on the same line at the beginning of Highlights. If they cannot fit on the same line, only then should the established name appear directly underneath the proprietary name. If the dosage form and route of administration are edited to simply "topical gel," it will likely all fit on one line.
- In the editing of the label, it appears that the hard return was lost after the line for "Initial U.S. Approval" before the heading for "Indications and Usage."

Dosage and Administration

- We recommend adding a bullet to this section about Ziana's not being for oral, ophthalmic, or vaginal use.

• ~~_____ (2.1)"~~

We suggest that the recommended amount of product to be used be added here, e.g.,
~~_____~~ Without this information, the
"dose" is missing. Additionally, the cross-reference at the end should be "(2)," not
"(2.1)."

b(4)

Contraindications

The language here differs slightly from the Contraindication in the Full Prescribing Information (FPI). The FPI says "... in patients with regional enteritis, ulcerative colitis, or a history of antibiotic-associated colitis." Is the true contraindication in patients with a history of any of these three conditions or in patients with active enteritis or colitis, or a history of AAC? Please clarify and reword accordingly.

We note that the label for another topical clindamycin product (Clindagel) also includes a contraindication in patients with a history of hypersensitivity to clindamycin or lincomycin. Should this be added here or was it intentionally deleted?

b(4)

Warnings and Precautions

- ~~_____~~
Please reword this sentence to delete the phrase ~~_____~~ as is currently preferred for labeling language.
- The recommendation to discontinue Ziana if severe diarrhea occurs should be added to the warning on colitis. Each entry under Warnings and Precautions in Highlights should state the problem and give advice on how to manage it.

b(4)

Adverse Reactions

- This list of adverse reactions includes all reactions that are listed in Table 1 in the FPI. It is not a requirement that all adverse reactions be listed in Highlights; a higher cut-off incidence rate can be used.

Drug Interactions

- The wording for these drug interactions seems awkward. We suggest something like,

~~_____~~
Ziana should not be used in combination with erythromycin-containing ~~_____~~ products because of its clindamycin component."

b(4)

CONTENTS

Once the FPI is completed, please revise the Contents to ensure that all numbering is correct and that section and subheading titles match exactly to those in the FPI.

FULL PRESCRIBING INFORMATION

General

- A recent joint initiative of FDA with the Institute for Safe Medication Practices recommends against using trailing zeroes when writing doses to avoid possible misinterpretation (e.g., "2.0" being read as "20"). Please check throughout the label to delete all trailing zeroes from dose descriptions.
- The trade name for this product is presented inconsistently in the label (e.g., Ziana, ZIANA, ZIANA Gel, ZIANA™ Gel). Please revise for consistency throughout, noting that the product name should not be in bold type in the labeling text.
- For labeling sections where information will be presented separately for clindamycin and tretinoin (e.g., Pregnancy, Clinical Pharmacology, Nonclinical Toxicology), we suggest using subheadings for each drug using underlining and/or italicizing. Note that these subheadings should not be in bold type and should not be numbered within Contents (e.g., "8.1.1 Clindamycin" and "8.1.2 Tretinoin").

1 Indications and Usage

- The Clindagel label's indication section also includes a sentence about how other products should be considered because of the risk of diarrhea and colitis. Should a similar statement be included for Ziana?

2 Dosage and Administration

As in the Highlights, the statement about not using for oral, ophthalmic, or vaginal use should be added here.

3 Dosage Forms and Strengths

- We suggest that the available tube sizes be added here for consistency with the corresponding Highlights section.

4 Contraindications

- Please see comment above about the Highlights Contraindications section.

5.1 Colitis

- ~~_____~~

b(4)

We suggest that this sentence be revised to, "When significant diarrhea occurs, Ziana should be discontinued." Saying "_____ here is inaccurate because this product contains two drugs.

• [

3

b(4)

6.1 Clinical Studies Experience

- The regulations require that this section be titled, "_____"
- Please add "Table 1" to the title of the table.
- Table 1 includes some adverse reactions that were more common with placebo (vehicle). As recommended in the recently finalized Guidance on the Adverse Reactions section of labeling, "Any reactions for which the placebo rate equals or exceeds the rate for the drug should not be included in the Adverse Reactions section unless there is some compelling factor (e.g., timing) that suggests that the event is caused by the drug." Please delete all such reactions from Table 1. This criterion should be incorporated into the table title, e.g. "... reported in at least 1% of patients and more commonly than with placebo..."
- *"Cutaneous safety and tolerance evaluations were conducted at each study visit in all of the clinical trials by assessment of erythema, scaling, itching, burning, and stinging..."*

Is this section on dermatologic tolerance common in topical product labels? Are these data adequately supported?

7.1 Concomitant Topical Medication

- *"Concomitant topical medication, medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices or lime should be used with caution _____"*

b(4)

Can the "_____ be discussed in more detail here? The discussion seems incomplete.

7.3 Neuromuscular Blocking Agents

- _____

b(4)

We recommend this sentence be reworded to: "_____ The _____ in the proposed sentence refers specifically to clindamycin, which cannot be discontinued alone.

8.1 Pregnancy

- This product has been assigned a Pregnancy Category C, presumably because of the tretinoin component. We suggest, however, that the pregnancy categories also be given for each individual component (C for tretinoin and B for clindamycin), along with the relevant human and animal data.

- ~~_____~~
We recommend this sentence be changed to ~~_____~~ for clarity.

b(4)

- Is the distinction of ~~_____~~ important here? If not, we recommend deletion of this subheading. If it remains in the label, it should not be in bold type as noted above.

8.4 Pediatric Use

- This section should describe any differences in efficacy or safety in adolescent patients from adult patients in the clinical trials, if any such differences were seen.
- This section can be expanded to direct the reader to the Clinical Trials section where information on Ziana's use in adolescents is described, e.g., ~~_____~~ *[See Clinical Studies (14)].*

b(4)

10 Overdosage

- The information presented here is not really appropriate for the Overdosage section, which should describe signs/symptoms of overdosage and how to manage them. Please revise accordingly.

11 Description

- ~~_____~~

b(4)

Please consider the best way to present the drug names and strengths of each in the label (consulting appropriate disciplines as needed). We suggest "Ziana (clindamycin phosphate 1.2% and tretinoin 0.025%) gel."

12 Clinical Pharmacology

- As available, please include information on mechanism of action and pharmacokinetics for both clindamycin and tretinoin in this section. The proposed language does not include information for both drugs in these sections.

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

•

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└

b(4)

We note that this sentence says that 1 g daily is the _____ clinical dose," while Pregnancy sections says that 1 g daily is just the "recommended" clinical dose. Is the qualifier _____ needed here? Please revise accordingly for consistency.

•

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└

b(4)

The clinical study citations should be deleted from this sentence.

14 Clinical Studies

- In the listing of the co-primary efficacy variables, the lesion counts are listed first, and the Evaluator's Global Severity (EGS) score is listed second; however, in the results tables, the EGS is presented first and the lesion count findings are second. Please revise to keep the order consistent within this section.
- We suggest adding more detail on the EGS scale (e.g., range of possible scores, grades, definitions, etc.).
- Please consider eliminating "Success" as an achievable study outcome because it is promotional in tone. Instead, we suggest using the definitions presented within the study descriptions (e.g., "Cleared or Almost Cleared").
- In Tables 3 and 4, the outcome measures on lesion counts need to be more clearly defined. Specifically, these data are described as _____ along with the actual numbers. We suggest either changing the description to "% reduction" or putting a "-" sign in front of each number (e.g., -52.6). Although the reader could probably infer the direction of change as being negative, the presentation should be as accurate and explicit as possible.
- In this section the Evaluator's Global Severity score is sometimes called the "EGSS" and sometimes the "EGS." Please revise for consistency.

b(4)

17 Patient Counseling Information

- This section needs to be revised and will be reviewed when completed.
- Please note that this review addresses only the physician labeling, not the patient labeling.

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/s/

Iris Masucci
10/10/2006 03:22:18 PM
DDMAC REVIEWER

Laurie Burke
10/11/2006 07:44:08 PM
INTERDISCIPLINARY

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MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

****PRE-DECISIONAL AGENCY MEMO****

Date: October 4, 2006

To: Shalini Jain, DDDDP

From: Andrew Haffer, DDMAC

Re: Comments on proposed draft labeling for Ziana Gel

DDMAC has reviewed the proposed draft container/carton labeling, PI, and PPI for Ziana Gel. DDMACs comments are based on the proposed draft labeling distributed by Shalini Jain on 9/6/06. Our tracked changes and comments are provided directly in the attachments as follows.

Attachment I – One comment on the carton/container labeling

Attachment II – Comments on the PI provided directly in the proposed document

Attachment III – Comments on the PPI provided directly in the proposed document

If you have any questions about DDMACs comments please do not hesitate to call.

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Attachment I:

Comments on Container/Carton labeling:

Many cartons and containers include the following text:

This description of the dose to use, i.e., a ~~pea-sized amount~~ is also utilized in the PI. However, the PPI discusses "squeezing about an inch or less." An inch strip of medication would include considerably more gel than a ~~pea-sized amount~~. Exactly how much drug product was utilized in the clinical trials? Does that amount equate to a pea-sized amount or 1 inch or less? The sponsor should revise all of their descriptions of the size of the dose to use to accurately reflect the amount of gel utilized in the clinical trials supporting approval of this product.

b(4)

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Attachment II:

DDMAC comments on the proposed draft PI

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✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

Attachment III:

DDMAC comments on the proposed draft PPI

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✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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/s/

Andrew Haffer
10/4/2006 10:53:05 AM
DDMAC REVIEWER

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

FACSIMILE TRANSMITTAL SHEET

Date: September 22, 2006

To: Barry Calvarese, M.S.
Vice President, Regulatory and Clinical Affairs
Dow Pharmaceutical Sciences
1330 Redwood Way
Petaluma, CA 94954-1169
Phone: (707) 793-2600, ext. 610
Fax: (707) 793-0145

From: Shalini Jain, Regulatory Project Manager
Phone: (301) 796-0692
Fax: (301) 796-9894/9895

This transmission includes 5 pages (including this page)

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FDA Facsimile Memorandum

Date: September 22, 2006
To: Barry Calvarese, M.S.
Dow Pharmaceutical Sciences
From: Shalini Jain, Project Manager
Subject: NDA 50-802, Ziana

Mr. Calvarese:

This fax memo provides a list of revisions for the proposed labeling for NDA 50-802. Please revise the package insert information as per attached.

Please respond by September 29.

Respectfully,

Shalini Jain
Regulatory Project Manager
Food and Drug Administration
Division of Dermatology and Dental Products (DDDP)
WO22, Room 5183
10903 New Hampshire Ave.
Silver Spring, MD 20993
P (301) 796-0692
F (301) 796-9894/9895
shalini.jain@fda.hhs.gov

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Subject: Proposed Labeling Format Review
NDA 50-802 Ziana (clindamycin phosphate and tretinoin) Gel

Highlights:

- The Highlights limitation statement should not include dosage form, just name of drug product. Delete the word “Gel”. [See 21 CFR 201.57(a)(1)]
- The drug names must be followed by the drug’s dosage form and route of administration (e.g., Gel, Topical). Do not include the strengths (e.g., 1.2% and 0.025%). [See 21 CFR 201.57(a)(2)]
- The preferred format for presenting the drug names is without all capital letters and without the trademark or other symbol. [Best Practices]
- For Initial U.S. Approval, this application is not approved. Delete ~~“~~ [See 21 CFR 201.57(a)(3)]

- Delete “ ~~_____~~ : This statement is out of place.

b(4)

- Under Indications and Usage the pharmacologic class statement is omitted. The new rule [21 CFR 201.57(a)(6)] requires that if a product is a member of an established pharmacologic class, the following statement must appear under the Indications and Usage heading in the Highlights:

“(Drug/Biologic Product) is a (name of class) indicated for (indication(s)).”

Please propose an established pharmacologic class that is scientifically valid AND clinically meaningful to practitioners or rationale why pharmacologic class should be omitted from the Highlights.

- Under Dosage Forms and Strengths, “2, 30, 60 gram tubes” must be added. [See 21 CFR 201.57(c)(4)]
- Regarding Contraindications, “theoretical” possibilities must not be listed (i.e., hypersensitivity). [See 21 CFR 201.57(a)(9)] If the contraindication is not theoretical, then it must be reworded to explain the type and nature of the adverse reaction. The same applies to the FPI Contraindications section. [See 21 CFR 201.57(c)(5)]
- Avoid using the word ~~_____~~ for subsection headings in Highlights, Contents and the FPI. Create headings that are descriptive and identify the content. [Best Practices]

b(4)

- Under Warnings and Precautions (heading 5.1 Colitis) the text should not be bolded or underlined. Use regular text. The same applies to the Warnings and Precautions FPI (subsection 5.1). [Best Practices]
- Under Adverse Reactions, the term “adverse event” is used instead of “adverse reaction”. Criteria used for reporting all adverse reactions listed must be listed. Also, a description of clinical trials should not be included under Adverse Reactions in Highlights. Refer to the “Guidance for Industry: Adverse Reactions Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format,” available at <http://www.fda.gov/cder/guidance> and revise the Adverse Reactions section in Highlights and the FPI accordingly. [See 21 CFR 201.57(a)(11)]
- ~~_____~~ b(4)
- The required statement must read **See 17 FOR PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**. Please fix. [See 21 CFR 201.57(a)(14)]
- The revision date will be the month/year that the NDA is approved, not September 2006. [See 21 CFR 201.57(a)(15)]
- Please submit the completed Highlights Data Element Table. To complete the Highlights data elements, please refer to the following two documents at the FDA Data Standards Council website (<http://www.fda.gov/oc/datacouncil>) under Structured Product Labeling: “Companion Document for SPL Release 2 Implementation Guide for Highlights DRAFT” and “SPL Highlights Data Element Table”. This table must be filled out with the terms that have been proposed for the Highlights data elements. The companion document provides information on the terminology to be used. If you need assistance completing the Highlights data elements portion of your application, please contact spl@fda.hhs.gov.

Full Prescribing Information: Contents:

- Under Use in Specific Populations, delete subsection ~~_____~~ in the Contents and the FPI since it is not applicable. [See 21 CFR 201.56(d)(4)] b(4)
- Under Clinical Pharmacology, delete subsection ~~_____~~ in the Contents and the FPI since it is not applicable. [See 21 CFR 201.57(d)(4)]

Full Prescribing Information (FPI):

- The preferred presentation of cross-references in the FPI is in all italics. For example, [*see Warnings and Precautions (5)*], not ~~_____~~. Because cross-references are embedded in the text in the FPI, the use of ~~_____~~ b(4)

italics to achieve emphasis is encouraged. Please correct your cross-references throughout the labeling. [Implementation Guidance]

- Under Dosage Forms and Strengths the inactive ingredients should not be listed. Inactive ingredients go under the Description section of the labeling. [See 21 CFR 201.57(c)(4)]
- Delete unnecessary references. Include only references that are important to the prescriber. [See 21 CFR 201.57(c)(16)]
- Regarding Patient Counseling Information, include information for prescribers to convey to patients to use the drug safely and effectively. Your Patient Counseling Information section is currently written for the patient, not the prescriber. [See 21 CFR 201.57 (c)(18)]
- Under Patient Counseling Information, any FDA-approved patient labeling must be referenced in this section. [See 21 CFR 201.57 (c)(18)]
- For the Patient Counseling Information, you need to add a subsection for FDA-approved patient labeling. [See 21 CFR 201.57 (c)(18)] Also incorporate this subsection heading into the Contents.

Appears This Way
On Original

Date: September 21, 2006

From: Robin Anderson, RN, MBA
Label Initiatives Specialist
Study Endpoint and Label Development (SEALD)
Office of New Drugs, CDER

Through: Laurie B. Burke, RPh, MPH
Director, SEALD

To: Shalini Jain
Regulatory Project Manager
Division of Dermatology and Dental Products

Subject: Proposed Labeling Format Review
NDA 50-802 Ziana (clindamycin phosphate and tretinoin) Gel

This memo provides a list of revisions for the proposed labeling that should be conveyed to the applicant. Please contact me at 796-0534 with questions or concerns.

Highlights:

- The Highlights limitation statement should not include dosage form, just name of drug product. Delete the word "Gel". [See 21 CFR 201.57(a)(1)]
- The drug names must be followed by the drug's dosage form and route of administration (e.g., Gel, Topical). Do not include the strengths (e.g., 1.2% and 0.025%). [See 21 CFR 201.57(a)(2)]
- The preferred format for presenting the drug names is without all capital letters and without the trademark or other symbol. [Best Practices]
- For Initial U.S. Approval, this application is not approved. Delete ~~_____~~ [See 21 CFR 201.57(a)(3)]
- Delete "~~_____~~
~~_____~~". This statement is out of place.
- Under Indications and Usage the pharmacologic class statement is omitted. The new rule [21 CFR 201.57(a)(6)] requires that if a product is a member of an established pharmacologic class, the following statement must appear under the Indications and Usage heading in the Highlights:

“(Drug/Biologic Product) is a (name of class) indicated for (indication(s)).”

b(4)

b(4)

Please propose an established pharmacologic class that is scientifically valid AND clinically meaningful to practitioners or rationale why pharmacologic class should be omitted from the Highlights.

- Under Dosage Forms and Strengths, “2, 30, 60 gram tubes” must be added. [See 21 CFR 201.57(c)(4)]
- Regarding Contraindications, “theoretical” possibilities must not be listed (i.e., hypersensitivity). [See 21 CFR 201.57(a)(9)] If the contraindication is not theoretical, then it must be reworded to explain the type and nature of the adverse reaction. The same applies to the FPI Contraindications section. [See 21 CFR 201.57(c)(5)]
- Avoid using the word ‘’ for subsection headings in Highlights, Contents and the FPI. Create headings that are descriptive and identify the content. [Best Practices] b(4)
- Under Warnings and Precautions (heading 5.1 Colitis) the text should not be bolded or underlined. Use regular text. The same applies to the Warnings and Precautions FPI (subsection 5.1). [Best Practices]
- Under Adverse Reactions, the term “adverse event” is used instead of “adverse reaction”. Criteria used for reporting all adverse reactions listed must be listed. Also, a description of clinical trials should not be included under Adverse Reactions in Highlights. Refer to the “Guidance for Industry: Adverse Reactions Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format,” available at <http://www.fda.gov/cder/guidance> and revise the Adverse Reactions section in Highlights and the FPI accordingly. [See 21 CFR 201.57(a)(11)]
- ~~_____~~ b(4)
- The required statement must read **See 17 FOR PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.** Please fix. [See 21 CFR 201.57(a)(14)]
- The revision date will be the month/year that the NDA is approved, not September 2006. [See 21 CFR 201.57(a)(15)]
- Please submit the completed Highlights Data Element Table. To complete the Highlights data elements, please refer to the following two documents at the FDA Data Standards Council website (<http://www.fda.gov/oc/datacouncil>) under Structured Product Labeling: “Companion Document for SPL Release 2 Implementation Guide for Highlights DRAFT” and “SPL Highlights Data Element Table”. This table must be filled out with the terms that have been

proposed for the Highlights data elements. The companion document provides information on the terminology to be used. If you need assistance completing the Highlights data elements portion of your application, please contact spl@fda.hhs.gov.

Full Prescribing Information: Contents:

- Under Use in Specific Populations, delete subsection ~~.....~~ in the Contents and the FPI since it is not applicable. [See 21 CFR 201.56(d)(4)]
- Under Clinical Pharmacology, delete subsection ~~.....~~ in the Contents and the FPI since it is not applicable. [See 21 CFR 201.57(d)(4)]

b(4)

Full Prescribing Information (FPI):

- The preferred presentation of cross-references in the FPI is in all italics. For example, [*see Warnings and Precautions (5)*], not [see *Warnings and Precautions (5)*]. Because cross-references are embedded in the text in the FPI, the use of italics to achieve emphasis is encouraged. Please correct your cross-references throughout the labeling. [Implementation Guidance]
- Under Dosage Forms and Strengths the inactive ingredients should not be listed. Inactive ingredients go under the Description section of the labeling. [See 21 CFR 201.57(c)(4)]
- Delete unnecessary references. Include only references that are important to the prescriber. [See 21 CFR 201.57(c)(16)]
- Regarding Patient Counseling Information, include information for prescribers to convey to patients to use the drug safely and effectively. Your Patient Counseling Information section is currently written for the patient, not the prescriber. [See 21 CFR 201.57 (c)(18)]
- Under Patient Counseling Information, any FDA-approved patient labeling must be referenced in this section. [See 21 CFR 201.57 (c)(18)]
- For the Patient Counseling Information, you need to add a subsection for FDA-approved patient labeling. [See 21 CFR 201.57 (c)(18)] Also incorporate this subsection heading into the Contents.

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this page is the manifestation of the electronic signature.**

/s/

Robin E Anderson
9/22/2006 11:35:49 AM
CSO

Laurie Burke
9/22/2006 02:17:17 PM
INTERDISCIPLINARY

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**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III**

FACSIMILE TRANSMITTAL SHEET

Date: September 12, 2006

To: Barry Calvarese, M.S.
Vice President, Regulatory and Clinical Affairs
Dow Pharmaceutical Sciences
1330 Redwood Way
Petaluma, CA 94954-1169
Phone: (707) 793-2600, ext. 610
Fax: (707) 793-0145

From: Shalini Jain, Regulatory Project Manager
Phone: (301) 796-0692
Fax: (301) 796-9894/9895

This transmission includes 2 pages (including this page)

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED BY APPLICABLE LAW. If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is ***unauthorized and strictly prohibited***. If you have received this facsimile in error, **please notify Shalini Jain by telephone at 301-796-0692 immediately**, return it c/o the Dermatology and Dental Product Division, 10903 New Hampshire Ave, WO22, Rm 5183, Silver Spring, MD 20993 by US Mail.

FDA Facsimile Memorandum

Date: September 12, 2006
To: Barry Calvarese, M.S.
Dow Pharmaceutical Sciences
From: Shalini Jain, Project Manager
Subject: NDA 50-802, Ziana

Mr. Calvarese:

1. Please revise the package insert information listed below:
 1. Drug names and dosage form in the HIGHLIGHTS OF PRESCRIBING INFORMATION section (Lines 6 and 7) should be in bold face shown as following:
Ziana
(Clindamycin Phosphate and Tretinoin) Gel, 1.2% and 0.025%
 2. The chemical name for clindamycin phosphate in Lines 329-332 of "Section 11 Description" should be revised to:

Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*- α -D-galacto-octopyranoside 2-(dihydrogen phosphate)

The hyphen (-) between Methyl and 7-chloro should be removed.
2. Either provide revised final mock-up container and carton labels or commit to provide them prior to final approval.

Please respond by September 14.

Respectfully,

Shalini Jain
Regulatory Project Manager
Food and Drug Administration
Division of Dermatology and Dental Products (DDDP)
WO22, Room 5183
10903 New Hampshire Ave.
Silver Spring, MD 20993
P (301) 796-0692
F (301) 796-9894/9895
shalini.jain@fda.hhs.gov



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

FACSIMILE TRANSMITTAL SHEET

Date: September 8, 2006

To: Barry Calvarese, M.S.
Vice President, Regulatory and Clinical Affairs
Dow Pharmaceutical Sciences
1330 Redwood Way
Petaluma, CA 94954-1169
Phone: (707) 793-2600, ext. 610
Fax: (707) 793-0145

From: Shalini Jain, Regulatory Project Manager
Phone: (301) 796-0692
Fax: (301) 796-9894/9895

This transmission includes 2 pages (including this page)

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FDA Facsimile Memorandum

Date: September 8, 2006
To: Barry Calvarese, M.S.
Dow Pharmaceutical Sciences
From: Shalini Jain, Project Manager
Subject: NDA 50-802, Ziana

Mr. Calvarese:

We note that SPL has not been submitted representing the content of your proposed labeling. By regulation [21 CFR 314.50(l), 314.94(d), and 601.14(b); Guidance for Industry: *Providing Regulatory Submissions in Electronic Format — Content of Labeling* (April 2005); <http://www.fda.gov/ohrms/dockets/dockets/92s0251/92s-0251-m000032-vol1.pdf>], you are required to submit to FDA prescribing and product information (i.e., the package insert or label) in SPL format. During the initial implementation phase of the PLR (until the end of 2006), FDA advises applicants to make a good faith effort to provide PLR-compliant SPL with their marketing applications or efficacy supplements. FDA will work closely with applicants during the review cycle to correct all SPL deficiencies before approval. Please email spl@fda.hhs.gov for individual assistance. Also, please submit evidence of your good faith effort to provide PLR compliant SPL by 09/14/06.

Respectfully,

Shalini Jain
Regulatory Project Manager
Food and Drug Administration
Division of Dermatology and Dental Products (DDDP)
WO22, Room 5183
10903 New Hampshire Ave.
Silver Spring, MD 20993
P (301) 796-0692
F (301) 796-9894/9895
shalini.jain@fda.hhs.gov

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION			
TO (Division/Office): Andrew Haffer Mail: DDMAC, HFD-42, WO22, room 1456			FROM: Shalini Jain, Regulatory Project Manager		
DATE 09/06/06	IND NO.	NDA NO. 50--802	TYPE OF DOCUMENT Original NDA	DATE OF DOCUMENT 5/06/06	
NAME OF DRUG Ziana (clindamycin 1%, tretinoin 0.025%) gel	PRIORITY CONSIDERATION S		CLASSIFICATION OF DRUG 3	DESIRED COMPLETION DATE PDUFA Goal Date 11/06/06	
NAME OF FIRM: DOW Pharmaceutical Sciences					
REASON FOR REQUEST					
I. GENERAL					
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): trade name consult					
II. BIOMETRICS					
STATISTICAL EVALUATION BRANCH			STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):			<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS					
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES			<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE					
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP			<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS					
<input type="checkbox"/> CLINICAL			<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS:					
<p>The label and carton and container and PI and patient information files were all received as an eCTD and are in the EDR. I will also send a separate email with the files as well to facilitate review. Please note that the label submission is also in the PLR format and SEALD team will also be advised. These revised labels and carton and container artwork were received 9/5/06.</p>					
SIGNATURE OF REQUESTER Shalini Jain			METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL DFS <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER			SIGNATURE OF DELIVERER		

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/s/

Shalini Jain

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 WO22, RM 4447		FROM: Shalini Jain, Regulatory Project Manager		
DATE 09/06/06	IND NO.	NDA NO. 50-802	TYPE OF DOCUMENT original NDA	DATE OF DOCUMENT 05/06/06
NAME OF DRUG Ziana (clindamycin 1%, tretinoin 0.025%) gel	PRIORITY CONSIDERATION S	CLASSIFICATION OF DRUG 3	DESIRED COMPLETION DATE PDUFA GOAL DATE 11/06/06	
NAME OF FIRM: Dow Pharmaceutical Sciences				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: This request is for tradename and label, carton and container review. The sponsor's information was submitted electronically and separate emails were sent with the labels and artwork for the carton, container, PI and PPI on 9/6/06. Please note the sponsor did not submit the label and artwork files until 9/5/06. Diane Smith in DMETS notified of late submission by sponsor of name, label and artwork on 9/6/06.				
PDUFA DATE: 11/06/06 ATTACHMENTS: Draft Package Insert, Container and Carton Labels CC: Archival IND/NDA 50802 HFD-540/Division File HFD-540/RPM HFD-540/Reviewers and Team Leaders				
NAME AND PHONE NUMBER OF REQUESTER Shalini Jain		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS ONLY <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		

301-796-0692	
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

5/28/05

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this page is the manifestation of the electronic signature.**

/s/

Shalini Jain

9/6/2006 04:18:56 PM

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 WO22, RM 4447		FROM: Shalini Jain, Regulatory Project Manager		
DATE 09/06/06	IND NO.	NDA NO. 50-802	TYPE OF DOCUMENT original NDA	DATE OF DOCUMENT 05/06/06
NAME OF DRUG Ziana (clindamycin 1%, tretinoin 0.025%) gel	PRIORITY CONSIDERATION S	CLASSIFICATION OF DRUG 3	DESIRED COMPLETION DATE PDUFA GOAL DATE 11/06/06	
NAME OF FIRM: Dow Pharmaceutical Sciences				
REASON FOR REQUEST				
I. GENERAL				
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II. BIOMETRICS				
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<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
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<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
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V. SCIENTIFIC INVESTIGATIONS				
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NAME AND PHONE NUMBER OF REQUESTER Shalini Jain		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS ONLY <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		

301-796-0692	
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

5/28/05

Appears This Way
On Original

NDA FILEABILITY CHECKLIST

NDA Number: 21-739 **Drug Name:** Clin-RA (clindamycin phosphate, 1%;
retinoic acid, 0.025%) Gel

Applicant: Dow Pharmaceutical Sciences

IS THE CMC SECTION OF THIS APPLICATION FILEABLE? (Yes or No) No __ Yes_X_

Table 1 Fileability Checklist

The following parameters are necessary for initiating a full review, e.g. complete enough for review but may have deficiencies.

	PARAMETER	YES	NO	COMMENT
1	Is the NDA organized adequately for its CMC content?	X		
2	Are the CMC sections adequately indexed & paginated?	X		
3	Is the CMC sections legible?	X		
4	Are all facilities identified with full street addresses, contact names & CFN#s?	X		
5	Is there a statement that all facilities are prepared for GMP inspections?	X		
6	Has an environmental assessment or categorical exclusion been provided?	X		
7	Does the drug substance section contain controls?	X		COAs + Refers to relevant DMFs (see below)
8	Does the drug product section contain controls?	X		
9	Has stability data been submitted to justify the requested expiry date?		X	12 month long term/ 6 month accelerated
10	Has the applicant provided all requested data by the division during the IND & pre-NDA phases?	X		
11	Have draft container labels been provided?	X		Label unacceptable to DMETS
12	Has a draft package insert been provided?	X		
13	Has an Investigational Formulations section been included?	X		
14	Are there three Methods Validation documents?	X		
15	Is a statistical consult required?		X	
16	Is there a separate microbiological section? Is a micro consult required?		X	

EER REPORT ATTACHED

Table 2 STABILITY DATA REQUIRED FOR FILEABILITY

	STABILITY DATA REQUESTED	YES	NO
1	Does the NDA include 12 or more months of stability data?	X	
2	Does the stability data cover the expiry date?		X
3	Does the stability data include only the largest & smallest container sizes?	X	
4	Does the stability data include all packages sizes?	X	
5	Are there tabular data for each size and batch?	X	
6	Are there graphical data for each size and batch?		X
7	Is a statistical consult required?		X
8	Is a stability protocol included?	X	
9	Are the stability-indicating assays described?	X	
10	Is there the three-point stability commitment?	X	

Table 3 DMF INFORMATION

DMF #	DMF HOLDER	TYPE	LOA DATE	DATE OF LAST REVIEW
			August 29, 2003	September 8, 2003
			July 15, 2002	August 15, 2003 (inadequate) March 12, 2004 (inadequate)
			January 26, 2001	October 7, 2003
			July 16, 2002	July 10, 2000
			May 29, 2003	June 5, 2002

b(4)

No CMC issues were identified for inclusion in the 74-day letter

Mid-cycle review completion date: July 13, 2004
 Estimated Review Completion Date: October 15, 2004

Saleh A. Turujman, Ph.D.
 Review Chemist

Wilson H. DeCamp, Ph.D.
 Chemistry Team Leader

Attachment: EER report. The overall recommendation of withhold was made because the initial ~~site, in~~ ~~which~~ ~~was~~ ~~provided~~ ~~in~~ ~~the~~ ~~original~~ ~~submission~~, was not the actual manufacturing site of tretinoin. The correct site, in ~~which~~ ~~was~~ ~~subsequently~~ ~~provided~~ ~~by~~ ~~the~~ ~~applicant~~. The correction is reflected in the attached EER report.

b(4)

Cc: Original NDA 21-739
 HFD-540/Division File
 HFD-540/Chm/SATurujman
 HFD-540/ActChmTL/NSchmuff
 HFD-540/ProjMgr/JSmith
 HFD-830/ActDivDir/DLin

4 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

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

/s/

Saleh Turujman
4/17/04 08:31:47 PM
CHEMIST

For your concurrence

Norman Schmuff
4/19/04 08:47:27 AM
CHEMIST

Appears This Way
On Original