

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

75276

ADMINISTRATIVE DOCUMENTS

APPROVAL SUMMARY

REVIEW OF PROFESSIONAL LABELING DIVISION OF LABELING AND PROGRAM SUPPORT LABELING REVIEW BRANCH

SUPERSEDES November 15, 1999 submission

ANDA Number: 75-276

Date of Submission: March 7, 2003

Applicant's Name: Altana, Inc.

Established Name: Betamethasone Dipropionate Gel, 0.05% (Augmented)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (15 g and 50 g) – Satisfactory as of March 7, 2003 submission [Vol 2.1; Revised 2/03 and 11/02, respectively ; Code # U4452 and X4451, respectively]

Carton Labeling: (15 g and 50 g) – Satisfactory as of March 7, 2003 submission [Vol 2.1; Revised 11/02 ; Code # IU4452 and IX4451, respectively]

Professional Package Insert Labeling: Satisfactory as of March 7, 2003 submission

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Diprolene Gel, 0.05%
- NDA Number: 19-408
- NDA Drug Name: Betamethasone Dipropionate Gel, 0.05% (Augmented)
- NDA Firm: Schering Corporation
- Date of Approval of NDA Insert and supplement #006: November 22, 1991
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labeling: Side-by-side comparison
- Revisions needed post-approval: **YES**
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 19-408

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
4489070	May 13, 2003	None	None	Paragraph III	Same as

Exclusivity Data– NDA 19-408

Code	Reference	Expiration	Labeling Impact
	There is no unexpired exclusivity for this product.		

POST REVISIONS:

INSERT:

1. General Comment:

Revise the term _____ to read " Pediatric patients" wherever it appears in your labeling to be in accordance with CRF 201.57 (9).

2. Pediatric Use:

Revise the first sentence to read "Data regarding use of Betamethasone Dipropionate Gel (augmented) in pediatrics patients are not available, so use of this product in patients under the age of 12 is not recommended" rather than "Safety and effectiveness of Betamethasone Dipropionate Gel (Augmented) in children have not been established, therefore its use in children under 12 is not recommended"

3. Geriatric Use:

To be in accordance with CRF 201.57 (10), add the following paragraph after the "pediatric use" section:

Geriatric Use: "Clinical studies of Betamethasone Dipropionate Gel (Augmented) included 65 subjects who were 65 years of age and over and 15 subjects who were 75 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. However, greater sensitivity of some older individuals cannot be ruled out."

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		x	
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		x	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?			
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		x	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		x	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x

Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	x		

NOTES/QUESTIONS TO THE CHEMIST:

Does the stability data support the proposed storage recommendation "Store between 2° and 25°C (36° and 77°F)"?

Yes 4/29/03

FOR THE RECORD:

1. Labeling review based on the approved labeling of the reference listed drug Diprolene Gel, 0.05% - Schering Corporation: NDA 19-408; Revised 1/00 (PDR Electronic Library); Approved 11/22/91.) There were minor changes made to the reference listed drug's labeling revised 1/00 (PDR Electronic Library). The changes are as follows:

- A change from the term "children" to "pediatric patients"
- Pediatric Use - The first sentence was changed from "Safety and effectiveness of Diprolene Gel in children have not been established, therefore its use in children under 12 is not recommended" to "Data regarding use of Diprolene Gel in pediatrics patients are not available, so use of this product in patients under the age of 12 is not recommended".

The applicant has been asked to revised their labeling to be consistent with the reference listed drug labeling, revised 1/00 (PDR Electronic Library).

Also, the applicant has been asked to add a "Geriatric use" section to be in accordance with CFR 201.57 (10) (B). In addition, the sponsor (NDA 19-408) has submitted supplement S-015, adding a Geriatric Use section. Denise Cook, M.D. recommended that the wording the sponsor proposed for the Geriatric Use section of the labeling be approved. However, the supplement is still open.

2. Packaging
The RLD packages its product in 15 g and 50 g tubes.

The applicant is proposing to market its product in 15 g and 50 g aluminum, blind-end tubes.

4. Labeling
The Orange Book only uses Augmented only in describing the Diprolene AF. However, since the descriptor is used with the RLD but is not a part of the established name, the applicant has been asked to place it at the end of the established name and strength in parentheses.

5. Inactive Ingredients
There does not appear to be a discrepancy between inactives listed in the DESCRIPTION section of the PI and the C&C Statements.

6. USP Issues
RLD - Store between 2° and 25°C (36° and 77°F).
ANDA - Same as the RLD

7. Patent/Exclusivity Issues - Diprolene Gel has 1 currently active patent: # 4489070 expiring May 13, 2003. Altana has certified that they will not introduce the product into the market prior to their expiration.
-
-

Date of Review:

Date of Submission: March 7, 2003 (Amendment)

Primary Reviewer:

ISI

Date: 3/26/03

Team Leader:

Date:

of days for J. Stone 3/24/03

cc: ANDA: 75-276
DUP/DIVISION FILE
HFD-613/BWeitzman/JGrace (no cc)

Review

RECORD OF TELEPHONE CONVERSATION

<p>On this date, I contacted Altana Inc. (Altana) and made reference to their ANDA 75-276 and to the teleconference on May 3, 2002.</p> <p>I informed Ms. Carmen that because Altana will require another month or two to collect additional data to support their specification, the application will be closed out. In addition, I informed Ms. Carmen that when the data is submitted, that amendment will reopen the application.</p> <p>Ms. Carmen acknowledged my comments.</p>	DATE: 5/23/02
	ANDA NUMBER 75-276
	TELECON INITIATED BY AGENT
	PRODUCT NAME: Betamethason Dipropionate Gel, 0.05%
	FIRM NAME: Altana Inc.
	FIRM REPRESENTATIVES: Virginia Carmen, Associate Director, Regulatory Affairs
	TELEPHONE NUMBER: 631-454-7677 ext. 2091
	FDA REPRESENTATIVES Sarah Ho
	SIGNATURES: S.Ho <i>SH</i> 5/23/02

Orig: ANDA 75-276

Cc: Division File

Chem. I Telecon Binder

RECORD OF TELEPHONE CONVERSATION

<p>On this date, we contacted Altana Inc. (Altana) and made reference to their ANDA 75-276.</p>	<p>DATE: 5/3/02</p>
<p>We informed Ms. Bialesky that Frank Holcombe is of the opinion that the upper limit for the assay release value should be %.</p>	<p>ANDA NUMBER 75-276</p>
<p>Ms. Bialesky explained that Altana did not want to make a commitment to % based on only the batches that were submitted.</p>	<p>TELECON INITIATED BY AGENT</p>
<p>We proposed that Altana could tighten the value to 112% for the tentative approval then submit an amendment to change the value once more data is collected.</p>	<p>PRODUCT NAME: Betamethason Dipropionate Gel, 0.05%</p>
<p>Ms. Bialesky will discuss with her colleagues.</p>	<p>FIRM NAME: Altana Inc.</p>
<p>We requested that she inform us of their decision.</p>	<p>FIRM REPRESENTATIVES: Audrey Bialesky, Regulatory Manager</p>
	<p>TELEPHONE NUMBER: 631-454-7677 ext. 2091</p>
	<p>FDA REPRESENTATIVES Paul Schwartz <i>PS 5/6/02</i> Sarah Ho <i>SH 5/6/02</i></p>
	<p>SIGNATURES: P.Schwartz S.Ho</p>

Orig: ANDA 75-276
 Cc: Division File
 Chem. I Telecon Binder

RECORD OF TELEPHONE CONVERSATION/MEETING

<p>Virginia Carman was contacted to clarify their proposed specs which were listed differently on diferent forms. She was also asked to identify the degradants. She was also informed that USP now has a method for related substances in the drug substance and if they used that method they wouldn't have to do full validation.</p> <p>She was subsequently asked to lower the stability limit for other impurities. She said that since USP allows 1% for individual impurities for the DS, % is not unresonable for stability. She agreed to send in her argument in a telephone amendment.</p>	<p>DATE 4/19,4/24,4/26/01</p>
	<p>AADA NUMBER 75276</p>
	<p>IND NUMBER</p>
	<p>TELECON</p>
	<p>INITIATED BY MADE</p> <p>— APPLICANT/ — BY</p> <p> SPONSOR TELE.</p> <p><u>X</u> FDA IN</p> <p> PERSON</p>
	<p>PRODUCT NAME Betamethasone Dipropionate Gel, 0.05%</p>
	<p>FIRM NAME Altana</p>
	<p>NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD Virginia Carman, Associate Director, Reg. Affairs</p>
	<p>TELEPHONE NUMBER (516) 454-7677</p>
	<p>SIGNATURE Paul Schwartz, <i>PS</i> phd. Team leader</p>

APPROVAL SUMMARY

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 75-276

Date of Submission: November 15, 1999 (Amendment)

Applicant's Name: Altana, Inc.

Established Name: Betamethasone Dipropionate Gel, 0.05% (Augmented)

hand
APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes

Container Labels: (15 g and 50 g) – Satisfactory as of November 15, 1999 submission

Carton Labeling: (15 g and 50 g) – Satisfactory as of November 15, 1999 submission

Professional Package Insert Labeling: Satisfactory as of November 15, 1999 submission

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Diprolene Gel, 0.05%

NDA Number: 19-408

NDA Drug Name: Betamethasone Dipropionate Gel, 0.05% (Augmented)

NDA Firm: Schering Corporation

Date of Approval of NDA Insert and supplement #006: November 22, 1991

Has this been verified by the MIS system for the NDA? Yes

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels: Side-by-side comparison

Basis of Approval for the Carton Labeling: Side-by-side comparison

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?	x		
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		x	
Is this name different than that used in the Orange Book?	x		
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	x		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?			
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		x	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)	x		
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	

Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	x		

NOTES/QUESTIONS TO THE CHEMIST:

The reference listed drug packages its product in 15 g and 45 g tubes. However, the applicant is proposing to package its product in 15 g and 50 g tubes.

FOR THE RECORD:

1. **Labeling review based on the approved labeling of the reference listed drug Diprolene Gel, 0.05% - Schering Corporation; revised 8/91; approved 11/22/91.) This is the first generic application for this product.**

2. **Packaging**
The RLD packages its product in 15 g and 45 g tubes.

The applicant is proposing to market its product in 15 g and 50 g aluminum, blind-end tubes rather than the 45 g tubes used by the RLD. This has been brought to the attention of the chemist.

4. **Labeling**
The Orange Book only uses Aaugmented@ in describing the Diprolene AF. However, since the descriptor is used with the RLD but is not a part of the established name, the applicant has been asked to place it at the end of the established name and strength in parentheses.

5. **Inactive Ingredients**
There does not appear to be a discrepancy between inactives listed in the DESCRIPTION section of the PI and the C&C Statements.

6. **USP Issues**
RLD - Store between 2° and 25°C (36° and 77°F).
ANDA - Same as the RLD

7. **Bioequivalence Issues - Pending**

8. **Patent/Exclusivity Issues - Diprolene Gel has 2 patents: #4489070 expiring December 18, 2001 and #4482539 expiring November 3, 2001. Altana has certified that they will not introduce the product into the market prior to their expiration.**

Date of Review:

April 12, 2000

Primary Reviewer:

/S/

Secondary Reviewer:

Date of Submission:

November 15, 1999 (Amendment)

Date:

4/12/00

Date:

Team Leader:

/S/

Date:

4/24/2000

cc: ANDA: 75-276
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review

**REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 75-276

Date of Submission: January 29,
1998

Applicant's Name: Altana, Inc.

Established Name: Betamethasone Dipropionate Gel, 0.05%
(Augmented)

Labeling Deficiencies:

1. GENERAL COMMENTS:

- a. The established name of this product is Betamethasone Dipropionate Gel. Throughout your labeling, please refer to your drug product as betamethasone dipropionate gel (augmented).
- b. Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when the USAN name stands alone as on labels or on the title of the package insert.
- c. Replace the _____ statement with the symbol "Rx only" or "R only". We refer you to the Guidance For Industry, "Implementation of Section 126, Elimination of Certain Labeling Requirements...", at the internet site, <http://www.fda.gov/cder/guidance/index.htm> for guidance.

2. CONTAINER (15 g and 50 g)

- a. Please ensure that the established name and strength appears as the most prominent information on your label. For example:

BETAMETHASONE DIPROPIONATE GEL, 0.05% (AUGMENTED*)

- b. See GENERAL COMMENTS.
- 3. CARTON (15 g and 50 g)
 - a. See GENERAL COMMENTS.
 - b. See CONTAINER comments.
- 4. INSERT
 - a. GENERAL COMMENT

Revise to delete the strength, "0.05%", appearing with the established name of your product throughout the text except the product title and HOW SUPPLIED section.
 - b. DESCRIPTION

Revise the first sentence of the second paragraph to read, ...molecular formula... rather than ...empirical formula...
 - c. PRECAUTIONS
 - i. General

Revise the first sentence of the eighth paragraph to read, ...antifungal... (delete dash).
 - ii. Carcinogenesis, Mutagenesis, and Impairment of Fertility
 - A) Revise to delete from the subsection heading.
 - B) Revise to delete the use of the terminal zero (i.e., "1" rather than and "2" rather than .
 - iii. Pregnancy

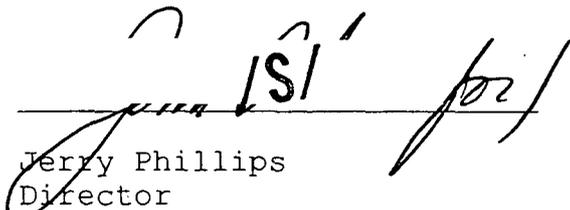
Revise the first sentence of the third paragraph to read, ...pregnant women.

Please revise your labels and labeling, as instructed above, and submit 4 draft copies for a tentative approval of this application. If draft labeling is provided, please be

advised that you will be required to submit 12 final printed copies of all labels and labeling at least 60 days prior to full approval of this application. In addition, you should be aware that color and other factors (print size, prominence, etc.) in final printed labeling could be found unacceptable and that further changes might be requested prior to approval.

Please note that the Agency reserves the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

A handwritten signature in black ink, appearing to read "Jerry Phillips", is written over a horizontal line. The signature is stylized and includes a large "S" or "SI" in the middle.

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?	x		
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23		x	
Is this name different than that used in the Orange Book?	x		
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	x		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?			
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		x	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).	x		
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		x	

Labeling (continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)	x		
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		x	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		x	
Do any of the inactives differ in concentration for this route of administration?		x	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		x	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?		x	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List C _{max} , T _{max} , T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	x		

NOTES/QUESTIONS TO THE CHEMIST:

The reference listed drug packages its product in 15 g and 45 g tubes. However, the applicant is proposing to package its product in 15 g and 50 g tubes. Is the proposed larger package size agreeable with you?

FOR THE RECORD:

1. Labeling review based on the approved labeling of the reference listed drug Diprolene Gel, 0.05% - Schering Corporation; revised 8/91; approved 11/22/91.) This is the first generic application for this product.

2. Packaging

The RLD packages its product in 15 g and 45 g tubes.

The applicant is proposing to market its product in 15 g and 50 g aluminum, blind-end tubes rather than the 45 g tubes used by the RLD. This has been brought to the attention of the chemist.

4. Labeling

The Orange Book only uses "augmented" in describing the Diprolene AF. However, since the descriptor is used with the RLD but is not a part of the established name, the applicant has been asked to place it at the end of the established name and strength in parentheses.

5. Inactive Ingredients

There does not appear to be a discrepancy between inactives listed in the DESCRIPTION section of the PI and the C&C Statements.

6. USP Issues

RLD - Store between 2° and 25°C (36° and 77°F).
ANDA - Same as the RLD

7. Bioequivalence Issues - Pending

8. Patent/Exclusivity Issues - Diprolene Gel has 2 patents: #4489070 expiring December 18, 2001 and #4482539 expiring November 3, 2001. Altana has certified that they will not introduce the product to the market prior to the patent expirations.

Date of Review:

May 19, 1998

Date of Submission:

January 29, 1998

Primary Reviewer:

IS/

Date:

3/20/98

Team Leader:

IS/

Date:

5/20/98

cc:

ANDA: 75-276
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review