

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
75279

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION/MEETING

<p>Dr. Schwartz informed the firm the following issues need to be addressed before approval this application:</p> <ol style="list-style-type: none"> 1. The packaging protocol on page 1154 should be withdrawn. 2. There are no stability data using the J. L. Clark's tube/cap. The firm should either withdraw this packaging system or provide the corresponding stability data. 3. The certificate of analysis of drug substance should include the tests for the residual solvents indicated in the manufacturer's certificate of analysis. 4. The manufacturing instruction indicates that a holding tank will be used after the completion of mixing process. The firm should provide a statement to assure that a bulk product will not be stored more than 30 days or a certain days justified by stability data. 5. Active ingredient testing commitment on page 912 should be withdrawn since this is a cGMP issue. <p>The firm agreed to look into these issues and will respond them by a telephone amendment probable as early as tomorrow morning.</p>	<p>DATE: May 25, 1999</p>
	<p>ANDA NUMBER: 75-279</p>
	<p>IND NUMBER: N/A</p>
	<p>TELECON</p>
	<p>INITIATED BY: <input type="checkbox"/> APPLICANT/SPONSOR <input checked="" type="checkbox"/> FDA</p>
	<p>MADE: <input checked="" type="checkbox"/> BY TELEPHONE <input type="checkbox"/> IN PERSON</p>
	<p>PRODUCT NAME: Clobetasol Propionate Gel, 0.05%</p>
	<p>FIRM NAME: Taro Pharmaceuticals Inc.</p>
	<p>NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Lorraine Sachs, Associate Director Allen Rudman, Deputy Director Paul Schwartz, Team Leader Naiqi Ya, Chemist</p>
	<p>TELEPHONE NUMBER: (914) 345-9001</p>
<p>SIGNATURE:</p> <p align="right">  5/25/99  5/25 Naiqi Ya, Ph.D. Paul Schwartz, Ph.D. </p>	

RECORD OF TELEPHONE CONVERSATION/MEETING

<p>With Dr. Schwartz and Dr. Ya attending; we called Taro and, again, recommended that the total impurities limit be reduced to NMT %.</p> <p>Alternatively, we you could propose a limit of NMT % with the sum of synthetic precursors in the calculation.</p> <p>The firm said they would our comments under advisement and respond.</p> <p>ANDA T-con Binder</p>	<p>DATE: May 11, 1999</p> <hr/> <p>ANDA NUMBER: 75-279</p> <hr/> <p>IND NUMBER: N/A</p> <hr/> <p style="text-align: center;">TELECON</p> <hr/> <p>INITIATED BY: <input type="checkbox"/> APPLICANT/SPONSOR <input checked="" type="checkbox"/> FDA</p> <hr/> <p>MADE: <input checked="" type="checkbox"/> BY TELEPHONE <input type="checkbox"/> IN PERSON</p> <hr/> <p>PRODUCT NAME: Clobetasol Propionate Gel 0.05%</p> <hr/> <p>FIRM NAME: TARO</p> <hr/> <p>NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Lorraine Sachs, Regulatory Yabi Jacobi Derek Ganes Terry Feldman</p> <hr/> <p>TELEPHONE NUMBER: (914)-345-9001</p> <hr/> <p>SIGNATURE: <div style="text-align: center;">  Joseph Buccine, PM </div> </p>
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APPROVAL SUMMARY

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

ANDA Number: 75-279

Date of Submission: August 21, 1998

Applicant's Name: Taro Pharmaceuticals, Inc.

Established Name: Clobetasol Propionate Gel, 0.05%

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, 30 g, and 60 g)

Satisfactory as of August 21, 1998, submission

Carton Labeling: (15 g, 30 g, and 60 g)

Satisfactory as of August 21, 1998, submission

Professional Package Insert Labeling:

Satisfactory as August 21, 1998, submission

Revisions needed post-approval:

TITLE - Revise the second line to read,
FOR ~~TOPICAL~~ USE ONLY. NOT FOR OPHTHALMIC, ORAL, OR
INTRAVAGINAL USE

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Temovate Gel

NDA Number: 20-337

NDA Drug Name: Clobetasol Propionate Gel, 0.05%

NDA Firm: Glaxo Dermatology

Date of Approval of NDA Insert: April 29, 1994

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?		x	
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	

FOR THE RECORD:

1. Labeling review based on labeling of the reference listed drug (Temovate® Gel, 0.05% - Glaxo Dermatology; revised June 1994; approved April 29, 1994; acknowledged and retained May 3, 1995).

2. Packaging
The RLD packages its product in 15 g, 30 g, and 60 g tubes.

The applicant is proposing to package its product in aluminum blind-ended tubes of the same package sizes.

3. Labeling

The labeling for the three products produced by Taro appear to be differentiated.

Per 21 CFR 201.55, firm was asked to revise their prescribing information statement to read,
USUAL DOSAGE: Apply a thin layer of clobetasol propionate gel to the affected skin areas twice daily and rub in gently and completely. See...information.

4. Inactive Ingredients
There is no discrepancy in inactive between DESCRIPTION and the composition statement.

5. USP Issues
Clobetasol propionate is the subject of a USP monograph. Although the gel form of this drug product is not USP, Stiefel has been asked to revise the molecular weight and chemical name to comply with the USP.

Storage recommendations are the same as those of the RLD, Store between 15-30°C (59-86°F).

USP recommends that clobetasol propionate be preserved in tight, light-resistant containers. Chemist has been asked to ensure that proposed container complies.

6. Bioequivalence Issues - Pending

7. Patent/Exclusivity Issues - None pending.

Date of Review:
January 22, 1999

Date of Submission:
August 21, 1998

Primary Reviewer:

Date:

Team Leader:

Date:

IS/

4/22/99

J/IS/

1/22/99

cc:

ANDA: 75-279
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: 75-279

Date of Submission: December 19,
1997

Applicant's Name: Taro Pharmaceuticals Inc.

Established Name: Clobetasol Propionate Gel, 0.05%

Labeling Deficiencies:

1. CONTAINER (15 g, 30 g, 60 g)
 - a. Revise the content statement to read,
Each gram contains: Clobetasol propionate
0.5 mg in...
 - b. Revise the prescribing information statement to
read, USUAL DOSAGE: Apply a thin layer of
clobetasol propionate gel to the affected skin
areas twice daily and rub in gently and
completely. See...information.
2. CARTON (15 g, 30 g, 60 g)

See CONTAINER comments.
3. INSERT
 - a. TITLE

Revise the second line to read,
FOR TOPICAL USE ONLY.
 - b. DESCRIPTION
 - i. Revise the second paragraph to use the second
chemical name listed in the USP.
 - ii. Revise the first sentence of the third
paragraph to read, ...molecular formula...
 - iii. Revise the molecular weight to read, 466.98,
to be in accord with the USP.
 - iv. Revise the fourth paragraph to read,

Each gram, for topical administration,
contains clobetasol propionate 0.5 mg in...

Please revise your labels and labeling, as instructed above,
and submit in final print.

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.

/S/
for

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?		x	
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
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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	
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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:

Please ensure that the tubes in which the product will be packaged are tight and light-resistant per USP recommendation.

FOR THE RECORD:

1. Labeling review based on labeling of the reference listed drug (Temovate® Gel, 0.05% - Glaxo Dermatology; revised June 1994; approved April 29, 1994; acknowledged and retained May 3, 1995).

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5. USP Issues

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Storage recommendations are the same as those of the RLD, Store between 15-30°C (59-86°F).

USP recommends that clobetasol propionate be preserved in tight, light-resistant containers. Chemist has been asked to ensure that proposed container complies.

6. Bioequivalence Issues - Pending

7. Patent/Exclusivity Issues
None pending.

Date of Review:
April 29, 1998

Date of Submission:
December 19, 1997

Primary Reviewer:

Date:

/S/

4/29/98

Team Leader:

Date:

/S/

4/30/98

CC:

ANDA 75-279
DUP/DIVISION FILE
HFD-613/LGolson/JGrace (no cc)

Review