CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-224

ADMINISTRATIVE DOCUMENTS

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Application: **ANDA 75224/000**
Stamp: **09-OCT-1997** Regulatory Due:
Applicant: **TARO PHARMS (CA)**
130 EAST DR, L6T 1C3
BRAMALEA, ONTARIO, CA

Priority:
Org Code: **600**
Action Goal:
District Goal: **09-DEC-1998**
Brand Name:
Established Name: **CLOBETASOL PROPIONATE**
Generic Name:
Dosage Form: **SOL (SOLUTION)**
Strength: **0.05%**

FDA Contacts: **T. AMES (HFD-617) 301-827-5849 , Project Manager**
U. VENKATARAM (HFD-647) 301-827-5849 , Team Leader

Overall Recommendation:

ACCEPTABLE on 18-FEB-1998 by M. EGAS (HFD-322) 301-594-0095

Establishment:
6, M1H
, CA

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **14-NOV-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE OTHER TESTER**

Establishment

DMF No:
AADA No:

Profile: **CSN** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **18-FEB-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **DRUG SUBSTANCE MANUFACTURER**

Establishment:

):
No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **14-NOV-1997**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: **DRUG SUBSTANCE OTHER TESTER**

ESTABLISHMENT EVALUATION REQUEST SUMMARY REPORT

Establishment:
TARO PHARMACEUTICALS INC
130 EAST DR, L6T 1C3
BRAMALEA, ONTARIO, CA

DMF No:
AADA No:

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date **17-NOV-1997**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**

Responsibilities: **FINISHED DOSAGE MANUFACTURER**

ANDA APPROVAL SUMMARY

ANDA:	CHEMIST:	DATE:
75-224	Neeru B. Takiar	September 28,1998

DRUG PRODUCT:
Clobetasol Propionate

FIRM:
Taro Pharmaceuticals USA Inc.

DOSAGE FORM:	STRENGTH:
Topical Solution	0.05%

cGMP:
EER was found acceptable by M.Egas on 2/18/98.

BIO:
Request for waiver was granted by Andre Jakson on 3/3/98.

VALIDATION - *(Description of dosage form same as firm's):*
The drug product is compendial.

STABILITY:
The firm has provided 3 months satisfactory accelerated stability data and 9 months room temperature stability data for 0.05% topical solution (lot # L113-5907) in HDPE bottles of 25 mL and 100 mL sizes. The stability data support an expiration of 24 months.

LABELING:
Labeling was found satisfactory by L. Golson on 7/16/98.

STERILIZATION VALIDATION *(If applicable)*:
N/A

SIZE OF BIO BATCH *(Firm's source of NDS ok?)*:
The firm has provided the master formula and manufacturing procedure for production batch size of and copies of the exhibit batch record (lot # L113-5907) for 40 Kg using Sicor drug substance lot # 5383/MI. The DMF found satisfactory on 3/31/98. The firm will be using the same equipment and procedure.

SIZE OF STABILITY BATCHES *(If different from bio batch, were they Manufactured via the same process?)*:
N/A

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME?:
The manufacturing process is same.

Signature of chemist:	Signature of supervisor:
Neeru B. Takiar 10/26/98	Paul Schwartz, Ph.D.

A:\ANDAAPP.SUM

PS 9/28/98

Application: ANDA 75224/000
Stamp: 09-OCT-1997 Regulatory Due:
Applicant: TARO PHARMS (CA)
130 EAST DR, L6T 1C3
BRAMALEA, ONTARIO, CA

Priority: Org Code: 600
Action Goal: District Goal: 09-DEC-1998
Brand Name:
Established Name: CLOBETASOL PROPIONATE
Generic Name:
Dosage Form: SOL (SOLUTION)
Strength: 0.05%

FDA Contacts: T. AMES (HFD-617) 301-827-5849 , Project Manager
U. VENKATARAM (HFD-647) 301-827-5849 , Team Leader

Overall Recommendation:

ACCEPTABLE on 18-FEB-1998 by M. EGAS (HFD-322) 301-594-0095

Establishment: DMF No:

, M1H AADA No:
A

Profile: CTL OAI Status: NONE Responsibilities:
Last Milestone: OC RECOMMENDAT 14-NOV-1997 DRUG SUBSTANCE OTHER TESTER
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Establishment: DMF No:

77 AADA No:

Profile: CSN OAI Status: NONE Responsibilities:
Last Milestone: OC RECOMMENDAT 18-FEB-1998 DRUG SUBSTANCE MANUFACTURER
Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

Establishment:

o:

Profile: CTL OAI Status: NONE Responsibilities:
Last Milestone: OC RECOMMENDAT 14-NOV-1997 DRUG SUBSTANCE OTHER TESTER
Decision: ACCEPTABLE
Reason: BASED ON PROFILE

Establishment: 9614240 DMF No:
TARO PHARMACEUTICALS INC
130 EAST DR, L6T 1C3

9614240 AADA No:

TARO PHARMACEUTICALS INC

BRAMALEA, ONTARIO, CA Responsibilities:

FINISHED DOSAGE MANUFACTURER

Profile: **LIQ** OAI Status: **NONE**

Last Milestone: **OC RECOMMENDAT 17-NOV-1997**

Decision: **ACCEPTABLE**

Reason: **DISTRICT RECOMMENDATION**

APPROVAL SUMMARY

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

ANDA Number: 75-224 Date of Submission: March 23, 1998 and July 13, 1998 (Amendments)

Applicant's Name: Taro Pharmaceuticals, Inc.

Established Name: Clobetasol Propionate Topical Solution USP, 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:

1. 25 mL - Satisfactory as of March 23, 1998 submission
2. 50 mL - Satisfactory as of July 13, 1998 submission

Carton Labeling:

1. 25 mL - Satisfactory as of March 23, 1998 submission
2. 50 mL - Satisfactory as of July 13, 1998 submission

Professional Package Insert Labeling:

Satisfactory as of July 13, 1998 submission

BASIS OF APPROVAL:

Was this approval based upon a petition? Yes

What is the RLD on the 356(h) form: Temovate Scalp Application, 0.05%

NDA Number: 19-966

NDA Drug Name: Clobetasol Propionate Topical Solution USP, 0.05%

NDA Firm: Glaxo, Inc. - Dermatology Product Development

Date of Approval of NDA Insert: February 22, 1990

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: 19-966

Basis of Approval for the Carton Labeling: 19-966

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.			

NOTES/QUESTIONS TO THE CHEMIST: None

FOR THE RECORD:

1. Labeling review based on the approved labeling of NDA #19-966 for the RLD (Temovate® Scalp Application, 0.05% - Glaxo Wellcome; revised January 1990; approved Feb. 22, 1990).

2. Packaging
   The RLD packages its product in 25 mL and 50 mL plastic squeeze bottles.

   The applicant is proposing to package its product in 25 mL white LDPE and 50 mL white HDPE oval containers with dropper tips.

3. Labeling
   Since the route of administration for this product is clearly identified in the product name of the RLD, Taro included "For Use on the Scalp" on the principal display panel of its container labels and carton labeling as requested.

   To clarify that the product is 0.05% w/w, Taro expresses its product strength as "...0.05% (0.5 mg/g)" on its container label and carton labeling as requested.

   In the ADVERSE REACTIONS section of the labeling, Taro revised the ultimate paragraph to use percentages rather than actual study data figures since studies were not conducted. This is in keeping with revised labeling drafted by OGD.

4. Inactive Ingredients
There does not appear to be a discrepancy in inactives between the DESCRIPTION section of the insert labeling and the Components and Composition Statements.

This product contains isopropyl alcohol.

5. USP Issues
USP - Preserve in tight containers. Store at CRT. Do not refrigerate.
RLD - Store between 4°-25°C (39°-77°F). Do not use near an open flame.
ANDA - Same as USP. Firm included the "open flame" statement.

6. Bioequivalence Issues - Waiver granted March 3, 1998.

7. Patent/Exclusivity Issues - None

Date of Review:
July 16, 1998

Date of Submission:
March 23, 1998 and July 13, 1998 (Amendments)

Primary Reviewer:

Date:
7/16/98

Team Leader:

Date:
7/17/98

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cc:

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

ANDA Number: 75-224 Date of Submission: October 8, 1997

Applicant's Name: Taro Pharmaceuticals, Inc.

Established Name: Clobetasol Propionate Topical Solution USP, 0.05%

Labeling Deficiencies:

1. CONTAINER (25 mL and 50 mL)

   a. Revise to include on the principal panel in prominent lettering, "FOR USE ON THE SCALP".

   b. Revise the "Contains" statement to read, ...0.05% (0.5 mg/g) in a...

   c. Revise the "See package insert" statement to read, "USUAL DOSAGE: See package insert...

   d. Revise "Do not use near an open flame" to appear in equal prominence as the rest of your storage recommendation .

2. CARTON (25 mL and 50 mL)

   See CONTAINER comments.

3. INSERT

   a. DESCRIPTION

      i. Revise the chemical name to the second name listed in the official monograph for clobetasol propionate in USP 23, supplement #2.

      ii. Revise the first sentence of the third paragraph to read, ...molecular formula...molecular weight of 466.98.

b. CLINICAL PHARMACOLOGY

Revise the first sentence of the second paragraph to read, Clobetasol propionate, a corticosteroid, has been... (Note: add comma)

c. INDICATIONS AND USAGE

Revise so that the ultimate sentence of the first paragraph, "This product is not..." is a new paragraph.

d. PRECAUTIONS (General)

Revise the first sentence of the eighth paragraph to read, "As with other potent topical corticosteroids, clobetasol... (Note: add comma)

e. ADVERSE REACTIONS

Revise the second paragraph to read, ...sensation, which occurred in approximately 10% of the patients; scalp pustules, which occurred in approximately 1% of the patients; and tingling and folliculitis, each of which occurred in 0.7% of the patients. Less...and eye irritation.

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/

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

Clobetasol Propionate
0.05% Topical Solution
ANDA # 75224
Reviewer: Andre Jackson
WP # 75224W-097

Taro Pharmaceuticals
Bramalea, Ontario
Submission Date:
October 8, 1997

REVIEW OF A WAIVER REQUEST

The firm is requesting a waiver of the in-vivo bioequivalence requirements for their clobetasol proprionate topical solution , which is a corticsteriod which is indicated for short-term topical treatment of inflammatory and pruritic manifestations of moderate to severe corticosteroid-responsive dermatoses of the scalp. The waiver request is based upon comparable formulation to the reference product Temovate[R] manufactured by Glaxo-Wellcome.

Comments:

1. The product meets the criteria for waiver of the in vivo bioequivalence study requirements set forth in CFR 320.22b(3)(i)(ii)(iii).

a. The test product is a solution intended solely for application to the skin.

b. It contains an active ingredient in the same concentration and dosage form as a drug product that is subject to an approved full new drug application.

c. It contains no inactive ingredient or other change in formulation from the drug product that is the subject of the approved full new drug application that may significantly affect absorption of the active moiety.

2.The comparative formulations for the 0.05% Topical Solution is presented in Table 1.

Table 1. Comparative formulations for the reference and test clobetasol propionate topical solutions.

0.05% Topical Solution	Reference	Test
Clobetasol Propionate	0.05%	0.05%
Carbomer	0.13%	0.18%
Isopropyl Alcohol	39.3%	39.3%
Sodium hydroxide	adjust for pH	adjust for pH
Purified Water	q.s.	q.s.

Comment

1. The test product contains 0.05% higher concentration of carbomer which is a thickening agent and this is within the 5% window for Q/Q and probably would have little effect on absorption.

Recommendation:

The Division of Bioequivalence agrees that the information submitted by Taro Pharmaceuticals demonstrates that clobetasol propionate topical solution; 0.05% falls under 21 CFR Section 320.22(b)(3)(i)(ii)(iii) of the Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence study for the 0.05% topical solution of the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems the test formulation to be bioequivalent to Temovate[R] manufactured by Glaxo-Wellcome.

Andre Jackson
Review Branch I
Division of Bioequivalence

RD INITIALED YCHUANG
FT INITIALED YCHUANG Date 3/3/98

Concur: /S/ Date 3/3/98

Dale P. Conner, Pharm D.
Director
Division of Bioequivalence

CDER Establishment Evaluation Report for November 13, 1997

Application: ANDA 75224/000
Stamp: 09-OCT-1997 Regulatory Due:
Applicant: TARO PHARMS (CA)
130 EAST DR, L6T 1C3
BRAMALEA, ONTARIO, CA

Priority:
Action Goal:
Brand Name:
Established Name: CLOBETASOL PROPIONATE
Generic Name:
Dosage Form: SOL (SOLUTION)
Strength: 0.05%

Org Code: 600
District Goal: 09-DEC-1998

FDA Contacts: T. AMES (HFD-617) 301-827-5849 , Project Manager
U. VENKATARAM (HFD-647) 301-827-5849 , Team Leader

Overall Recommendation:

Establishment

DMF No:

AADA No:

Profile: NEC OAI Status: NONE
Last Milestone: SUBMITTED TO OC 13-NOV-1997

Responsibilities:
DRUG SUBSTANCE OTHER TESTER

Establishment

DMF No

AADA No:

Profile: CSN OAI Status: NONE
Last Milestone: SUBMITTED TO OC 13-NOV-1997

Responsibilities:
DRUG SUBSTANCE MANUFACTURER

Establishment:

DMF No:

LABORAT

AADA No:

Profile: NEC OAI Status: NONE
Last Milestone: SUBMITTED TO OC 13-NOV-1997

Responsibilities:
DRUG SUBSTANCE OTHER TESTER

Establishment: 9614240
TARO PHARMACEUTICALS INC
130 EAST DR, L6T 1C3
BRAMALEA, ONTARIO, CA

DMF No:

AADA No:

9614240 Responsibilities:

TARO PHARMACEUTICALS INC **FINISHED DOSAGE MANUFACTURER**

BRAMALEA, ONTARIO, CA

Profile: **LIQ** OAI Status: **NONE**
Last Milestone: **SUBMITTED TO OC 13-NOV-1997**

TELEPHONE MEMO

To: Lorraine Sachs (Taro Pharmaceuticals USA, Inc.) for Taro Pharmaceuticals Inc. (914) 345-9001

CC: ANDA 75-224 (Clobetasol Propionate Topical Solution USP, 0.05%)

From: Saundra T. Middleton

Date: November 7, 1997

Subject: Patent Certification

Ms. Sachs was asked to revise the patent certification and take out the word "fluocinonide" and insert Clobetasol Propionate.

Will fax copy and follow-through with hard copy.

E L E C T R O N I C M A I L M E S S A G E

Date: 13-Nov-1997 09:16am EST
From: William Rickman
RICKMAN
Dept: HFD-615 MPN2 113
Tel No: 301-827-5862 FAX 301-594-0174

TO: ELLA S WALKER (ORA) (EWALKER@ORA.FDA.GOV @INTERNET)
TO: ALFRED C KING (ORA) (AKING1@ORA.FDA.GOV @INTERNET)

Subject: RE: Methods Verification

OGD has accepted forfiling ANDA 74-224 for Clobetasol Propionate Topical Solution USP, 0.05% from:

Taro Pharmaceuticals USA, Inc.
Att: Lorraine Sachs
US Agent for: Taro Pharmaceuticals Inc.
5 Skyline Drive
Hawthorne, NY 10532
(914)345-9001

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

ANDA Number: 75-224 Date of Submission: October 8, 1997

Applicant's Name: Taro Pharmaceuticals, Inc.

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   d. Revise "Do not use near an open flame" to appear in equal prominence as the rest of your storage recommendation .

2. CARTON (25 mL and 50 mL)

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3. INSERT

   a. DESCRIPTION

      i. Revise the chemical name to the second name listed in the official monograph for clobetasol propionate in USP 23, supplement #2.

      ii. Revise the first sentence of the third paragraph to read, ...molecular formula...molecular weight of 466.98.

b. CLINICAL PHARMACOLOGY

Revise the first sentence of the second paragraph to read, Clobetasol propionate, a corticosteroid, has been... (Note: add comma)

c. INDICATIONS AND USAGE

Revise so that the ultimate sentence of the first paragraph, "This product is not..." is a new paragraph.

d. PRECAUTIONS (General)

Revise the first sentence of the eighth paragraph to read, "As with other potent topical corticosteroids, clobetasol... (Note: add comma)

e. ADVERSE REACTIONS

Revise the second paragraph to read, ...sensation, which occurred in approximately 10% of the patients; scalp pustules, which occurred in approximately 1% of the patients; and tingling and folliculitis, each of which occurred in 0.7% of the patients. Less...and eye irritation.

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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.

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., Opacoda, 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.			

NOTES/QUESTIONS TO THE CHEMIST: None

FOR THE RECORD:

1. Labeling review based on the approved labeling of NDA #19-966 for the RLD (Temovate® Scalp Application, 0.05% - Glaxo Wellcome; revised January 1990; approved Feb. 22, 1990).

2. Packaging
The RLD packages its product in 25 mL and 50 mL plastic squeeze bottles.

The applicant is proposing to package its product in 25 mL white LDPE and 50 mL white HDPE oval containers with dropper tips.

3. Labeling
Since the route of administration for this product is clearly identified in the product name of the RLD, Taro will be asked to include "For Use on the Scalp" on the principal display panel of its container labels and carton labeling.

To clarify that the product is 0.05% w/w, Taro has been asked to express its product strength as "...0.05% (0.5 mg/g)" on its container label and carton labeling.

In the ADVERSE REACTIONS section of the labeling, Taro has been asked to revise the ultimate paragraph to use percentages rather than actual study data figures since studies were not conducted. This is in keeping with revised labeling drafted by OGD.

4. Inactive Ingredients
There does not appear to be a discrepancy in inactives between the DESCRIPTION section of the insert labeling and the Components and Composition Statements.

This product contains

5. USP Issues
USP - Preserve in tight containers. Store at CRT. Do not refrigerate.
RLD - Store between 4°-25°C (39°-77°F). Do not use near an open flame.
ANDA - Same as USP. Firm included the "open flame" statement using a smaller font. It was asked to revise so that the statement appears as prominent as the rest of the storage