CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40386

CORRESPONDENCE

ANDA 40-386

Thames Pharmacal Co., Inc.
Attention: Srinivasa Rao
2100 Fifth Avenue
Ronkonkoma, NY 11779

SEP 16 1999

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated September 7, 1999 and your correspondence dated September 7, 1999.

NAME OF DRUG: Triamcinolone Acetonide Ointment USP, 0.5%

DATE OF APPLICATION: August 3, 1999

DATE (RECEIVED) ACCEPTABLE FOR FILING: August 6, 1999

We will correspond with you further after we have had the opportunity to review your application.

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Joe Buccine
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ack for filing 9/8/99 505(j)(2)(A) S. Middleton

Thames PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (516) 737-1155

Office of Generic Drug, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: Abbreviated New Drug Application for
"Triamcinolone Acetonide Ointment USP, 0.5%"

Dear Sir/Madam:

Pursuant to section 505 (j) of Federal Food, Drug and Cosmetic Act, we are herewith submitting an **abbreviated new drug application** for the above referenced drug product.

Included are the following:

1. Original ANDA (Blue Folder-FDA 2626)
2. Archival Copy (Blue Folder-FDA 2626)
3. Review Copy
   - (i) CMC (Red Folder-FDA 2626a)
   - (ii) Bioavailability/Bioequivalence (Orange Folder-FDA 2626c)

Field copy will be sent to the district office in a separate envelope.

Very truly yours,
Thames Pharmacal

7/30/99

SRINIVASA RAO, M.Pharm, MS, RPh., FASCP
Supervisor, Research and Development

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
AUG 3 1 1999
OGD

SUMMARY

Triamcinolone Acetonide Ointment USP, 0.5% (Aristocort A® Ointment 0.5%) is a topically administered product. Each gram of the product contains 5 mg of Triamcinolone Acetonide, USP as the active ingredient. Triamcinolone Acetonide is a corticosteroid. Its safety and efficacy has already been determined. Triamcinolone Acetonide Ointment USP 0.5% is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Triamcinolone Acetonide, USP is an official (USP 23, pg.no. 1575) item. Its chemical, pharmacological and toxicological properties have been previously established.

Two batches of Triamcinolone Acetonide Ointment USP, 0.5% were manufactured (Lot #'s M300 and M350) at Thames Pharmacal Co., Inc., Ronkonkoma plant, using Standard Operating Procedure as per CGMPs. Lot #'s M 300 and M 350 were put on accelerated stability to check their physical and chemical properties over a period of three months. Based on the results of stability studies, the product was found to be stable physically and chemically, well within specifications. Triamcinolone Acetonide Ointment USP, 0.5% complies with USP microbial limit test.

The product Triamcinolone Acetonide Ointment USP, 0.5%, will be available in 15 g, 30 g, 80 g and lb. package sizes upon approval.

Thames
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2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (516) 737-1155

FIELD CERTIFICATION STATEMENT

Thames Pharmacal Co., Inc., hereby certifies that the field copy is a true copy of the technical section described in section 314.94(a) (9) contained in the archival and review copies of the abbreviated application for "Triamcinolone Acetonide Ointment USP, 0.5%"

Very truly yours,
Thames Pharmacal Co., Inc.

S. [signature] 7/30/99

SRINIVASA RAO, M.Pharm, MS, RPh, FASCP
Supervisor, Research and Development

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

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NDA ORIG AMENDMENT
AB

February 25, 2000

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attn: Ms. Elaine Hu, Project Manager

Ref: Triamcinolone Acetonide Ointment USP, 0.5%
ANDA # 40-386 – **Bio-equivalency Amendment**

Dear Ms. Hu:

Pursuant to your bio-equivalency comments dated November 19, 1999, Thames Pharmacal Co., Inc. has the following response.

The inactive ingredients in the test formulation containing White Petrolatum, USP and Light Mineral Oil, NF is less likely to affect the safety of the drug product, Triamcinolone Acetonide Ointment USP, 0.5%, since a similar combination of inactives were previously approved by the Office of Generic Drugs.

At the present time, Triamcinolone Acetonide Ointment USP, 0.5% is marketed by two manufacturers.

Applicant	Application Number	Approval Date	Inactive Ingredient
Clay Park	**087385**	**Approved prior to January 1, 1982**	**White Petrolatum, USP and Light Mineral Oil, NF**
Altana	**085691**	**Approved prior to January 1, 1982**	**White Petrolatum, USP and Mineral Oil, NF**

Based on the above information, we feel that we have satisfactorily cited examples of drug products with similar test inactive ingredients, which are proven to be safe.

If you have any questions, feel free to contact me at (631) 737-1155.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M. Pharm, MS, R.Ph.

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (516) 737-1155

June 20, 2000

ORIG AMENDMENT
N/AC

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attn: Ms. Elaine Hu

Ref: **MAJOR AMENDMENT – ANDA # 40-386**
Triamcinolone Acetonide Ointment USP, 0.5%

Dear Ms. Hu:

Pursuant to the major amendment dated February 17, 2000, Thames Pharmacal Co., Inc. has the following responses:

A. Deficiencies

1. **Please revise your specifications for the drug substance to include test and specifications for chromatographic purity, residual solvents, and organic volatile impurities. Provide a revised COA with the results of those tests.**

Response
We have revised our drug substance specification sheet to include the following:

a) Chromatographic purity
   (i) Individual impurity NMT ___%
   (ii) Total impurities NMT ___%

b) Organic Volatile Impurities –

Since the manufacturer of the drug substance has assurance, based on knowledge of the manufacturing process and controlled handling, shipping and storage of the drug substance Triamcinolone Acetonide, USP, Thames Pharmacal will rely on the Certificate of Analysis provided by the drug substance manufacturer. _____ have residual solvents tested for each lot during the active release and they comply with the test limits, which are indicated in the Certificate of Analysis. As stated in the general statement (see page # 6-8) by both drug substance manufacturers, the residual solvents present in the drug substance meet the required specification.

2. **Please revise your bulk product specifications to include assay and specification for_____ _____ with RSD.**

Response
We have included _____ analysis with the RSD in our bulk drug product specification sheet (see page # 9-11).

3. **Please revise your finished drug product specifications to include limits and specifications for viscosity, and related substance and impurities and provide the results.**

Response
We have revised our finished drug product specification sheet to include specifications for viscosity and degradants level. Both individual and total degradants will be reported on this sheet. Please see page # 9-11.

4. **Please provide full term room temperature stability data.**

Response
Please see page # 12-19.

5. **Please provide cycle study data.**

Response
Enclosed please find the cycle study performed for the drug product, Triamcinolone Acetonide Ointment USP, 0.5%. As the results indicate, very little variation is seen in the potency of the active when the sample is subjected to extreme conditions. However, the 16-oz package size sample was retested and found to be within specification. We can conclude, based on the results obtained, that the drug product could withstand at both of the extreme temperatures. Please see page # 20-21.

6. **Please revise your stability specifications to include test and specification for viscosity, and related substances (individual and total). Provide the results with your additional stability data.**

   Response
   We have revised our stability cards to include viscosity and degradant levels of both total and individual degradants (please see page # 12-19).

7. **Please revise your stability specifications to indicate that the assay test will be conducted at the top, middle and bottom of the tubes.**

   Response
   We have revised our stability cards to include assay testing at the top, middle and bottom of the finished drug product.

8. **Please provide information on the container liner.**

   Response
   We have previously provided this information in our original application. Please see page # 626-629.

9. **What tests do you perform on your containers? Provide the results of such tests.**

   Response
   Enclosed please find test results of polypropylene and HDPE analysis, USP <661>, performed on our 1-lb jar container closure system. The testing performed includes:

   a) Water Vapor Permeation
   b) Heavy Metals
   c) Non-Volatile Residue
   d) Residue on Ignition
   e) Light Transmission

   _____ performed the above tests.

   The lot # (RCBI #) used to perform this test was not used to package our submission batch. But, the resin specifications and other specifications including the stock # are the same. All other packaging is packed in aluminum tubes, which do not require any testing, by the USP (see page # 22-32).

10. **Please provide the supplier of the drug substance on the stability report on pages 1140 through 1147.**

Response
We have revised our stability sheets to include supplier information of the drug substance manufacturer.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. **The firms referenced in your application should be in compliance with CGMP at the time of the approval.**

   Response
   We believe that the referenced firms are in compliance with CGMP.

2. **Please provide a categorical exclusion request under 21 CFR 225.31 (a). and certify that you are in compliance with all applicable local, state and federal environmental regulations.**

   Response
   Please see attached, see page # 33-34.

3. **USP methods are the regulatory methods and will prevail in the event of dispute.**

   Response
   We acknowledge your comments.

4. **We are waiting for your response to the letter from the Division of Bio-equivalence dated November 19, 1999.**

   Response
   We had responded to the Bio-equivalency deficiency on February 25, 2000.

5. **Please update your list of outside laboratories that will be used.**

   Response
   We will be using _____ as our outside testing laboratories.

Labeling Deficiencies

Response
As noted in our previous correspondence dated April 11, 2000 we were unable to obtain the labeling information for the 0.5% strength drug product. We believe that the information provided is likely to be similar to that of the 0.5% strength drug product.

We have also revised our labeling information as requested by your office to include:

a) "For external use only." on the principal display panel(s).
b) Changing the molecular weight to "434.51" on the insert labeling.
c) Revision of the heading to read: Pregnancy. Teratogenic Effects, Pregnancy Category C on the insert labeling.

We have included a side-by-side comparison of container, carton and insert labeling. Please see attached labeling page # 35-71.

We believe that we have responded to the major amendment deficiencies.

If you have any questions, feel free to contact me at (631) 737-1155 x 45.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M. Pharm, M.S., R.Ph.
Director of Regulatory Affairs

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (631) 737-1155 FAX (631) 737-3185

NDA ORIG AMENDMENT
N/A

June 1, 2001

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Attention: Ms. Pat Block

Re: Telephone Amendment – ANDA #40-386
Triamcinolone Acetonide Ointment USP, 0.5%

By fax: 301-594-0183

Dear Ms. Block:

Pursuant to our conversation dated May 30, 2001, Thames Pharmacal Co., Inc. has the following as its response:

Tests on residual solvents including Acetone (NMT____ppm), Methanol (NMT____ ppm) and Dimethylformamide (NMT____ppm) will be performed on three batches of the drug substance Triamcinolone Acetonide, USP and the results will be reported in our annual report for this drug product.

If you have any questions, please call me at (631) 737-1155.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M. Pharm, M.S., R.Ph.
Director, Regulatory Affairs

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (631) 737-1155 FAX (631) 737-3185

NDA ORIG AMENDMENT
N/FA

May 31, 2001

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Attention: Ms. Pat Block

Re: Telephone Amendment – ANDA #40-386
Triamcinolone Acetonide Ointment USP, 0.5%

Dear Ms. Block:

Pursuant to our conversation dated May 30, 2001, Thames Pharmacal Co., Inc. has the following as its response:

Tests on residual solvents including Acetone (NMT ____ ppm), Methanol (NMT ____ ppm) and Dimethylformamide (NMT ____ ppm) will be performed on three batches of the drug substance Triamcinolone Acetonide, USP and the results will be reported in our annual report for this drug product.

If you have any questions, please call me at (631) 737-1155.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M. Pharm, M.S., R.Ph.
Director, Regulatory Affairs

B21

Thames
PHARMACAL CO., INC.

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May 8, 2001

NC

NEW CORRESP

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Pat Block

Re: **Telephone Amendment – ANDA # 40-374**
Triamcinolone Acetonide Ointment USP, 0.025%

Dear Ms. Block:

Pursuant to our conversation dated May 8, 2001, Thames Pharmacal has the following as its response:

1. We are withdrawing _____ as our contract testing laboratory.

If you have any questions, please call me at (631) 737-1155.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M. Pharm, M.S., R.Ph.
Director of Regulatory Affairs

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (516) 737-1155

April 12, 2001

NDA ORIG AMENDMENT
N/FA

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Elaine Hu

Ref: TELEPHONE AMENDMENT – ANDA # 40-386
Triamcinolone Acetonide Ointment USP, 0.5%

Dear Ms. Hu:

Pursuant to our conversation dated April 11, 2001, Thames Pharmacal has the following as its response:

A. Since _____ is no longer in business, we are unable to use their services. Henceforth, we are withdrawing _____ _____ as our contract laboratory from our application.

B. The New Jersey division of _____ _____

If you have any questions, please feel free to contact me at (631) 737-1155.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M. Pharm, M.S., R.Ph.
Director, Regulatory Affairs

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (516) 737-1155

March 9, 2001

ORIG AMENDMENT
N/FA

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Elaine Hu

Ref: FAX AMENDMENT – ANDA # 40-386
Triamcinolone Acetonide Ointment USP, 0.5%

Dear Ms. Hu:

Pursuant to your fax amendment dated December 21, 2000, Thames Pharmacal Co., Inc. has the following as its response.

A. Deficiencies:

1. Please be informed that you cannot rely on the certificate of analysis provided by the drug substance manufacturer until you validated the manufacturer. Please revise your specifications for the drug substance to include test and specifications for residual solvents and organic volatile impurities.

Response

We have validated our manufacturers of the drug substance by performing organic volatile impurities and residual solvents as per USP 24 Supplement II (test procedure <467> Method I).

Three batches of Triamcinolone Acetonide, USP of each manufacturer were tested by an outside contract laboratory (_____) and all lots tested conformed to the specification.

Since we have validated the drug substance manufacturer and, moreover, this OVI testing is not included in the monograph for the drug substance Triamcinolone Acetonide, USP, we, at the present time, will rely on the certificate of analysis provided by the drug substance manufacturer (page# 3-15).

2. **Please tighten your limits for individual and total degradants for the finished drug product.**

Response

We have tightened our individual and total degradants for the finished drug product to__ % and__ % respectively (page# 16).

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. **Please provide a categorical exclusion request under 21 CFR 25.31 (a) and certify that you are in compliance with all applicable local, state and federal environmental regulations.**

Response

Please see attached certification (page# 17).

Labeling Deficiencies:

Please submit your labels and labeling in final print.

Response

Please see attached labels and labeling (page# 18-67).

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____ 3/9/01
Srinivasa Rao, M. Pharm, M.S., R.Ph.
Director, Regulatory Affairs

1 copy

Thames
HARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

2100 FIFTH AVENUE, RONKONKOMA, NY 11779 (516) 737-1155

BIOAVAILABILITY N/AB

August 31, 2000

Office of Generic Drugs, CDER, I
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attn: Dr. Krista M. Scardina

Ref: BIOEQUIVALENCY AMENDMENT- ANDA# 40-386
Triamcinolone Acetonide Ointment USP, 0.5%

Dear Dr. Scardina:

Pursuant to the Bioequivalency Amendment dated August 31, 2000, Thames Pharmacal Co., Inc., has the following as its response:

As per our telephone conversation, we will refer Clay Park Laboratory, NY for our ANDA# 40-386 as the Reference Listed Drug (RLD).

At the present time we believe that we do not require any labeling changes due to this change. We are also enclosing form-356h with the corrected RLD change.

If you have any questions, feel free to contact me at 631 737 1155

Very Truly yours,

Thames Pharmacal Co., Inc.

By: _____
Srinivasa Rao, M.Pharm., M.S., R.Ph.
Director of Regulatory Affairs