CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40310

CORRESPONDENCE

OUTSIDE NEW YORK
(800) 225-1003

Thames PHARMACAL CO., INC.

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

May 15, 1998

OFFICE OF GENERIC DRUGS
Document Control Room
Metropark North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NEW CORRESP
N C

Re: Hydrocortisone Ointment USP, 2.5%
ANDA #40-310

Dear Sir/Madam,

Pursuant to my conversation with Denise Huie (CSO), the following additional information is enclosed:

1.	Proposed Production Batch Sizes	Page No. 1
2.	Reprocessing Statement	Page No. 2
3.	Side by Side Comparison Between Proposed Drug and Reference Listed Drug	Page No. 3
4.	Page 164 (Inactive Ingredient Source) of the original application submission is revised to include the address of the manufacturers.	Page No. 4
5.	"Description of Inprocess Testing" is revised to include the Sampling Schedule.	Page No. 5-7

We hope this information will satisfy the requirements.

Very truly yours,
Thames Pharmacal

5/15/98
Kalpana Rao
VP of Scientific Affairs

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GENERIC DRUGS

OUTSIDE NEW YORK
(800) 225-1003

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

April 17, 1998

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
"Hydrocortisone Ointment USP, 2.5%".

Dear Sir/Madam,

Pursuant to section 505 (b) 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. Form 356 H (Revised 4/97)
2. Archival Copy (Volume No. 1) (Blue Folder)
3. Archival Copy (Volume No. 1.2) (Blue Folder)
4. Technical Review Copy (Volume No. 2.1) (Red Folder)
5. Technical Review Copy (Volume No. 2.2) (Orange Folder)
6. Methods Validation copy - 2.

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

Very truly yours,
Thames Pharmacal

4/17/98

Kalpana Rao
Vice President of Scientific Affairs

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APR 21 1998

Thames
ARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

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

February 1,1999

DR Label

NDA ORIG AMENDMENT
AC

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

Re: Hydrocortisone Ointment USP, 2.5%
ANDA #40-310

Dear Sir/Madam:

Reference is made to your letter dated November 2, 1998. Thames herewith submits the response as a major amendment to the deficiencies noted in your letter dated November 2, 1998:

A. 1. Thames acknowledges agency's comment regarding DMF [ ]holder for Hydrocortisone drug substance. We are enclosing a copy of correspondence received from [ ] who is an authorized agent for [ ] (DMF [ ] in the USA, which indicates the responses to all the deficiencies noted by the FDA.

P. No. 1

2. Drug Substance Hydrocortisone:

a. Page 157 and 158 of the original submission indicates that [ ] were approved sources for Hydrocortisone drug substance for other ANDA products. A general statement was made regarding OVI (Organic Volatile Impurities) testing on behalf of [ ] This was an oversight to include in the original submission since currently [ ] performs the OVI (Organic Volatile Impurities) testing. [ ] is not an additional manufacturer of the drug substance for this ANDA.

b. Copies of Certificates of Analysis from Thames for Hydrocortisone with complete testing are enclosed. P. No. 2 - 5

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3. Drug Product:

a. Justification for ~ % excess Hydrocortisone in the Product:

Hydrocortisone Ointment is currently produced at 0.5% and 1% strengths by Thames Pharmacal. Therefore, the process used for the preparation of the R&D batch can be trusted to consistently produce a uniform product. The assay results attained on it ~ % is ~ % recovery of the amount of Hydrocortisone placed into the product (a % excess was used). Based on the assay results, full recovery of active is seen. Therefore, 0.5% excess of the labeled amount of active will be used during manufacturing to compensate for any mechanical and human error. Also, please note that this amount will not have any toxic effects.

b. Copies of final batch weight checks are enclosed.

P. No. 6 - 7

c. Copies of blend uniformity in-process testing with specifications for assay and ~ values are enclosed.

P. No. 8

d. The length of the time the finished bulk product will be held is 21 days before filling. If any changes in the set length of time occur, it will be validated prior to filling.

4. Finished product testing and specifications were revised to include the following:

a. Specifications for known, individual unknown and total impurities.

b. Viscosity testing.

Copies are enclosed.

P. No. 9 - 10

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

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

5. Stability tests were revised to include:

a. The specification for Microbial Testing.

b. The orientation of the container.

c. Tests and specifications for individual known, individual unknown, and total impurities testing.

d. Viscosity testing.

e. Assay testing at top, middle and bottom of tubes.

Copies are enclosed P. No. 11-16

6. Copy of memo explaining the duplicate assay results at 3 months and assay results fluctuations from onetime interval to another of 16 oz. jar. P. No. 17

7. Copies of updated stability data. P. No. 11-16

8. Copy of stability commitment to include in statement

a): "One additional batch will be placed on stability yearly thereafter.

P. No. 18

B. Thames acknowledges the agency's comment regarding the firm's compliance with CGMP at the time of approval.

LABELING DEFICIENCIES:

Revised Container & Carton draft labeling to include the Agency's suggestions, are enclosed.

P. No. 19-32

In order to facilitate the review, a side-by-side comparison of proposed labeling with our last submission with all differences annotated and explained also enclosed.

P. No. 33-34

Thames
ARMACAL CO., INC.

OUTSIDE NEW YORK
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BIOEQUIVALENCY

Thames also acknowledges agency's comments regarding the bioequivalency information.

We believe that we have responded to all the deficiencies noted and hope to have an expedited review.

Sincerely Yours,

THAMES PHARMACAL CO., INC.

KaD 2/1/99

KALPANA RAO
Vice President of Scientific Affairs

Thames
PHARMACAL CO., INC.

OUTSIDE NEW YORK
(800) 225-1003

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

November 30, 2000

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

Re: Minor Amendment – ANDA # 40-310
Hydrocortisone Ointment USP, 2.5%

Dear Ms. Hu:

In response to the Minor Amendment dated March 17, 2000 we are hereby notifying you of the following information.

Pursuant to a conversation on November 30, 2000 with Lawrence Farina, Pre-Approval Manager, Food and Drug Administration, Syosset, NY, I was informed that the District Office has recommended Thames Pharmacal Co., Inc. as a CGMP compliance firm.

If you have any questions, feel free to contact me at (631) 737-1155 x45.

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

FACSIMILE AMENDMENT

November 3, 1999

NDA ORIG AMENDMENT
N/AM

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

Re: Hydrocortisone Ointment USP, 2.5% ANDA #40-310

Dear Mr. Buccine:

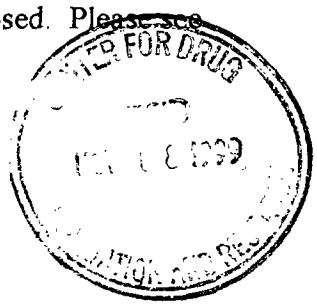
Thames Pharmacal Co., Inc. is herewith responding to deficiencies noted in your facsimile amendment dated August 8, 1999.

A1. Please submit the test method validation and for the degradation testing for the drug product. Provide updated long-term stability data which includes degradation testing.

A1. Response
Reference is made to our written/fax communication dated August 23, 1999 and telephone conversation dated September 10, 1999.

Method validation was performed for the analytical method which is used for stability and finished product testing. Please refer to pages # 515-527 on the original application submission date April 17, 1998 for data. A written procedure is enclosed. Please see pages # 5-6A.

Degradation study (stress testing) was performed earlier. Please see pages # 525-526 of the original application. Degradation studies were repeated for acid and base stress conditions. Please see attached pages # 7-11. Also see pages # 12-18 for long-term stability data. Revised bulk and finished drug product specifications with changes in viscosity specifications are enclosed. Please see pages # 19-21.



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A2. You have stated that at

Also, you have stated that

Please submit any updated room temperature stability data with complete testing.

A2. Response
We have noticed this fluctuation in our package size only.

The product does not Please refer to pages # 12-18 for long-term stability data.

A3. Please submit revised stability test forms with the name of the active manufacturer/supplier. "N/A" is not acceptable.

A3. Response
Please see attached long-term stability with revised active manufacturer/supplier information.

A4. For the drug substance, please submit the organic volatile impurity test results; the COA states "see attached." Also, submit chromatographic purity results; "conforms" is not acceptable.

A4. Response
The Organic Volatile Impurities test results provided to us by is included. Page # 22.

Changes were made in our raw material specification sheet to read chromatographic purity results for individual and total impurities. We are also enclosing chromatographic purity results for Lot R5696 used in making the drug product. Please see pages # 23-25.

A5. Please submit the physicochemical tests and/or certifications for the container/closure systems' components.

A5. Response

As per our telephone conversation dated September 10, 1999 and faxed communication dated August 23, 1999, physicochemical tests for the container/closure system for the 16-oz package size was performed. An outside contract laboratory was engaged to perform USP <661> physicochemical testing on our 16 oz container/closure system. Since we did not have the same RCBI # 5595 on our 16-oz polypropylene jars that were used for submission, a different RCBI # 6172 was used to do the physicochemical tests. Please see page # 26-36.

Certifications for the 1 oz and 20 g sizes were submitted earlier. Please refer to the original application dated April 17, 1998 pages # 205-225.

Labeling Deficiencies

Twelve (12) copies of final printed labels and labeling are enclosed. Please see pages # 37-80.

Please note that is no longer in business and, therefore, we are unable to use their services. Henceforth, we are **withdrawing** as our contract laboratory from our application.

Very truly yours,

Thames Pharmacal Co., Inc.

By: _____

Srinivasa Rao
Director, Regulatory Affairs