CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 75042

CORRESPONDENCE

August 19, 1998

Office of Generic Drugs
Food and Drug Administration
Document Control Room
MPN II
7500 Standish Place, room 150
Rockville, Maryland
USA 20855-2773

TARO PHARMACEUTICALS INC.
130 EAST DRIVE
BRAMALEA, ONTARIO
L6T 1C3

Reference: **ANDA 75-042**
Hydrocortisone Valerate Cream USP, 0.2%
Telephone Amendment

Dear Sir:

Reference is made to our ANDA dated December 23, 1996 and the amendments dated March 5, 1997, November 7, 1997, March 30, 1998, April 16, 1998, May 11, 1998, June 15, 1998 and July 30, 1998 for Hydrocortisone Valerate Cream USP, 0.2%.

Reference is also made to the telephone conversation of August 19, 1998 between Dr. A. Rudman of the Agency and Dr. T. Feldman and Lorraine Sachs of Taro Pharmaceuticals Inc. in which the following clarification and information have been requested by the Agency.

Comment 1: Establish in-process specifications for blend uniformity

In-process and bulk specifications for Hydrocortisone Valerate Cream USP, 0.2% have been revised to include the test and limits for blend uniformity. Please see **supplementary page 1**.

Comment 2: Establish stability limits for viscosity

Based on the viscosity data collected to date, limits for viscosity have been included in the stability specifications (please see **supplementary pages 2-3**).

Comment 3: Include limits for USP OVI's in the specifications for the active raw material

The only USP solvent used by the active raw material supplier n the synthesis of Hydrocortisone Valerate is (please see attached letter from **supplementary pages 4-5**) for this solvent e limit of NMT (as per the USP). Taro's specifications for the raw material Hydrocortisone Valerate have been revised to include the USP limit for (please see **supplementary page 6**).

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1-800-268-1975
VOICE MAIL
905-791-5181
TELEFAX NO.
905-791-5008

Comment 4: Since the Packaging Modification Protocol submitted on page 1511 of the original ANDA has been found unacceptable in this case, it should be revised or withdrawn from the file.

We withdraw the Packaging Modification Protocol submitted in the ANDA. The components to be used in packaging of this product will be supplied by

This completes our Telephone Amendment dated August 19, 1998. We hope that all Agency's concerns have been addressed satisfactorily and are looking forward to approval of this ANDA. If there are any questions with regards to this amendment, please do not hesitate to contact the undersigned or our U.S. agent

Taro Pharmaceuticals U.S.A., Inc.,
attention: Lorraine Sachs, RAC
Associate Director, Regulatory Affairs
5 Skyline Drive
Hawthorne, New York 10532

(914) 345-9001

This Telephone Amendment is being submitted in two copies. In addition a third (Field copy) is enclosed.

Sincerely yours,
TARO PHARMACEUTICALS INC.

Derek Ganes, Ph. D.
V.P., Regulatory Affairs

/Vesna Lucic

cc. Acting Director, FDA, Office of International Programs

TARO PHARMACEUTICALS INC
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July 30, 1998

Office of Generic Drugs
Food and Drug Administration
Document Control Room
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7500 Standish Place, room 150
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USA 20855-2773

TARO PHARMACEUTICALS INC.
130 EAST DRIVE
BRAMALEA, ONTARIO
L6T 1C3

N/FA

Reference: **ANDA 75-042**
Hydrocortisone Valerate Cream USP, 0.2%
Telephone Amendment

Dear Sir:

Reference is made to our ANDA dated December 23, 1996 and the amendments dated March 5, 1997, November 7, 1997, March 30, 1998, April 16, 1998, May 11, 1998 and June 15, 1998 for Hydrocortisone Valerate Cream USP, 0.2%.

Reference is also made to the telephone conversation between Mr. Buccine of the Agency and Lorraine Sachs of Taro Pharmaceuticals Inc. in which the commitment regarding the blend uniformity specifications has been requested by the Agency.

Taro Pharmaceuticals Inc. hereby commits to establish in-process limits for blend uniformity after approval of the above mentioned ANDA. At that time the established limits will be submitted to the Agency as a Changes Being Effected Supplement.

This completes our Telephone Amendment dated July 30, 1998. We hope that all Agency's concerns have been addressed satisfactorily and are looking forward to approval of this ANDA. If there are any questions with regards to this amendment, please do not hesitate to contact the undersigned or our U.S. agent

Taro Pharmaceuticals U.S.A., Inc.,
attention: Lorraine Sachs, RAC
Associate Director, Regulatory Affairs
5 Skyline Drive
Hawthorne, New York 10532

(914) 345-9001

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Sincerely yours,
TARO PHARMACEUTICALS INC.

Derek Ganes, Ph. D.
V.P., Regulatory Affairs

/Vesna Lucic

cc. Acting Director, FDA, Office of International Programs

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Taro Pharmaceuticals Inc.

Fax Cover Sheet

ORIG AMENDMENT
M/FA

DATE: June 15, 1998June 15, 1998 **TIME:**

TO: Mr. Joe Buccine **PHONE:**
FAX: (301) 827-4337

FROM: Vesna Lucic **PHONE:** (905) 791-5181 Ext. 459

TARO Pharmaceuticals **FAX:**

RE: Hydrocortisone Valerate Cream USP 0.2% ANDA # 75-042

CC:

Number of pages including cover sheet: [58]

Message

Please find attached a "Facsimile Amendment" for the above mentioned ANDA. A hard copy will follow in the mail.

Sincerely ,

TARO Pharmaceuticals Inc.

N. Lucic

Vesna Lucic

Regulatory Affairs Associate

Page(s) 4

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

Chemistry deficiency

review

May 11, 1998

TARO PHARMACEUTICALS INC
130 EAST DRIVE
BRAMALEA, ONTARIO
L6T 1C3

Office of Generic Drugs
Food and Drug Administration
Document Control Room
MPN II
7500 Standish Place, room 150
Rockville, Maryland
USA 20855-2773

Reference: **ANDA 75-042**
Hydrocortisone Valerate Cream USP, 0.2%
Telephone Amendment

Dear Sir:

Please find enclosed Taro Pharmaceuticals' Telephone Amendment, dated May 11, 1998, for the above-referenced application.

As required by 21 CFR 314.96(d)(5), Taro is forwarding a copy of the technical data (including 356h form). Taro Pharmaceuticals Inc. certifies that the technical sections contained in this copy are true copies of the same sections submitted to OGD. If there are any questions relating to the information submitted, please contact our US Agent:

Taro Pharmaceuticals U.S.A., Inc.,
attention: Lorraine Sachs, RAC
Associate Director, Regulatory Affairs
5 Skyline Drive
Hawthorne, New York 10532
(914) 345-9001

Sincerely yours,
TARO PHARMACEUTICALS INC.

Derek Ganes, Ph. D.
V.P., Regulatory Affairs

Encl. : Field Copy

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Page(s) 4

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

Chemistry review

Page(s) 2

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Chemistry review

March 30 , 1998

ORIG AMENDMENT
N/FA

Office of Generic Drugs
Food and Drug Administration
Document Control Room
MPN II
7500 Standish Place, room 150
Rockville, Maryland
USA 20855-2773

TARO PHARMACEUTICALS INC
130 EAST DRIVE
BRAMALEA, ONTARIO
L6T 1C3

Reference: **ANDA 75-042**
Hydrocortisone Valerate Cream USP, 0.2%
Facsimile Amendment

Dear Sir:

Please find enclosed Taro Pharmaceuticals' response to a recent deficiency letter from the FDA, dated March 23, 1998, for the above-referenced application.

As required by 21 CFR 314.96(d)(5), Taro is forwarding a copy of the technical data (including 356h form). Taro Pharmaceuticals Inc. certifies that the technical sections contained in this copy are true copies of the same sections submitted to OGD. If there are any questions relating to the information submitted, please contact our US Agent:

Taro Pharmaceuticals U.S.A., Inc.,
attention: Lorraine Sachs, RAC
Associate Director, Regulatory Affairs
5 Skyline Drive
Hawthorne, New York 10532
(914) 345-9001

Sincerely yours,
TARO PHARMACEUTICALS INC.

Derek Ganes, Ph. D.
V.P., Regulatory Affairs

Encl. : Field Copy

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November 7, 1997

TARO PHARMACEUTICALS INC.
130 EAST DRIVE
BRAMALEA, ONTARIO
L6T 1C3

Office of Generic Drugs
Food and Drug Administration
Document Control Room
MPN II
7500 Standish Place, room 150
Rockville, Maryland
USA 20855-2773

Reference: **ANDA 75-042**
Hydrocortisone Valerate Cream USP, 0.2%
Major Amendment

Dear Sir:

Reference is made to our ANDA dated 12/23/1996 and the amendment dated 3/5/1997 for Hydrocortisone Valerate Cream USP, 0.2%.

Reference is also made to the Agency's letter dated August 21, 1997 in which the Agency stated that the application is deficient and, therefore, not approvable under section 505 of the Act for the following reasons:

CHEMISTRY COMMENTS

Page(s) 9

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

Chemistry

LABELING DEFICIENCIES:

COMMENT # 1 GENERAL COMMENTS

i. Delete the terminal zero throughout your labeling when expressing a strength (e.g., 2 mg rather than 2.0 mg).

ii. You are encouraged to use boxing, contrasting colors, or other means to differentiate the dosage forms of your product.

COMMENT # 2 CONTAINER (15 g, 45 g, 60 g tubes)

See GENERAL COMMENT.

COMMENT # 3 CARTON (15 g, 45 g, 60 g)

See GENERAL COMMENT.

COMMENT # 4 INSERT

a. GENERAL COMMENT
The reference numbers throughout your insert are difficult to read. Revise to enhance their readability.

TARO PHARMACEUTICALS INC.
TELEPHONE
905-791-8276
1-800-268-1975
TELEFAX NO.
905-791-5008

March 5, 1997

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

AMENDMENT

TARO PHARMACEUTICALS INC.
130 EAST DRIVE
BRAMALEA, ONTARIO
L6T 1C3

505(j)(2)(a)(ok)
Anna Marie N. Weick
3/11/97

Reference: ANDA 75-042
Hydrocortisone Valerate Cream USP, 0.2%
"Response to Refuse to File Letter"

Dear Sir/Madam:

Reference is made to our Abbreviated New Drug Application submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Hydrocortisone Valerate Cream USP, 0.2% dated December 23, 1996.

Reference is also made to your "Refuse to File" letter dated February 28, 1997, in which you requested a letter of authorization from designating the n to act as their agent in granting access to their DMF.

Attached is a letter of authorization from designating the to act as their agent in granting access to their DMF.

This response is being submitted in two copies. A copy of your "Refuse to File" letter dated February 28, 1997, and FDA 356h form are also attached.

If you have any questions or require further information, please do not hesitate to contact the undersigned or our US agent at the following address:

Taro Pharmaceuticals USA Inc.
Attention: Timothy A. Anderson, M.Sc., M.B.A.
5 Skyline Drive
Hawthorn, NY 10532

Tel: (914) 345-9001
Fax: (914) 345-8728

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MAR 07 1997
MAR 06 1997
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Sincerely,

Derek A. Ganes, Ph.D.
Director, Regulatory Affairs

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