CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number: NDA 20489/S3

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-489/S-003

TheraTech, Inc.
Attention: Dorothy A. Frank, M.S., R.A.C.
Director, Regulatory Affairs
417 Wakara Way, Suite 100
Salt Lake City, UT 84108

MAY 2 1997

Dear Ms. Frank:

We acknowledge your supplemental new drug application dated October 25,1996, received October 28, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Androderm® (testosterone transdermal system), 5.0 mg.

We also refer to your amendment dated April 30, 1997 and received May 1, 1997, in response to our letter dated April 28, 1997.

The User Fee goal date for this application is November 1, 1997.

This supplement provides for marketing an additional strength of the product 5 mg/day and labeling changes in the CLINICAL PHARMACOLOGY and DOSE AND ADMINISTRATION sections.

We have completed the review of this supplemental application and it is approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Terri F.Rumble, B.S.N., Regulatory Health Project Manager, at (301) 827-4260.

Sincerely,

5-2-97

Lisa D. Rarick, M.D.
Director
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-489
HFD-580/Div. Files
HFD-580/CSO/T.Rumble
HFD-580/Mitra/Rhee/Barnette
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: Rumble/May 2, 1997/20379
Initialed by: Rarick/Barnette,5.2.97/Mitra,5.2.97/Rhee, 5.2.97/Pauls,5.2.97
final: Rumble,5.2.97

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:NDA 20489/S3

CHEMISTRY REVIEW(S)

ORIGINAL MAY 2 1997

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS

REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS
CHEMIST'S REVIEW

1. NDA NUMBER: 20-489

2. NAME AND ADDRESS OF APPLICANT
TheraTech, Inc.
417 Wakara way
Salt Lake City, UT 84108

3. SUPPLEMENT NUMBER/DATE/DATE ASSIGNED
Amendment to SCP-003/4-30-97/5-01-97

4. NAME OF THE DRUG: Androderm^R (testosterone transdermal system)
5. NONPROPRIETARY NAME: Testosterone Transdermal System
6. SUPPLEMENT PROVIDES FOR: The purpose of this Prior Approval Supplement is to get approval to market an additional strength of the product (5 mg./day) that was not included in the NDA 20-489. The NDA 20-489 was approved for marketing 2.5 mg/day strength only.
7. AMENDMENTS/REPORTS/ DATE: This amendment provides the response to the deficiencies recorded in the prior review.
8. PHARMACOLOGICAL CATEGORY
Androgen

9. HOW DISPENSED
Prescription

10. RELATED IND/NDA/DMF/SUPPLEMENT
None
11. DOSAGE FORM : Transdermal
12. POTENCY
5 mg/day

13. CHEMICAL NAME AND STRUCTURE
$C_{19}H_{28}O_2$
MW = 288.43

Androst-4-en-3-one, 17- hydroxy-, (17 β) -

14. COMMENTS

In order to improve patient acceptance the 5 mg/day patches were developed using the same approved composition but increasing the surface area by two fold. The 2.5 mg/day system has been approved through 20-489. The clinical studies were conducted with two 2.5 mg/day systems and proving its bioequivalence with the 5 mg/day system.

The following changes were made to address the deficiencies in supplement

SCP 003:

1. Quantitative composition table was revised as recommended.
2. Dimension has been included in the regulatory specification
3. Specification for related substances has been provided and adopted in the Regulatory Specification as recommended.

15. CONCLUSIONS AND RECOMMENDATIONS

The supplement can be approved since all the deficiencies were corrected.

REVIEWER'S NAME / SIGNATURE/ DATE COMPLETED

AMIT K. MITRA /S/ 5-2-97

17. R/D INIT BY:

CC: A. K. MITRA/HFD-580
M.J.RHEE/HFD-580
T. RUMBLE/HFD-580
NDA 20-489

ORIGINAL

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCTS

REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS CHEMIST'S REVIEW

AUG - 8 1997

1. NDA NUMBER: 20-489

2. NAME AND ADDRESS OF APPLICANT
TheraTech, Inc.
417 Wakara way
Salt Lake City, UT 84108

3. SUPPLEMENT NUMBER/DATE/DATE ASSIGNED
General Communication (SNC) S-002 and S-003 /6-24-97/6-27-97

4. NAME OF THE DRUG: Androderm^R (testosterone transdermal system)
5. NONPROPRIETARY NAME: Testosterone Transdermal System
6. GENERAL COMMUNICATION PROVIDES FOR: Reevaluating the requirement by the District Laboratories for reference standards for the Methods Validation (see Appendix 1).
7. AMENDMENTS/REPORTS/ DATE: NDA 20-489, S-002 and S-003
8. PHARMACOLOGICAL CATEGORY
Androgen

9. HOW DISPENSED
Prescription

10. RELATED IND/NDA/DMF/SUPPLEMENT
None
11. DOSAGE FORM : Transdermal
12. POTENCY
2.5 and 5 mg/day

13. CHEMICAL NAME AND STRUCTURE
$C_{19}H_{28}O_2$
MW = 288.43

Androst-4-en-3-one, 17- hydroxy-, (17 β) -

14. COMMENTS

TheraTech should send the requested reference standards to the District Laboratories except two (those are not commercially available) as suggested below.

The following changes were made to address the deficiencies in supplement SCP 003:

TheraTech wants the reviewer to reconsider the reference standard requirement by the District Laboratory.

15. CONCLUSIONS AND RECOMMENDATIONS

TheraTech should send the following reference standards and samples to each of the District Analytical Laboratories:

1. Testosterone: Reference standard: 500 mg
2. Epitestosterone- 100 mg
3. Androstene- 3, 17- dione- 100 mg
4. 6-α-hydrotestosterone- 100 mg
5. 6-β-hydrotestosterone- 100 mg
6. 6-β-hydroperoxytestosterone- 50 mg
7. Finished product- 5 mg- 60 patches

This recommendation should be conveyed to the San Juan and Philadelphia District Laboratories.

REVIEWER'S NAME / SIGNATURE/ DATE COMPLETED

AMIT K. MITRA 18-8-97

17. R/D INIT BY: 8/8/97 /S/

CC: A. K. MITRA/HFD-580
M.J.RHEE/HFD-580
T. RUMBLE/HFD-580
NDA 20-489
San Juan District Laboratory
Philadelphia District Laboratory

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20489/S3

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

MAY 2 9 1997

CLINICAL PHARMACOLOGY and BIOPHARMACEUTICS REVIEW

NDA: 20-489

Compound: Androderm® (testosterone transdermal system, 2.5 and 5.0 mg) ORIGINAL

Submission Date: 4/30/97 (Amendment Serial No. 003)

Sponsor: TheraTech, Inc.

Type of Submission: Labeling Changes

Reviewer: K. Gary Barnette, Ph.D.

NDA 20-489, Androderm® 2.5 mg (testosterone transdermal delivery system) was approved for marketing September 29, 1995. The system approved is intended to deliver 2.5 mg of testosterone per day. It was shown that in order to achieve serum testosterone levels within the range of normal circadian rhythm of testosterone, a majority of the patients must wear two systems at a time for a total testosterone dose of 5.0 mg per day. Therefore, the sponsor developed a 5.0 mg system and received approval for this system on May 2, 1997.

The following change in the *Absorption* sub-section of the **Pharmacokinetic** sub-section of the **CLINICAL PHARMACOLOGY** section of the labeling was made in a letter to the sponsor dated April 28, 1997 (addition bolded);

> *Absorption*
> Following Androderm (testosterone transdermal system) application to non-scrotal skin, testosterone is continuously absorbed during the 24-hour dosing period. Daily application of two **Androderm 2.5 mg** systems at approximately 10 PM results...etc.

The current submission to NDA 20-489, dated April 30, 1997 contains the following proposed labeling change to the aforementioned labeling recommendation;

> *Absorption*
> Following Androderm (testosterone transdermal system) application to non-scrotal skin, testosterone is continuously absorbed during the 24-hour dosing period. Daily application of ~~two~~ **Androderm** ~~**2.5 mg systems**~~ at approximately 10 PM results...etc.

Reviewer Comment: I concur with the sponsor's proposal.

Recommendation: The submission to NDA 20-489 (Amendment Serial No. 003), dated April 30, 1997 has been reviewed by the Office of Clinical Pharmacology and Biopharmaceutics/Division of Pharmaceutical Evaluation II (OCPB/DPEII). It is the opinion of OCPB/DPEII that the proposed change in the *Absorption* sub-section of the **Pharmacokinetic** sub-section of the **CLINICAL PHARMACOLOGY** section of the Androderm (testosterone transdermal delivery system) is appropriate. OCPB/DPEII's agreement to the proposed change was communicated to the sponsor in a letter dated May 2, 1997.

K. Gary Barnette, Ph.D.
Office of Clinical Pharmacology and Biopharmaceutics
Division of Pharmaceutical Evaluation II

RD initialed by Angelica Dorantes,Ph.D., Team Leader 5/29/97
FT signed by Angelica Dorantes, Ph.D., Team Leader Dorantes 5/29/97

cc: **NDA 20-489, HFD-580 (Fourcroy, Rumble), HFD-870 (M.Chen, Barnette, Dorantes), Drug file (CDR, Barbara Murphy).**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20489/S3

ADMINISTRATIVE DOCUMENTS

MEMORANDUM OF TELECONFERENCE MINUTES

Meeting Date: April 30, 1997
Time: 3:15 - 3:45 pm
Location: Parklawn 17B43

Application: NDA 20-489/S003 - Androderm™ , 5.0 mg strength

Type of Meeting: guidance

Meeting Chair: Lisa Rarick, M.D. - Director, Division of Reproductive and Urologic Drug Products (DRUDP; HFD-580)

External Chair: Dorothy Frank, Regulatory Affairs, TheraTech

Meeting Recorder: Terri Rumble, Project Manager, DRUDP, HFD-580

FDA Participants:
Lisa Rarick, M.D. - Director, DRUDP; HFD-580
Moo-Jhong Rhee, Ph.D. - Chemistry Team Leader, Division of New Drug Chemistry II (DNDC II) @ DRUDP (HFD-580)
Amit Mitra, Ph.D.- Chemist, DNDCII @ DRUDP (HFD-580)
Terri F. Rumble, Project Manager, DRUDP, HFD-580

External Participants:

Dorothy Frank, Director, Regulatory Affairs, TheraTech Inc.
Rex Mauthe, Regulatory Affairs Associate, TheraTech, Inc.
Steven Sanders, Executive Director Project Management, TheraTech, Inc.
William Good, Vice President, Development, TheraTech, Inc.

Background: TheraTech was issued a not approvable letter on April 28, 1997 for NDA 20-489/S003 for the 5.0 mg strength of Androderm. They faxed a proposed response addressing the NA deficiencies on April 29, 1997 in preparation for the following teleconference.

Meeting Objectives:
To determine whether sponsor can adequately address deficiencies for this supplemental NDA.

Discussion Points:

- sponsor is ready to change the quantitative composition table by removing the ranges for the active ingredients
- the rationale for requesting a % for alcohol and water is that this would account for some of the product that may be lost in the process
- the sponsor's proposal to add length and width dimension specifications for the entire system as well as the active drug delivery area based on the qualified die dimensions used for the manufacture of the systems is acceptable
- the proposed specifications for related substances are acceptable
- the proposed labeling change will be reviewed by Biopharm upon submission

Decisions (agreements) reached:

- the proposed changes will be reviewed upon submission of an amendment, but appear adequate
- DRUDP will perform an expedited review of this amendment upon receipt of an amendment

Action Items:

	Item	Responsible Person	Due Date
1.	amend supplement	sponsor	will send 5/1/97
2.	review amendment	DRUDP	expedited review(5/3097)

Minutes Prepared: _____ /S/

Chair Concurrence: _____ 5/21/97

Attachments: facsimile from sponsor dated 4/29/97

cc: Original NDA 20-489
HFD-580/Div. Files
HFD-580/PM/Rumble
HFD-580/Rarick/Jolson/Mitra/Rhee/Dorantes/Barnette

Drafted by: Rumble/5.20.97/20489tcn.s03
Concurrences: Rarick,5.21.97/Mitra,5.20.97/Rhee,5.20.97//Pauls,5.20.97
final: Rumble,5.22.97

TELECONFERENCE MEETING MINUTES

MEMORANDUM OF TELECONFERENCE MINUTES

Meeting Date: April 1, 1997
Time: 1:20-1:30 pm
Location: Parklawn 17B43

Application: NDA 20-489/S002, S003 - Androderm™ 2.5 mg and 5.0 mg strengths

Type of Meeting: guidance regarding dissolution specifications

Meeting Chair: K. Gary Barnette, Ph.D., Pharmacokinetics Reviewer, Division of Pharmaceutical Evaluation II (DPE II) @ DRUDP (HFD-580)

External Chair: Dorothy Frank, Regulatory Affairs, TheraTech

Meeting Recorder: Terri Rumble, Project Manager, DRUDP, HFD-580

FDA Participants:

K. Gary Barnette, Ph.D., Pharmacokinetics Reviewer, Division of Pharmaceutical Evaluation II (DPE II) @ DRUDP (HFD-580)
Terri F. Rumble, Project Manager, DRUDP, HFD-580

External Participants:

Dorothy Frank, Director, Regulatory Affairs, TheraTech Inc.
Dr. Don Mantle, Vice President, Quality Assurance/Quality Control, TheraTech, Inc.
Dr. John Moellmer, Director, Analytical Research and Development, TheraTech, Inc.
William Good, Vice President, Development, TheraTech, Inc.

Background: TheraTech has submitted two supplemental NDA applications to this Division, S-002, which included a new *in vitro* dissolution method for post-approval, quality control testing of batches of Androderm 2.5 mg, and the S-003 supplement, which included bioequivalence and dissolution data for 5.0 mg

Meeting Objectives:

1. Inform the sponsor of the Division's recommendation to change the drug release specification for the hr time from %
2. Request the sponsor to officially submit an amendment for this change or the justification for another proposal

Discussion Points:

- FDA accepts the release specifications for the 0-3 hr and 0-7 hr times, but recommends changing the specification for hr time to % (proposed was %) for both 2.5 mg and 5.0 mg
- FDA understands that the skin is a rate-limiting factor effecting drug absorption
- the sponsor indicated that they could probably meet these specifications; they need to do their own calculations looking at the data

Decisions (agreements) reached:

- sponsor will respond with an amendment to both supplements either accepting the proposed recommendation or a rationale for a different specification for review by Dr. Barnette

Action Items:

	Item	Responsible Person	Due Date
1.	submit amendments	sponsor	4/11/97
2.	review amendment	Drs. Barnette, Dorantes	4/18/97
2.	action letter	Rumble, review team	4/21/97

Minutes Preparer. _____ /S/

Chair Concurrence: _____

Attachments/Handouts: Biopharmaceutics Review, 3.27.97

cc: Original
HFD-580/Div. Files
HFD-580/Meeting Minutes files
HFD-580/PM/Rumble
HFD-580/Rarick/Jolson/Mitra/Rhee/Barnette/Dorantes

Drafted by: Rumble/4.1.97/20489tcn.s02
Concurrences: Barnette, 4.2.97./Pauls, 4.2.97.
final: Rumble, 4/10/97.

TELECONFERENCE MEETING MINUTES

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20489/S3

CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

APR 2 0 1997

NDA 20-489/S-003

TheraTech, Inc.
Attention: Dorothy A. Frank, M.S., R.A.C.
Director, Regulatory Affairs
417 Wakara Way, Suite 100
Salt Lake City, UT 84108

Dear Ms. Frank:

Please refer to your supplemental new drug application dated October 25, 1996, received October 28, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Androderm® (testosterone transdermal system), 5.0 mg.

We also refer to your amendments dated February 5, 1997 and April 10, 1997.

The User Fee goal date for this application is April 28, 1997.

The supplemental application provides for an additional strength of Androderm® (5 mg/day). This new strength was not included in the original NDA 20-489, which was approved for marketing of the 2.5 mg/day strength only.

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

We also have the following comments that should be addressed:

Labeling

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of such action FDA may take action to withdraw the application. Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

This change may not be implemented until you have been notified in writing that this supplemental application is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Terri F.Rumble, B.S.N., Regulatory Health Project Manager, at (301) 827-4260.

Sincerely,

/S/ 4/28/97

Moo-Jhong Rhee, Ph.D.
Chemistry Team Leader
Division of Reproductive and Urologic Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Original NDA 20-489
HFD-580/Div. Files
HFD-580/CSO/T.Rumble
HFD-580/Mitra/Rhee/
HFD-870/Barnette/Dorantes
HFD-820/ONDC Division Director
HFD-92/DDM-DIAB
DISTRICT OFFICE

Drafted by: Rumble/April 24, 1997/20489ap.003
Initialed by: Rhee,4.25.97,4.28.97/Jolson,4.28.97/Mitra,4.24.97/Barnette,4.25.97
final: Rumble,4.28.97

NOT APPROVABLE (NA)

ORIGINAL

REVIEWS COMPLETED
CSO ACTION: AP letter
☒ LETTER ☐ N.A.I. ☐ MEMO
CSO INITIALS DATE

THERATECH

RESEARCH PARK
417 WAKARA WAY
SALT LAKE CITY
UTAH 84108

(801) 588-6200
FAX (801) 583-6042

April 30, 1997

ORIG AMENDMENT

Lisa Rarick, M.D.
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane Rockville, MD 20857

RE: NDA 20-489: Androderm® Testosterone Transdermal System, 2.5 mg/day, Amendment to S003

Dear Dr. Rarick:

Reference is made to our supplement, S003 to this application, dated October 25, 1996 which provides for a new 5 mg/day dosage strength. Reference is also made to your corresponding not approvable action letter for this supplement, dated April 28, 1997 and our telephone conference call with members of the Division on April 30, 1997.

TheraTech hereby amends this supplemental application with the following responses to the items outlined in the action letter. In addition, as part of this cover letter I have included minutes from our telephone conference call held today.

Chemistry

1. We are providing a revised quantitative composition table, in Attachment 1, which deletes all reference to ranges for the active and excipient ingredients of the gel formulation.

2. The Regulatory Specifications have been revised to include a length and width dimension specification for the system and also the drug delivery area based on the qualified heat seal die cutting tool dimensions. Methodology has been added to the document and the rationale for the specification included in Attachment 2.

3. Specifications for related substances have been generated and methodology added to the Regulatory Specification document provided in Attachment 2. The rationale for these specifications is provided in Attachment 3.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 0 1 1997
HFD-580

Labeling

As discussed in our 4/30/97 conference call, TheraTech has printed a limited number of the physician inserts in order to build launch quantities. As these labeling issues appear to be minor in nature, we will institute these changes, provided our recommendations are acceptable to the Division, at the time of next printing of the insert.

Minutes of 4/30/97 Telephone Conference

Present form FDA: Ms. Terri Rumble, Dr. Lisa Rarick, Dr. Moo-Jhong Rhee, Dr. Amit Mitra

Present form TheraTech: Ms. Dorothy Frank, Mr. Rex Mauthe, Dr. Steve Sanders, Dr. Bill Good

The meeting opened with introductions. TheraTech noted Dr. Rhee's suggestions for revising the quantitative composition table and agreed to make changes that would target nominal values with no range for all ingredients in the gel formulation. Dr. Mitra gave his rationale why he thought we could have a positive range from nominal on the water and

alcohol based on their volatility but the table presented should theoretically not contain ranges. Dr. Good responded that TheraTech had worked out volatility issues in our development formulations.

Dr. Good then explained the method that we had chosen to measure system dimensions as measuring the release liner since it was an exact replicate of the system. Dr. Mitra agreed that this would be acceptable and that the reason for the specification is so that TheraTech does not change the patch shape without prior approval.

Dr. Sanders then asked for a minor word change based on the labeling comments in the action letter. Dr. Rarick responded that Biopharm had made those comments so we must propose the change in our amendment. We also asked for any comment on our proposal to use present inserts and make changes at the next printing, Dr Rarick responded that it would be Biopharm's decision but didn't see that it should be any problem.

We closed the phone call with a discussion on the timing of the review of the amendment. TheraTech agrees to have the formal amendment to FDA by May 1, 1997. Dr. Rhee and Dr. Mitra agreed to review the amendment as quickly as possible. Dr. Rarick could not promise that the review would take any shorter time than 30 days. The amendment would receive a standard 6 month User Fee goal date but Dr. Rarick promised that the Division would work hard to clear the amendment as quickly as possible. The meeting then concluded.

If you have any questions regarding this amendment, please contact either Rex Mauthe or myself by phone (801) 588-6200 or fax (801) 583-8135.

Sincerely,

Dorothy C. Frank

Dorothy A. Frank, M.S., R.A.C.
Director, Regulatory Affairs

enclosures

ORIGINAL

ORIG AMENDMENT
SCS-003 BB

THERATECH

RESEARCH PARK
417 WAKARA WAY
SALT LAKE CITY
UTAH 84108

(801) 588-6200
FAX (801) 583-8042

April 10, 1997

Lisa Rarick, M.D.
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane Rockville, MD 20857

RE: NDA 20-489: Androderm® Testosterone Transdermal System, 2.5 mg/day, Amendments to Supplement S002 and S003

Dear Dr. Rarick:

Reference is made to our supplements, S002 & S003 to this application dated October 23 and 25, 1996, respectively. Reference is also made to our telephone conference call between FDA and TheraTech on April 1, 1997, with respect to the Release Rate Specifications for both the 2.5 mg/day product and the newly proposed 5 mg/day product.

Dr. Barnett of the Biopharmaceutics group requested that TheraTech include an upper specification on the 0-24 hour time point of our Release Rate specifications. Using the same specifications rationale as we did for the original specification, we have evaluated the data and concluded that a 0-24 hour specification of
% of label claim released is acceptable for both products. These limits were derived from from the mean of the data for the time point. TheraTech will continue to collect data for both products and will periodically re-evaluate the data against these specifications. If evidence suggests that the current specifications do not fit the product, TheraTech will submit appropriate data to the FDA to consider a change in the specification.

The first page of revised Regulatory Specifications/Test Methods documents for both the 2.5 mg/day and 5 mg/day product are included for your reference.

If you have any questions regarding this amendment, please do not hesitate to contact either Rex Mauthe or myself by phone (301) 588-6200 or fax (301) 583-8135.

Sincerely,

Dorothy A. Frank

Dorothy A. Frank, M.S., R.A.C.
Director, Regulatory Affairs

THERATECH

RESEARCH PARK
417 WAKARA WAY
SALT LAKE CITY
UTAH 84108

(801) 588-6200
FAX (801) 583-6042

Orig.
S-003
505 BB

February 5, 1997

Lisa Rarick, M.D.
Director, Division of Reproductive and Urologic Drug Products (HFD-580)
Office of Drug Evaluation II
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

RE: Amendment to Supplement S-003 to NDA 20-489
Androderm® Testosterone Transdermal System

Dear Dr. Rarick:

Reference is made to our approved new drug application for Androderm® Testosterone Transdermal System, submitted in accordance with Section 505(b) of the Federal Food, Drug, and Cosmetic Act. Reference is also made to our supplement to this application (S-003) dated October 25, 1996, submitted in accordance with 21 CFR 314.70(b). This supplement provided for a new system size with 15 cm^2 of active drug delivery area which provides nominal delivery of 5 mg of testosterone per day

As discussed over the past week with Dr. Gary Barnette, the bioavailability reviewer for this application, we hereby amend this supplement to provide a copy of the report from Endocrine Sciences that describes the method used for determining serum testosterone levels in the patients involved in the bioequivalence study, and provides validation and quality assurance information for this analytical method.

There are no other changes to this application.

Questions or comments concerning this supplement can be addressed to the undersigned or to Mr. Rex Mauthe, either of whom can be reached at telephone number (801) 588-6200 or fax number (801) 583-8135.

Sincerely,

Dorothy A. Frank

Dorothy A. Frank, M.S., R.A.C.
Director, Regulatory Affairs

enc.

CENTER FOR DRUG
REC'D
FEB 06 1997
HFD-580
EVALUATION AND RESEARCH