CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-791

CHEMISTRY REVIEW(S)

Memorandum

Date: December 16, 1997
To: NDA 20-791 (Testoderm TTS),
Amendment, December 15, 1997
From: Moo-Jhong Rhee, Ph.D., Chemistry Team Leader @HFD-580
Subject: Final in-vitro Release Rate Specification

12/15/97

Chemistry Review #2 indicates that the final in-vitro release rate specification is as follows:

hours	mg
hours	mg
hours	mg
hours	mg

However, based on further thoughts and Dr. Sam Haidar's guidance, the specification was revised as follows during the telephone conference on December 15, 1997:

hours	mg
hours	mg
hours	mg
hours	mg

This decision was based on calculations that lower limit is % less than the mean value of the lowest releasing batch (CN 830395) and upper limit is % above the mean value of the highest releasing batch (CN 847696). This agreement was confirmed by the amendment to the NDA dated December 15, 1997.

If the firm generates further data through the phase IV commitment and wants to extend the shelf-life to 24 months, the specification should be re-established based on all available data (however, it is expected to be within a predicted range from the current specification).

CC:
NDA 20-791
HFD-580/MRhee/AMitra/SHaidar/Trumble
file:n20791.memo

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCT (HFD-580)
REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS

NDA # 20-791 **Chemistry Review** # 2 **Review Date:** 12/8/97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment by Fax	12-03-97	12-04-97	12-04-97
Amendment by Fax	12-05-97	12-05-97	12-05-97

NAME AND ADDRESS OF APPLICANT
ALZA Corporation
950 Page Mill Road
Palo Alto, CA 95688-9470

DRUG PRODUCT NAME
Proprietary: Testoderm^R TTS
Non-proprietary/USAN: Testosterone Transdermal Delivery System
Compendium: does not apply
Code name/number:None
Chem. Type/Ther. Class: 3 S

ANDA SUITABILITY PETITION/DESI/PATENT STATUS: A patent approval for formulation compositions and methods for preparation is being sought (patent application number 4,379,454

PHARMACOL. CATEGORY/INDICATION: Androgen replacement therapy in male patients with an absence or deficiency of endogenous production.

DOSAGE FORM: Transdermal Delivery System

STRENGTHS: Testosterone Transdermal System 328 mg, 60 Cm^2, delivery rate approximately 5 mg/day.

ROUTE OF ADMINISTRATION: Transdermal, once a day application

DISPENSED: By prescription

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT.:
17 β hydroxyandrost-4-en-3-one
$C_{19}H_{28}O_2$, Molecular Weight: 288.43

SUPPORTING DOCUMENTS:
DMF
DMF
DMF
DMF
DMF

RELATED DOCUMENTS
IND
NDA 19-762 (Testoderm^R, Testosterone Transdermal System, ALZA Corporation)

CONSULTS
2. None

REMARKS/COMMENTS
Based on the Chemistry Review #1 several deficiencies were recorded. The response to the deficiencies are reviewed here.

CONCLUSION AND RECOMMENDATIONS
This application can be approved.

cc: NDA 20-791

HFD-580/A. K. Mitra/ 12/08/97
HFD-580/M. J. Rhee
HFD-580/T. Rumble
R/D. Init. By- 12/9/97

Amit K. Mitra, Ph.D

NOV 2 8 1997

DIVISION OF REPRODUCTIVE AND UROLOGIC DRUG PRODUCT (HFD-580)
REVIEW OF CHEMISTRY MANUFACTURING AND CONTROLS

NDA # 20-791 **Chemistry Review** # 1 **Review Date**: 11/28/97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Original	12-23-97	12-26-97	1-02-97
Amendment	7-02-97	7-07-97	7-07-97
Amendment	8-26-97	8-27-97	8-27-97
Amendment	9-12-97	9-15-97	9-15-97
Amendment	10-14-97	10-16-97	10-16-97
Amendment	11-3-97	11-4-97	11-5-97

NAME AND ADDRESS OF APPLICANT
ALZA Corporation
950 Page Mill Road
Palo Alto, CA 95688-9470

DRUG PRODUCT NAME
Proprietary: Testoderm® TTS
Non-proprietary/USAN: Testosterone Transdermal Delivery System
Compendium: does not apply
Code name/number:None
Chem. Type/Ther. Class: 3 S

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SUPPORTING DOCUMENTS:
DMF
DMF
DMF

DMF
DMF

RELATED DOCUMENTS
IND
NDA 19-762 (Testoderm®, Testosterone Transdermal System, ALZA Corporation)

CONSULTS
1. The proposed tradename Testoderm™ AT was sent to the Labeling and Nomenclature committee. The committee had no reason to find the tradename unacceptable . The division disagreed with the findings of the committee and suggested that the company pick names like Testoderm™ TTS or Testoderm™ TDS. The nomenclature committee did not find any reason to find Testoderm™ TDS unacceptable; however, the Testoderm™ TTS is unacceptable because of potential conflict with Tuesday, Thursday, Saturday. The company insisted on Testoderm™ TTS and the division accepted the tradename.
2. An EER was sent on 2-25-97. The response is back from compliance with satisfactory results of inspection.

REMARKS/COMMENTS
1. The application was declared fileable in a meeting held on filing meeting on 1/27/97.
2. As shown the firm must provide additional information before the application can be approved.
3. The Amendment dated 7-02-97 is a stability update reporting the stability information to 12 months for all three lots.
4. The Amendment dated 8-26-97 is for a request for categorical exclusion based on July 26, 1997, Federal Registrar notice.
5. The Amendment dated 9-12-97 is for labeling changes.
6. The Amendment dated 10-14-97 is an answer to various questions raised by Dr. A. Mitra to Alza through T.con. via CSO (Ms. T. Rumble).
7. The Amendment dated 11-3-97 is for update on stability data extending it up to 18 months for all five registration lots. The stability update on 3 validation lots using alternate pouch material (3 months for all three lots) was also provided. Based on the stability data of the registration lots, a 24 months shelf life was proposed.

CONCLUSION AND RECOMMENDATIONS
This application is approved. However, the firm should respond to the questions in the NDA review and all responses should be reviewed and found satisfactory.

cc: NDA 20-791
HFD-580/A. K. Mitra/ 11-28-97
HFD-580/M. J. Rhee
HFD-580/T. Rumble
R/D. Init. By-

Amit K. Mitra, Ph.D

11-28-97