

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020898

CHEMISTRY REVIEW(S)

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-898

CHEM. REVIEW #: 3

REVIEW DATE: 11/18/98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	9/22/98		
Amendment	9/29/98		
Amendment	10/7/98		
Amendment	11/13/98		

NAME & ADDRESS OF APPLICANT: Genzyme Corporation
One Kendall Square
Cambridge, MA 02139

DRUG PRODUCT NAME

Proprietary: Thyrogen
Nonproprietary/USAN: Thyrotropin alfa
Common Name: Recombinant Thyroid Stimulating Hormone
Code Name/#: hTSH
Chem. Type/Ther. Class: 1P

PHARMACOL. CATEGORY/INDICATION:

Hormone, stimulating thyroid cells to take up radioiodine and to secrete thyroglobulin. an adjunctive **diagnostic tool** for serum thyroglobulin testing in the follow-up of patients with thyroid cancer.

DOSAGE FORM:

Lyophilized powder for injection

STRENGTHS:

1.1 mg/vial (0.9 mg/mL after reconstitution)

ROUTE OF ADMINISTRATION:

intramuscular

DISPENSED:

X Rx OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL.WT:

See page 4 of Chemistry Review #1.

REMARKS/COMMENTS:

The amendment dated 9/22/98 provides for a background package containing information to be discussed in a tele-conference. The telephone conference was requested by the applicant after receiving an Approvable Letter dated 9/15/98.

The amendment dated 9/29/98 provides for raw data for the determination of specific activities for a number of lots of thyrotropin alfa. The specific activities for these lots were presented in a meeting held in the Agency on 9/9/98. The meeting was held to discuss the problems uncovered an inspection made by the reviewer and Ms. Karen Moksnes of the New England District to Genzyme's manufacturing facility at Framingham, MA on 8/26/98. The problems discovered after the review of raw data for the [redacted] performed on a number of lots of Thyrogen drug substance are described in the attached memo dated 10/27/98.

The amendment dated 10/7/98 provided for the formal response to the chemistry deficiencies outlined in the Approval letter dated 9/15/98.

The amendment dated 11/13/98 provides for a [redacted]
for the [redacted] used to establish an [redacted]

The labeling issues concerning the specific activity, established name and other items have been resolved in separate meetings and teleconferences.

CONCLUSIONS & RECOMMENDATIONS:

With a satisfactory response to the deficiencies listed in the Approvable Letter and phase IV commitments made by the applicant [redacted] the NDA can be approved from chemistry standpoint.

Orig. NDA 20-898
HFD-510/Division File
HFD-820/J. Gibbs
HFD-510/D.G. Wu
HFD-510/S. McCort

[redacted]
/S/
Duu-Gong Wu, Ph.D
Team Leader II, ONDCII

R/D Init by:

Filename: 20898ND3

APPEARS THIS WAY
ON ORIGINAL

McCart
MAY 13 1998

DIVISION OF METABOLISM AND ENDOCRINE DRUG PRODUCTS - HFD-510
Review of Chemistry, Manufacturing, and Controls

NDA #: 20-898 CHEM. REVIEW #: 1 REVIEW DATE: 5/12/98

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	12/12/97	12/16/97	
Amendment	1/12/98	1/13/98	

NAME & ADDRESS OF APPLICANT: Genzyme Corporation
One Kendall Square
Cambridge, MA 02139

DRUG PRODUCT NAME

Proprietary: Thyrogen
Nonproprietary/USAN: Thyrotropin alfa
Common Name: Recombinant Thyroid Stimulating Hormone
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CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT.

REMARKS/COMMENTS:

Thyrogen has been designated as an orphan drug by the Agency.

The amendment dated 1/12/98 provided for information requested by the Dr. Uratoni regarding microbiology consult review. Microbiology consult reviews has been completed and the Microbiology section was found not satisfactory (see Microbiology Review #1).

Genzyme has requested a category exclusion under 62FR 145, section 25.31(b) based on the calculation that the amount of waste entering the environment will be [redacted] (Vol. 1.3, page 176). No EA review is required.

CGMP for all facilities has been completed and all are found acceptable(see attached EES reports).

Trade name "Thyrogen" was also reviewed by the CDER Labeling and Nomenclature Committee and found acceptable(see attached).

CONCLUSIONS & RECOMMENDATIONS:

From chemistry standpoint, this NDA is approvable, pending a satisfactory response to deficiencies outlined in the Draft list of comments and deficiencies and other deficiencies related to Microbiology section (see Microbiology consult review #1).

Orig. NDA 20-898
HFD-510/Division File
HFD-820/J. Gibbs
HFD-510/D.G. Wu
HFD-510/S. McCort

/S/

Duu-Gong Wu, Ph.D
Team Leader II, ONDCII

R/D Init by:

Filename:20898ND1

APPEARS THIS WAY
ON ORIGINAL