CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 21-839

Microbiology Review(s)

Product Quality Microbiology Review

Consult review for HFD-510

22 July, 2005

NDA:	21-839 & 21-839 BC
Name of Drug:	Increlex™ (mecasermin (rDNA origin) injection
Review Number:	1
Submission Date:	February 24, 2005
Applicant:	Tercica
Name of Reviewer:	Vinayak Pawar
Conclusion:	The application is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. **NDA:** 21-839 & 21-839 BC

2. **REVIEW NUMBER:** 1

3. **REVIEW DATE:** 22 July, 2005

4. **TYPE OF SUPPLEMENT:** NA

5. **APPLICATION FOR:** Recombinant Insulin-like Growth Factor.

6. **APPLICANT/SPONSOR:**
Name: Tercica
Representative: Ira Wallis
Telephone: 650-624-4920

7. **MANUFACTURING SITE:** Baxter Pharmaceutical Solutions, Bloomington, IN

8. **DRUG PRODUCT NAME:**
Proprietary: Increlex™ injection
Non-proprietary: (mecasermin (rDNA origin)
Drug Priority Classification: Insulin-like Growth Factor-1

9. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

10. **METHOD(S) OF STERILIZATION:** [ ]

11. **PHARMACOLOGICAL CATEGORY:** Growth factor

B. 1. **DOCUMENT/LETTER DATE:** February 24, 2005
2. **RECEIPT DATE:** Electronic submission
3. **CONSULT DATE:** March 16, 2005
4. **DATE OF AMENDMENTS:** NA
5. **ASSIGNED FOR REVIEW:** March 18, 2005
6. **SUPPORTING/RELATED DOCUMENTS:** DMF [ ] NDA 21-839 BC

C. **REMARKS:** The consult requests a priority review of NDA 21-839 for Increlex™, a human insulin-like growth factor. This is an electronic submission in an eCTD format, for a drug substance which is manufactured at [ ] and drug product manufactured at Baxter Pharmaceutical Solutions in Bloomington, IN.

filename: C:\my documents\review\NDA\N021839R1

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Based on the product microbiology quality assessment the application is recommended for approval.

B. Recommendation on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug substance is prepared at [ ] and shipped to Baxter Pharmaceutical Solutions, Bloomington, IN where it is manufactured as Increlex™ drug product (see overview Figure 1). Increlex™ is a sterile aqueous, clear solution intended for subcutaneous injection. The formulated bulk containing the active ingredient rhIGF-1 and Benzyl Alcohol as preservative [ ] for storage. The bulk filtration and filling operations are conducted in [ ] The product is filled in 5mL vials, stoppered and then sealed with aluminum flip-off seal. The manufacturing process and in-process controls at — are seen in Figure 2.

B. Brief Description of Microbiology Deficiencies - None

C. Assessment of Risk Due to Microbiology Deficiencies- NA

III. Administrative

A. Reviewer's Signature /S/
Vinayak B. Pawar, Ph.D.

B. Endorsement Block /S/
Bryan S. Riley, Ph.D.

C. CC Block
cc:
Original NDA 21-839
HFD-510/Division File/Enid Galliers

6 Page(s) Withheld

✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

C

J

E.4. Microbial Limits for Non-Sterile Products
NA

F. RELEASE TESTS

F.1. Bacterial Endotoxin Test and Method
See section E.3.

F.2. Sterility Test Methods and Release Criteria
The Sterility test will be performed according to USP/Ph. Eur methods. There are no changes in the currently approved procedures.

F.3. Adventitious Safety Evaluation
The product is manufactured from Genentech C

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G. LABELING
NA

H. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS: None

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/s/

Vinayak Pawar
8/5/05 01:40:12 PM
MICROBIOLOGIST

Recommended for approval from microbiology standpoint

Bryan Riley
8/5/05 01:44:56 PM
MICROBIOLOGIST