CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-800

MICROBIOLOGY REVIEW

Product Quality Microbiology Review
Review for HFD-570

7 OCTOBER 2002

NDA: 20-800 amendment

Drug Product Name
Proprietary: Twinject
Non-proprietary: Epinephrine Injection USP
Drug Product Classification: S

Review Number: 2

Subject of this Review
Submission Date: 26 July 2002
Receipt Date: 29 July 2002
Consult Date: 18 September 2002
Date Assigned for Review: 27 September 2002

Submission History (for amendments only)
Date(s) of Previous Submission(s): 26 June 2001
Date(s) of Previous Micro Review(s): 28 September 2001

Applicant/Sponsor
Name: Hollister-Stiers
Address: PO Box 3145; Spokane, WA 99220
Representative: David Mirabell
Telephone: 509-482-1721

Name of Reviewer: Bryan S. Riley, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** N/A

2. **SUPPLEMENT PROVIDES FOR:** N/A

3. **MANUFACTURING SITE:** Abbott Laboratories; McPherson, KS

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** [redacted] IV administration

5. **METHOD(S) OF STERILIZATION:** [redacted]

6. **PHARMACOLOGICAL CATEGORY:** Adrenergic

B. **SUPPORTING/RELATED DOCUMENTS:** Microbiology review of NDA 20-800AZ dated 28 September 2001

C. **REMARKS:** This submission contains the applicants responses to product quality microbiology deficiencies.

filename: 20800r2.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – This submission is recommended for approval on the basis of product quality microbiology.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug product is [redacted]

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies – The drug product is [redacted] using an appropriately validated process. Therefore, the drug product presents a minimal risk from the standpoint of product quality microbiology.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Bryan S. Riley, Ph.D. (Microbiology Reviewer)
Peter H. Cooney, Ph.D. (Microbiology Supervisor)

C. CC Block
N/A

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bryan Riley
10/18/02 09:51:13 AM
MICROBIOLOGIST

Peter Cooney
10/18/02 01:55:16 PM
MICROBIOLOGIST

REVIEW TO HFD-570
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF/HFD-805
MICROBIOLOGY REVIEW #1 OF NDA

28 September 2001

A. 1. NDA: 20-800AZ

2. TYPE OF SUPPLEMENT: N/A

3. SUPPLEMENT PROVIDES FOR: N/A

4. APPLICANT/SPONSOR: Hollister-Stier Laboratories

5. MANUFACTURING SITE: Abbott Laboratories
McPherson, KS

6. DRUG PRODUCT NAME:
Proprietary: Twinject™
Nonproprietary: Epinephrine Injection
Drug Priority Classification: S

7. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: [redacted], IV administration, [redacted]

8. METHOD(S) OF STERILIZATION: [redacted]

9. PHARMACOLOGICAL CATEGORY: Adrenergic

B. 1. DOCUMENT/LETTER DATE: June 26, 2001
2. RECEIPT DATE: June 28, 2001
3. CONSULT DATE: July 11, 2001
4. DATE OF AMENDMENT: June 26, 2001
5. ASSIGNED FOR REVIEW: July 31, 2001
6. SUPPORTING/RELATED DOCUMENTS:

C. REMARKS: This amendment contains the sterility assurance information for the drug product.

D. CONCLUSIONS: This submission is approvable, pending resolution of microbiology deficiencies. Please see "Microbiologist's List of Deficiencies" at the end of this review.

Bryan S. Riley, Ph.D.
Microbiology Reviewer

cc.: Original NDA 20-800
HFD 570/Division File
HFD 570/Project Manager
HFD 570/Chemist
HFD 805/Consult File
HFD 805/ B. Riley

Drafted by: Bryan Riley, Ph.D.
R/D initialed by: Peter Cooney, Ph.D.

filename: C:\Data\Data\Word\NDA\20800AZ.doc

7 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

MAY 12 1997

REVIEW FOR HFD-570
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF HFD-805

Microbiologist's Review # 1 of NDA 20-800
May 12, 1997

A. 1. APPLICATION NUMBER: 20-800

APPLICANT: Bayer Corporation
Pharmeceutical Division
3525 N Regal Street
Spokane, WA 99207

2. PRODUCT NAMES: Epinephrine Injection — Epinephrine Injection, USP, 1:1000)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION: — subcutaneous or intramuscular.

4. METHOD(S) OF STERILIZATION: —

5. PHARMACOLOGICAL CATEGORY: Adrenergic, used in emergency treatment of allergen induced anaphylaxis and bronchospasm.

B. 1. DATE OF INITIAL SUBMISSION: December 5, 1996

2. AMENDMENT: none

3. RELATED DOCUMENTS: DMFs: —

4. ASSIGNED FOR REVIEW: February 6, 1997

5. DATE OF CONSULT REQUEST: January 14, 1997

C. REMARKS:

— Epinephrine Injection USP (1:1000) is a drug delivery system consisting of an automatic needle/injection device and existing marketed drug/syringe product, — Epinephrine Injection, USP (1:100). The product is contained in a sterile, 1 ml syringe, is designed to deliver two doses of 0.3 ml each. The — which is the subject of this NDA, is a new delivery system for — It delivers the first dose of epinephirine automatically and the second dose manually, if needed.

D. CONCLUSIONS:

Since the product is a legally marketed drug and it is not further manipulated prior to use in patients, there is no microbiological safety issues related to this NDA. The submission is recommended for approval with respect to microbiology. The Pre-approval inspection from the stand-point of —— manufacture of the ——is critical.

(S)

Brenda Uratani, Ph.D. (S)
Review Microbiologist

cc:

NDA 20-800
HFD-570/ Div. File
HFD-805 /Uratani
HFD-570/CSO/D. Toyer
drafted by: Brenda Uratani, 5/12/97
R/D initialed by P.Cooney, 5/12/97

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_____ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

TOYER

REQUEST FOR CONSULTATION

CO 1545 1-15-97

TO (Division/Office): Peter Cooney HFD-160			FROM: HFD-570 (Division of Pulmonary Drug Products) Denise P. Toyer, Project Manager	
DATE: January 14, 1997	IND NO.:	NDA NO.: 20-800	TYPE OF DOCUMENT: New submission	DATE OF DOCUMENT: December 6, 1996
NAME OF DRUG: — (epinephrine) injection 1:1000 (1 mL)	PRIORITY CONSIDERATION: Standard	CLASSIFICATION OF DRUG: 3S	DESIRED COMPLETION DATE: April 1, 1997 (Filed date 12-6-97)	
NAME OF FIRM: Bayer Pharmaceutical Division			Division Action Date 5-1-97 (CMC Pkg Insts)	

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER (SPECIFY BELOW): Injectable

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW	☐ CHEMISTRY REVIEW
☐ END OF PHASE II MEETING	☐ PHARMACOLOGY
☐ CONTROLLED STUDIES	☐ BIOPHARMACEUTICS
☐ PROTOCOL REVIEW	☐ OTHER:
☐ OTHER:	

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: Please review the attached information. — is an epinephrine product used for allergic emergencies. The autopen will provide two 0.3 ml injections. It will contain one automatic injection and one manual injection. An existing epinephriine is used in the assembled product.

cc: Original NDA 20-800
HFD-570/Div. Files
HFD-570/Toyer/Kim, Schumaker

CENTER FOR DRUG REC'D JAN 15 1997

SIGNATURE OF REQUESTER: (5)

METHOD OF DELIVERY (Check one): ☒ HAND

SIGNATURE OF RECEIVER: (5)

SIGNATURE OF DELIVERER: (5)