CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-539

MICROBIOLOGY REVIEW

Product Quality Microbiology Review
Review for HFD-180

12 DEC 2003

NDA: 21-539

Drug Product Name
Proprietary: Acetadote®
Non-proprietary: Acetylcysteine Injection
Drug Product Classification: 3P

Review Number: 2

Subject of this Review
Submission Date: 24 OCT 2003
Receipt Date: 28 OCT 2003
Consult Date: 30 OCT 2003
Date Assigned for Review: 05 NOV 2003

Submission History (for amendments only)
Date(s) of Previous Submission(s): 17 OCT 2002
Date(s) of Previous Micro Review(s): 27 JAN 2003

APPEARS THIS WAY
ON ORIGINAL

Applicant/Sponsor
Name: Cumberland Pharmaceuticals
Address: 209 10th Avenue, South
Suite 332
Nashville, TN 37203
Representative: Amy Rock, Ph.D.
Telephone: (615) 255-0068

Name of Reviewer: David Hussong

Conclusion: APPROVE

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** (Amendment to New NDA)

2. **SUPPLEMENT PROVIDES FOR:** (New NDA)

3. **MANUFACTURING SITE:**

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Injection solution (20%) for intravenous administration, supplied in 10 and 30 mL single use glass vials.

5. **METHOD(S) OF STERILIZATION:**

6. **PHARMACOLOGICAL CATEGORY:**

B. **SUPPORTING/RELATED DOCUMENTS:** N/A

C. **REMARKS:** The NDA submission was inadequate and resulted in deficiencies. A FAX was sent to the applicant on October 8, 2003, conveying eight deficiencies (plus subparts) to the applicant. In the text of this review, the deficiencies are copied from the original review and the applicant's replies are reviewed after each deficiency.

filename: 21-539rv2.doc

APPEARS THIS WAY
ON ORIGINAL

Executive Summary

I. Recommendations

A. Recommendation on Approvability - APPROVE

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - none

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The product is manufactured sterile by [redacted] g, using [redacted] to prepare the solution for filling. The subject presentation is for intravenous injection.

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
David Hussong/Microbiologist
Peter Cooney/Microbiology Supervisor

C. CC Block
cc:
Original NDA 21-539
HFD-180/Division File/NDA 21-539

APPEARS THIS WAY
ON ORIGINAL

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/s/

David Hussong
12/16/03 10:22:36 AM
MICROBIOLOGIST

Peter Cooney
12/16/03 11:47:59 AM
MICROBIOLOGIST

APPEARS THIS WAY
ON ORIGINAL

Product Quality Microbiology Review
Review for HFD-180

27 JAN 2003

NDA: 21-539

Drug Product Name
Proprietary: Acetadote®
Non-proprietary: Acetylcysteine Injection
Drug Product Classification: 3P

Review Number: 1

Subject of this Review
Submission Date: 17 OCT 2002
Receipt Date: 21 OCT 2002
Consult Date: 18 OCT 2002
Date Assigned for Review: 31 OCT 2002

Submission History (for amendments only)
Date(s) of Previous Submission(s): 27 JUN 2002
Date(s) of Previous Micro Review(s):
RTF memorandum, 30-JUL-2002

Applicant/Sponsor
Name: Cumberland Pharmaceuticals
Address: 209 10th Avenue, South
Suite 332
Nashville, TN 37203
Representative: Amy Rock, Ph.D.
Telephone: (615) 255-0068

APPEARS THIS WAY
ON ORIGINAL

Name of Reviewer: David Hussong

Conclusion: Approvable

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** (New NDA)

2. **SUPPLEMENT PROVIDES FOR:** (New NDA)

3. **MANUFACTURING SITE:**

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Injection solution (20%) for intravenous administration, supplied in 10 and 30 mL single use glass vials.

5. **METHOD(S) OF STERILIZATION:**

6. **PHARMACOLOGICAL CATEGORY:**

B. **SUPPORTING/RELATED DOCUMENTS:** N/A

C. **REMARKS:** The original submission was inadequate for review and additional sterilization process information was submitted in the amendment dated 17-OCT-2002. In the text of this review, reference to the original submission applies to the 27-JUN-2002 submission. Reference to the "amendment" refers to the 17-OCT-2002 submission.

filename: 21-539rv1.doc

APPEARS THIS WAY
ON ORIGINAL

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Approvable

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - none

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The product is manufactured sterile by ——— using ——— to prepare the solution for filling. The subject presentation is for intravenous injection.

B. Brief Description of Microbiology Deficiencies – There are numerous omissions in the sterilization validation and minor errors in the documentation of procedures. A more significant error appears in the acceptance criteria for the ——— test, which is part of the product specification. For additional details, refer to "LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS" at the end of this review.

C. Assessment of Risk Due to Microbiology Deficiencies – These deficiencies pose significant risks to the patient.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
David Hussong/Microbiologist
Peter Cooney/Microbiology Supervisor

C. CC Block
cc:
Original NDA 21-539
HFD-180/Division File/NDA 21-539

APPEARS THIS WAY
ON ORIGINAL

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/s/

David Hussong
2/11/03 02:08:32 PM
MICROBIOLOGIST

Peter Cooney
2/11/03 03:03:57 PM
MICROBIOLOGIST

APPEARS THIS WAY
ON ORIGINAL