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RESEARCH**

APPLICATION NUMBER:

21-872

MICROBIOLOGY REVIEW

Product Quality Microbiology Review Review for Neurology Drug Products Division

5 June 2006

NDA: 21-872 - Amended

Drug Product Name

Proprietary: Keppra Injection

Non-proprietary: Levetiracetam 100 mg/mL

Drug Product Priority Classification: S1

Review Number: 2

Dates of Submission(s) Covered by This Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
January 31, 2006	Unknown	February 6, 2006	February 17, 2006

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
July 14, 2005, Amendment Re-assigned on July 25, 2005 to V.Pawar	1	November 14, 2005 V.Pawar
December 20, 2004 Originally Assigned January 25, 2005 to S. Langille	1	November 14, 2005 V.Pawar

Applicant/Sponsor

Name: UCB Pharma, Inc.
Address: Smyrna, Georgia 30080
Representative: Linda F. Noa
Telephone: 770-970-8582

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: The application is recommended for approval from microbiology product quality standpoint.

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – The contract manufacturing site at Cardinal Health underwent a facility shut down to accommodate changes in the manufacturing areas and equipment. The data provided from these changes satisfy the requirement for sterility assurance of the product. Therefore, the application is recommended for approval from microbiology product quality standpoint.
- B. **Recommendations 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 ingredients are ~~_____~~ process using ~~_____~~ The ~~_____~~ product is then ~~_____~~ in vials, ~~_____~~ and ~~_____~~ The finished dosage form is subjected to ~~_____~~ The product manufacturing process is shown in Figure 1.
- B. **Brief Description of Microbiology Deficiencies** – See section H.
- C. **Assessment of Risk Due to Microbiology Deficiencies** - NA

III. Administrative

- A. **Reviewer's Signature** _____
Vinayak B. Pawar, Ph.D.
- B. **Endorsement Block** _____
James McVey.
- C. **CC Block**
N/A

7 Page(s) Withheld

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Withheld Track Number: Microbiology- 1

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/s/

Vinayak Pawar
6/7/2006 02:06:27 PM
MICROBIOLOGIST

Recommended for approval from microbiology product quality standpoint.

James McVey
6/8/2006 07:14:15 AM
MICROBIOLOGIST

Product Quality Microbiology Review

Review for HFD-120

21 November 2005

NDA: 21-872

Drug Product Name

Proprietary: Keppra Injection
Non-proprietary: Levetiracetam 100 mg/mL
Drug Product Priority Classification: S1

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
December 20, 2005		January 3, 2005	Originally Assigned January 25, 2005. S. Langille
July 14, 2005, requesting consultation meeting			Re-assigned on July 25, 2005. V.Pawar

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
NA	NA	NA

Applicant/Sponsor

Name: UCB Pharma, Inc.
Address: Smyrna, Georgia 30080
Representative: Linda F. Noa
Telephone: 770-970-8582

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: The application is approvable pending resolution of microbiology product quality issues (see Section H).

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA
 2. **SUBMISSION PROVIDES FOR:** New Drug Product
 3. **MANUFACTURING SITE:** Cardinal Health, Albuquerque, NM
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** 110mg/mL, Intravenous
 5. **METHOD(S) OF STERILIZATION:** 
 6. **PHARMACOLOGICAL CATEGORY:** Anti-Convulsion
- B. **SUPPORTING/RELATED DOCUMENTS:** Supplementary volume submitted for T-Con.
- C. **REMARKS:** The consult requests review of NDA 21-872 for a Keppra® in a new injectable presentation. Five volumes of the application relevant to the microbiology product quality review were submitted for review. The application was amended on July 14, 2005 to inform facility changes at Cardinal Health, a contract manufacturer for UCB Pharma, Inc. This amendment was assigned to me. After reviewing the supplement, a meeting was arranged with HFD-120 to discuss the changes in the manufacturing facility at Cardinal Health and to discuss the review plan. At this meeting, it was determined that there were major changes in the manufacturing facility and in order to meet the early January 2006 review deadline, the sponsor will need to provide sterility assurance data by the end of September 2005. This was conveyed via T-con to the sponsor. A meeting was called on November 15, 2005 by the Division to assess the review progress and to discuss FDA inspection issues. At this meeting, a decision was made to wrap up all the reviews and issue an approvable status.

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Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – The manufacturing site at Cardinal Health is undergoing a manufacturing facility shut down to accommodate changes in the manufacturing areas and equipment. In light of these changes the sterility related issues cannot be reviewed until the changes have been completed and re-validated. Therefore, the application is approvable pending resolution of items listed in Section H that are directly impacted by the changes at Cardinal manufacturing facility.
- B. **Recommendations 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 ingredients are ~~_____~~ and ~~_____~~ process using ~~_____~~. The ~~_____~~ product is then ~~_____~~ vials, ~~_____~~ and ~~_____~~ and ~~_____~~. The product manufacturing process is shown in Figure 1.
- B. **Brief Description of Microbiology Deficiencies** – See section H.
- C. **Assessment of Risk Due to Microbiology Deficiencies - NA**

III. Administrative

- A. **Reviewer's Signature** _____
Vinayak B. Pawar, Ph.D.
- B. **Endorsement Block** _____
Bryan S. Riley, Ph.D.
- C. **CC Block**
N/A

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/s/

Vinayak Pawar
11/21/2005 02:56:47 PM
MICROBIOLOGIST

Approvable pending resolution of items listed in microbiology review
section H.

Bryan Riley
11/21/2005 03:02:57 PM
MICROBIOLOGIST