CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-725

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

04 MAY 2007

NDA: 20-725 AZ, BZ and BI

Drug Product Name
Proprietary: CREON®
Non-proprietary: Pancrelipase delayed-release capsules, USP
Drug Product Priority Classification: 7P

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
17-NOV-2006	20-NOV-2006	16-JAN-2007	16-JAN-2007
21-MAR-2007	22-MAR-2007	N/A	23-MAR-2007
19-APR-2007	20-APR-2007	N/A	24-APR-2007

Submission History (for amendments only) – N/A

Applicant/Sponsor
Name: Solvay Pharmaceuticals, Inc.
Address: 901 Sawyer Rd
Marietta, GA 30062

Representative: Don Ruggirello
Sr. Director, Regulatory Affairs
Telephone: 770-578-5658

Name of Reviewer: Anastasia G. Lolas

Conclusion: Recommended for approval with one comment to be provided to the applicant (see Section 3 of review)

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: AZ amendment to original NDA

2. SUBMISSION PROVIDES FOR: Complete response to not-approvable letter, additional clinical and CMC information

3. MANUFACTURING SITE: Solvay Pharmaceuticals GmbH
Site Neustadt
Justus-von Liebig-Strasse 33
31535 Neustadt am Rubenberge
Germany

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

- Delayed-release capsules
- Oral
- 6000, 12000 and 24000 units

5. METHOD(S) OF STERILIZATION: N/A

6. PHARMACOLOGICAL CATEGORY: Digestants/Pancreatic enzymes

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: This is the first pancrelipase NDA application. The original NDA was submitted in 1997. This AZ amendment is a complete response to the not-approvable letter (October 2003) that included many CMC deficiencies. The applicant is submitting additional clinical data and a new CMC section. The drug substance manufacturer has changed.

This is an electronic submission in the CTD format. There is no PAL assessment in DFS. There is no microbiology review of the original NDA in DFS. The viral clearance studies in this submission are reviewed by OBP.

A multi-disciplinary information request was sent to the applicant on March 5, 2007 including the following microbiology questions:

1. *Identify the sampling process and method used to test the Creon® capsules for microbial limits* (b) (4)
2. *Provide a data summary of studies that verify the suitability of the microbial limits methods for testing the Creon® capsules.*

A BZ amendment was submitted on March 21, 2007. A desk copy was provided for review. The microbiology responses are located in Attachments 1-2 of

Volume 1 of 2. See relevant sections of review for an assessment of these responses.

A second information request was sent to the applicant on April 9, 2007 to request the following:

Provide microbial limits sampling and testing protocols for the finished dosage form. The in-process testing in the sampling plan provided does not test the assembled dosage form. Refer to the International Conference on Harmonization (ICH); Guidance on Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances as well as Decision Tree #8 for guidance on setting microbiological attributes for non-sterile dosage forms.

A response was received on April 19, 2007 as a BI amendment. See Section P.5 of the review for an assessment of this response.

file name: N020725R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – Recommended for approval based on product quality microbiology with one comment to be provided to the applicant (see Section 3 of review)

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 product is non-sterile. The microbial limits for the drug substance and the drug product are reviewed.

B. Brief Description of Microbiology Deficiencies – None

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

III. Administrative

A. Reviewer's Signature _____
Anastasia G. Lolas

B. Endorsement Block
James L. McVey

C. CC Block
N/A

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

/s/

Anastasia Lolas
5/4/2007 01:34:18 PM
MICROBIOLOGIST

James McVey
5/4/2007 02:45:40 PM
MICROBIOLOGIST