

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-175Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

February 3, 2012

NDA: 22-175/N-000

Drug Product Name

Proprietary: Pancrecarb

Non-proprietary: pancrelipase

Review Number: 4

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
November 18, 2011	November 18, 2011	November 23, 2009	November 23, 2011

Submission History (for amendments only) –

Submit Date(s)	Microbiology Review #	Review Date(s)
N/A	3	June 13, 2011
N/A	2	January 25, 2011
June 20, 2008	1	May 12, 2009

Applicant/Sponsor

Name: Digestive Care Inc.

Address: 1120 Win Drive, Bethlehem, PA 18017

Representative: Tibor Sipos Ph.D., President

Telephone: 610-882-5950

Name of Reviewer: Vinayak Pawar, Ph.D.

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original NDA Resubmission
2. **SUBMISSION PROVIDES FOR:** Microbial limits Testing Information.
3. **MANUFACTURING SITE:** Digestive Care Inc., Bethlehem, PA
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Capsules containing Bicarbonate-Buffered and Enteric-Coated Microspheres in strength of (b) (4) MS-8 (8,000 USP units of lipase); MS-16 (16,000 USP units of lipase) per capsule for oral administration.
5. **METHOD(S) OF STERILIZATION:** Oral product, not sterile.
6. **PHARMACOLOGICAL CATEGORY:** Exocrine pancreatic insufficiency.
- B. **SUPPORTING/RELATED DOCUMENTS:** DMF (b) (4)
- C. **REMARKS:** The submission was provided electronically in CTD format.

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Executive Summary

I. Recommendations

- A. Recommendation on Approvability** – The application is recommended for approval from microbiology product quality standpoint.
- 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 Pancrecarb® manufacturing process steps consist of [REDACTED] (b) (4) [REDACTED]. The oral drug product is in a capsule form not intended to be sterile.
- B. Brief Description of Microbiology Deficiencies** - None
- C. Assessment of Risk Due to Microbiology Deficiencies** - None

III. Administrative

- A. Reviewer's Signature** _____
Vinayak B. Pawar, Ph.D.
Senior Review Microbiologist,
CDER/OPS/NDMS
- B. Endorsement Block** _____
John W. Metcalfe, Ph.D.
Senior Review Microbiologist,
CDER/OPS/NDMS
- C. CC Block**
N/A

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/s/

VINAYAK B PAWAR
02/03/2012

JOHN W METCALFE
02/03/2012
I concur.

MEMORANDUM



DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: JUNE 13, 2011

TO: NDA 22-175

FROM: Vinayak B. Pawar, Ph.D.
Senior Microbiology Reviewer
CDER/OPS/New Drug Microbiology Staff

THROUGH: James McVey.
Team Leader,
CDER/OPS/New Drug Microbiology Staff

CC: Jagjit Grewal, M.P.H. , Senior Regulatory Health Project Manager
Division of Gastroenterology and Inborn Errors Products
CDER/OND/ODE III
DARRTS

SUBJECT: **Addendum 2 to Quality Microbiology Review dated 13 May 2009**
Product: Pancrecarb (pancrelipase) capsules
Sponsor: Digestive Care Inc.

In the quality microbiology review of NDA 22-175/N-000 dated 13 May 2009, DMF (b) (4) was found to be adequate (DMF review 08 June 2010). This finding was part of the basis for the recommendation to approve the application from a quality microbiology perspective.

The review of subsequent amendments to DMF (b) (4) resulted in a request for additional product quality microbiology information (IR dated 27 October 2010). This changed the status of NDA 22-175/N000 to approvable on January 25, 2011.

In the submission dated November 8, 2010, the DMF holder addressed all of the issues listed in the IR letter of 27 October 2010. From Microbiology Product Quality standpoint this submission was found adequate (OPS Microbiology Review dated June 3, 2011 - DARRTS Reference ID 2956822). Therefore, NDA 22-175/N000 status is changed to recommend for approval.

END

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/s/

VINAYAK B PAWAR
06/13/2011

JAMES L MCVEY
06/14/2011
I concur.

MEMORANDUM



**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

DATE: January 25, 2011

TO: NDA 22-175

FROM: Vinayak B. Pawar, Ph.D.
Senior Microbiology Reviewer
CDER/OPS/New Drug Microbiology Staff

THROUGH: Bryan S Riley, Ph.D.
Senior Microbiology Reviewer
CDER/OPS/New Drug Microbiology Staff

CC: Matthew Sherer – Regulatory Project Manager
DARRTS

SUBJECT: **Addendum to Quality Microbiology Review dated 13 May 2009**
Product: Pancrecarb (pancrelipase) capsules
Sponsor: Digestive Care Inc.

In the quality microbiology review of NDA 22-175/N-000 dated 13 May 2009, DMF (b) (4) was found to be adequate (DMF review 08 June 2010). This finding was part of the basis for the recommendation to approve the application from a quality microbiology perspective.

The review of subsequent amendments to DMF (b) (4) resulted in a request for additional product quality microbiology information (IR dated 27 October 2010). NDA 22-175/N000 cannot be recommended for approval until the product quality microbiology deficiencies cited in the 27 October 2010 information request have been adequately addressed.

END

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/s/

VINAYAK B PAWAR
01/26/2011

BRYAN S RILEY
01/26/2011
I concur.

Product Quality Microbiology Review

May 12, 2009

NDA: 22-175

Drug Product Name

Proprietary: Pancrecarb

Non-proprietary: pancrelipase

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
June 20, 2008	October 27, 2008	November 18, 2009	October 7, 2008 Rolling NDA

Submission History (for amendments only) – N/A

Applicant/Sponsor

Name: Digestive Care Inc.

Address: 1120 Win Drive, Bethlehem, PA 18017

Representative: Tibor Sipos Ph.D., President

Telephone: 610-882-5950

Name of Reviewer: Vinayak Pawar, Ph.D.

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

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original NDA
2. **SUBMISSION PROVIDES FOR:** An oral drug product.
3. **MANUFACTURING SITE:** Digestive Care Inc., Bethlehem, PA
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Capsules containing Bicarbonate-Buffered and Enteric-Coated Microspheres in strength of [REDACTED] (b) (4) [REDACTED] MS-8 (8,000 USP units of lipase); MS-16 (16,000 USP units of lipase) per capsule for oral administration.
5. **METHOD(S) OF STERILIZATION:** Oral product, not sterile.
6. **PHARMACOLOGICAL CATEGORY:** Exocrine pancreatic insufficiency.
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** The consult requests review of NDA 22-175 for pancrelipase in the form of an oral capsule. The application was submitted on June 20, 2008 as a rolling NDA. An official consult request was submitted on November 18, 2008 with a PDUFA goal date of October 27, 2009. No IQA was filed.

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Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – The application is recommended for review from microbiology product quality standpoint.
- 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 Pancrecarb® manufacturing process steps consist of [REDACTED] (b) (4) [REDACTED]. The oral rug product is in a capsule form not intended to be sterile.
- B. **Brief Description of Microbiology Deficiencies** - None
- C. **Assessment of Risk Due to Microbiology Deficiencies** - None

III. Administrative

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

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/s/

Vinayak Pawar

5/13/2009 03:13:03 PM

MICROBIOLOGIST

Please forward review comments in section H to the sponsor.

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

James McVey

5/13/2009 03:20:11 PM

MICROBIOLOGIST

I concur.