CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205494Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

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

DATE: 02 January 2014

TO: Jessica Benjamin, Project Manager, ODE III/DGIEP

Cc: Rebecca McKnight, Project Manager, ODNDQAII/BRIV
Yichun Sun, Chemist, ODNDQA

FROM: Robert J. Mello, Ph.D.
Senior Review Microbiologist
CDER/OPS/New Drug Microbiology Staff

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

SUBJECT: NDA 205494/N-000 Review
Submission Date: 19 September 2013
Received Date: 20 September 2013
Drug Product: Cerdelga (eliglustat tartrate)
Sponsor: Genzyme Corporation

The drug product, Cerdelga (eliglustat tartrate), is a hard gelatin capsule oral formulation. The Applicant has demonstrated adequate microbiological controls on the manufacturing process. (b) (4) The hypromellose is USP grade having (b) (4) The USP microcrystalline cellulose, USP lactose monohydrate and the hard gelatin capsules are tested for microbial limits (USP<61>, <62>) and the API does not support microbial growth. The Applicant performed microbial limits (ML) testing at release and during the stability program for the three stability batches. (b) (4) The following microbiology information request was transmitted to the Applicant in the NDA filing letter dated 12/03/2013.

> (b) (4) ***Since you have demonstrated adequate upstream microbial controls within your manufacturing process, you are advised to amend your Release Specifications Table 1 (Section 3.2.P.5.1) t*** (b) (4) ***Since you are conducting microbial limits testing within your long-term stability program, Table 1, Evolution of Eliglustat Hard Capsule Stability Specification" (Section 3.2.P.8.1, page 3/12) adequately establishes the microbial limit specification within the on-going, commercial stability program.***

The Applicant provided the following response on 12/20/2013:

Genzyme Response:

Genzyme agrees to [redacted] (b) (4) *the drug product release specifications and confirms that it will be performed as part of the ongoing commercial long term stability program. Genzyme proposes that all Module 2.3 and Module 3 sections which are impacted by this and future responses to Agency questions be submitted as product correspondence after the approval of NDA 205494.*

Acceptable

Reviewer's Comment: The in-process controls and the microbial limits testing within the ongoing stability program provide adequate assurance of microbial control of the manufacturing process. The Applicant's stated agreement is now a formal part of the NDA submission. The NDA submission is recommended for approval from microbiology product quality standpoint.

END

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/s/

ROBERT J MELLO
01/02/2014

BRYAN S RILEY
01/02/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY NON-STERILE DRUG PRODUCT FILING CHECKLIST

NDA Number: 205-494 **Applicant:** Genzyme Corporation 500 Kendall Street Cambridge, MA 02142 **Letter Date:** 19 September 2013

Drug Name: Cerdelga (eliglustat tartarate) **NDA Type:** 505(b)(1) **Stamp Date:** 20 September 2013

Dosage Form: oral hard capsule **Reviewer:** Robert J. Mello, Ph.D.

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		Submission is in eCTD format located in EDR
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		Section 3.2.P.3.3 (process description); Section 3.2.P.4 (excipients):
3	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		Section 3.2.P.5.1
4	Has the applicant submitted the results of analytical method verification studies?	X		Microbial Limits performed per USP<61> and <62>
5	Has the applicant submitted preservative effectiveness studies (if applicable)?	-	-	Not Applicable
6	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: The Applicant has demonstrated adequate microbiological controls on the manufacturing process. (b) (4) The hypromellose is USP grade having (b) (4). The USP microcrystalline cellulose, USP lactose monohydrate and the hard gelatin capsules are tested for microbial limits (USP<61>, <62>) and the API does not support microbial growth. The Applicant performed microbial limits (ML) testing at release and during the stability program for the three stability batches. (b) (4) The Applicant will be advised to amend their Release Specifications Table 1 (Section 3.2.P.5.1) to indicate that microbial limits testing will be performed only within the stability program.

Product Quality Microbiology Information Request: (b) (4) Since you have demonstrated adequate

upstream microbial controls within your manufacturing process you are advised to amend your Release Specifications Table 1 (Section 3.2.P.5.1) to [redacted] (b) (4)

Since you are conducting microbial limits testing within your long-term stability program, Table 1, *Evolution of Eliglustat Hard Capsule Stability Specification"* (Section 3.2.P.8.1, page 3/12) adequately establishes the microbial limit specification within the on-going, commercial stability program.

Robert J. Mello, PhD., Senior Review Microbiologist Date

John W. Metcalfe, Ph.D., Senior Review Microbiologist Date

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/s/

ROBERT J MELLO
10/25/2013

JOHN W METCALFE
10/25/2013
I concur.