CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-575

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

29 January 2010

NDA: **22-575/N000**

Drug Product Name
Proprietary: VPRIV
Non-proprietary: velaglucerase alfa

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
30-JUL-2009	30-JUL-2009	04-SEP-2009	08-SEP-2009
31-AUG-2009	31-AUG-2009	04-SEP-2009	08-SEP-2009
20-NOV-2009	20-NOV-2009	NA	NA
18-DEC-2009	18-DEC-2009	NA	NA
22-DEC-2009	22-DEC-2009	NA	NA
13-JAN-2010	13-JAN-2010	NA	NA
27-JAN-2010	27-JAN-2010	NA	NA

Submission History (for amendments only) – NA

Applicant/Sponsor
Name: Shire Human Genetic Therapies, Inc.
Address: 700 Main Street
Cambridge MA 02139
Representative: Nikhil Mehta
Telephone: (617) 613-4531

Name of Reviewer: Denise Miller

Conclusion: Approve (with a comment to be forward to the sponsor, see page 26)

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Original New Drug Application

2. **SUBMISSION PROVIDES FOR:** Aseptic filling and lyophilization procedures for velaglucerase alfa

3. **MANUFACTURING SITE:**

b(4)

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
Dosage form: lyophilized powder for infusion
Route of administration: Intravenous
Strength/Potency: 200 and 400 units/vial

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

6. **PHARMACOLOGICAL CATEGORY:** enzyme replacement therapy

B. **SUPPORTING/RELATED DOCUMENTS:** b(4)

C. **REMARKS:**
1) This application was a rolling submission in e-CTD format.

2) Information Request (IR) #1 was sent in the 74 day letter. The method suitability testing for sterility and the endotoxin testing in addition to the container closure integrity testing were requested. These reports were submitted in an amendment dated 20-NOV-2009.

3) has only brief descriptions of their validation and environmental monitoring programs. These summaries were also in the NDA. Data for the most current equipment qualifications, media fills and floor plans were not included in either the DMF or the NDA. In a discussion with the DMF holder, does not submit this information to their DMF but the information is provided to the NDA sponsor. requested that such information be requested from Shire. As a result, IR #2 b(4)

was sent to Shire on 11 DEC-2009 requesting the most current media fills containing a lyophilization simulation, [redacted] floor plans, and the most recent qualifications for t[redacted] the lyophilization [redacted]. A response was submitted in an amendment dated 18-DEC-2009.

4) The media fill data submitted on 18-DEC-2009 documented an aborted media fill in May 2009 as a result of a critical failure (fire) [redacted]

The qualification data submitted on 18-DEC-2009 [redacted] b(4)
predated this event and subsequent repair and was invalid. IR #3 was sent to Shire requesting the post repair revalidation reports [redacted].
These reports were provided in an amendment dated 13-JAN-2010. It was noted that effective 03-DEC-2009, [redacted] has changed its name and the letter head on the reports submitted reflect this.

5) Amendment submitted on 22-DEC-2009 was a stability data update.

6) IR#4 was sent to Shire on 22-JAN-2010 requesting justification for the validation cycle parameters [redacted]. The IR also b(4)
requested the acceptance criteria for D-value and spore population for incoming biological indicators. A response was submitted in an amendment dated 27-JAN-2010

filename: N022575N000R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommend to approve from a quality microbiology 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 manufacturing process for velaglucerace alfa includes sterilization —— , aseptic filling, and lyophilization. b(4)

B. Brief Description of Microbiology Deficiencies - None

C. Assessment of Risk Due to Microbiology Deficiencies - NA

III. Administrative

A. Reviewer's Signature _____
Denise A. Miller

B. Endorsement Block _____
Bryan S. Riley, Ph.D.

C. CC Block
N/A

22 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Microbiology Review Section-_____

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22575	ORIG-1	SHIRE HUMAN GENETIC THERAPIES INC	VELAGLUCERASE ALFA

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

/s/

DENISE A MILLER
02/03/2010

BRYAN S RILEY
02/03/2010
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 022-575/N000 **Applicant:** Shire HGT Inc. **Letter Date:** 31-AUG-209

Drug Name: Veleglucerase alpha **NDA Type:** 505 (b)(1) **Stamp Date:** 31-AUG-2009

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?	√		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	√		References DMF
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	√		
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		√	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?		√	Preservative eff. NA Container closure were performed data/reports not included
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	√		
7	Has the applicant submitted the results of analytical method verification studies?		√	
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?	NA		
9	Is this NDA fileable? If not, then describe why.	√		

Comments to be forwarded to the sponsor:

1) Please provide the method suitability report for USP <71> Sterility testing
2) Please provide the method suitability report for USP <85> Endotoxin testing
3) Please provide the container closure testing report.

Denise A. Miller, Microbiologist Date

Bryan S. Riley, Ph.D. Date

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

/s/

DENISE A MILLER
09/17/2009

BRYAN S RILEY
09/17/2009
I concur.