CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-058

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

27 March 2007

NDA: 22-058

Drug Product Name
Proprietary: Supprelin® LA.
Non-proprietary: Histrelin acetate subcutaneous implant.
Drug Product Priority Classification: S.

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
30 June 2006	03 July 2006	21 July 2006	28 July 2006
01 March 2007	05 March 2007		

Applicant/Sponsor
Name: Valera Pharmaceuticals, Inc.
Address: 8 Clarke Dr.
Cranbury, NJ. 08512
Representative: William B. Gray
Telephone: 609-235-3206

Name of Reviewer: John W. Metcalfe, Ph.D.

Conclusion: Recommended for Approval.

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Original NDA.

2. **SUBMISSION PROVIDES FOR:** A new drug product.

3. **MANUFACTURING SITE:**
Following are the sites for manufacturing of the subject drug product:

Table 3.2.P.3.1- 1 Production Sites Involved in Fabrication, Packaging, Testing and Distribution

Name and Address	Responsibility
Valera Pharmaceuticals 8 Clarke Drive Cranbury, New Jersey 08512 USA	Fabrication, packaging, labelling, release testing.

[redacted] b(4)

Site for finished product sterility and bacterial endotoxins testing:

[redacted] b(4)

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Subcutaneous implant.
- 50 mg.

5. **METHOD(S) OF STERILIZATION:** [redacted] b(4)

6. **PHARMACOLOGICAL CATEGORY:** Indicated for the treatment of central precocious puberty (CPP) in children of both genders.

B. SUPPORTING/RELATED DOCUMENTS: Microbiology reviews of NDA 21-732 (dated 14 July 2004 and 14 September 2004).

C. REMARKS:

The following is taken from Module 3.2.P.8.1, page 2:
"FDA approved Valera's histrelin subcutaneous implant (50 mg), under the proprietary name Vantas (NDA #21-732, approved on October 12, 2004), for the palliative treatment of advanced prostate cancer. The Vantas product is almost identical to Supprelin LA. That is, both products are histrelin subcutaneous implants, they are manufactured using the same starting materials, and packaged in the same container/closure immersed in the identical packaging solution, hypertonic 1.8% sodium chloride solution. The only difference between Vantas and Supprelin LA is that the new product releases drug at a higher rate than the Vantas product [redacted] b(4)
[redacted] Container/closure, API, and excipient compatibility have been addressed in the Vantas stability program as well as the ongoing Supprelin LA stability program and no significant compatibility issues have been found."

The implant insertion device is the same device which is currently approved for use with the applicant's implant manufactured under NDA 21-732 (page 3 of Module 3.2.R.4).

Correspondence was sent to the applicant on 23 February 2007 by the Division of Metabolic and Endocrine Drug Products to convey the following comment and question:

A product quality microbiology review of NDA 22-058 has been performed. Following are a comment and questions related to the manufacture of this drug product and its sterility assurance:
Comment:
The implant hydration process involving storage in sodium chloride of the units for 2 weeks at 38±2°C prior to [redacted] *is long and provides an opportunity for significant microbial growth to occur on the implant prior to sterilization. The subject submission provides some bioburden assessment data on three lots of product (pages 34-42 of Module 3.2.R.2), however no information is provided regarding when in the process the bioburden samples are taken or what the bioburden action level is.* b(4)

Questions:
- *Is the process used in the manufacture of Supprelin® LA (NDA 22-058) identical to that used for Vantas® (approved NDA 21-732)?*
- *Will pre-sterilization bioburden testing be performed on each lot of Supprelin® LA? When (exactly) during the manufacturing process is the bioburden sample taken? What is the pre-sterilization bioburden action level? What is the action plan in the event of excursion of this action level?*

On 01 March 2007, the applicant filed an amendment (#004) to the application in response to these questions. The applicant responses to these questions are incorporated and reviewed in relevant sections of this review.

APPEARS THIS WAY ON ORIGINAL

File Name: N022058R1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – NDA 22-058 is recommended for approval on the basis of microbiological product quality.

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 manufacturing process is quite complex. Reference is made to the relevant section of this review for a description. The individual product units are

B. Brief Description of Microbiology Deficiencies – There are no microbiology deficiencies identified.

C. Assessment of Risk Due to Microbiology Deficiencies – Not applicable.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Stephen Langille, Ph.D.

C. CC Block
N/A

12 Page(s) Withheld

X Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Microbiology-1

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/s/

John Metcalfe
4/4/2007 09:35:39 AM
MICROBIOLOGIST

Stephen Langille
4/4/2007 01:15:56 PM
MICROBIOLOGIST