

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-211

MICROBIOLOGY REVIEW(S)

Date: August 21, 2009

To: Gorski Lori, Project Manager

From : Vinayak Pawar, OPS, NDMS

Re: Product Quality Microbiology Comment sent to Sirion Therapeutics in Division's letter dated July 20, 2009.

Comment: Bacterial Endotoxins testing is required for ophthalmic products. Please provide assurance that Ganciclovir Ophthalmic Gel has no more than — EU/mg of endotoxin in the product. Provide test methods you used to assay the endotoxin content in the product.

b(4)

Response: Sirion responded in a letter dated August 6, 2009. The sponsor provided Control of Drug Product Specifications section (3.2.P.5.1) which included a USP LAL Method MTM-200033 indicating an acceptable specification for Ganciclovir at — EU/mL. This response is acceptable.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-22211

ORIG-1

SIRION
THERAPEUTICS

ZIRGAN (GANCICLOVIR
OPHTHALMIC GEL)0.15%

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/s/

VINAYAK B PAWAR
09/08/2009

JAMES L MCVEY
09/09/2009
I concur.

Product Quality Microbiology Review

July 29, 2009

NDA: 22-211/N-000

Drug Product Name

Proprietary: Ganciclovir

Non-proprietary: ganciclovir ophthalmic gel 0.15%

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
June 25, 2008	June 26, 2008	December 03, 2008	December 05, 2008

Applicant/Sponsor

Name: Sirion Therapeutics

Address: 9314 E Broadway Ave., Tampa, FL 33619

Representative: Christine, Miller, Pharm D, Sr. VP, Drug Development.

Telephone: 813-496-7328 ext 236

Name of Reviewer: Vinayak. B. Pawar, Ph.D.

Conclusion: The NDA is approvable pending resolution of the deficiency listed in section 3 of this review.

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original NDA
2. **SUBMISSION PROVIDES FOR:** Ganciclovir, ophthalmic gel
3. **MANUFACTURING SITE:** Allied Medical Products, Irvine, CA
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Ophthalmic Gel containing 0.15% Ganciclovir. b(4)
5. **METHOD(S) OF STERILIZATION:** _____
6. **PHARMACOLOGICAL CATEGORY:** Indicated for the topical treatment of acute herpetic keratitis.
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** The consult for review of this Original NDA 22-211 (electronic submission dated June 25, 2008) was submitted on December 3, 2008. This NDA from IND 75,762 was granted an orphan status for a product intended for the treatment of acute herpetic keratitis. In an IQA was filed by Linda NG on August 13, 2008 she states that the consult for this NDA was sent to NDMS staff by Lori Gorski on July 30, 2008. However, the request for this review was sent through an email dated December 3, 2008.

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Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – The NDA is approvable pending resolution of the deficiency listed in section 3 of this 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 drug product is formulated at 1.5 mg of Ganciclovir per gram of clear colorless gel with benzalkonium chloride as preservative. The bulk formulation is sterilized in

b(4)

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- B. **Brief Description of Microbiology Deficiencies** - None
 - C. **Assessment of Risk Due to Microbiology Deficiencies** – N/A

III. Administrative

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

11 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22211	ORIG 1	SIRION THERAPEUTICS	ZIRGAN (GANCICLOVIR OPHTHALMIC GEL)0.15%

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/s/

VINAYAK B PAWAR
08/04/2009

STEPHEN E LANGILLE
08/05/2009