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RESEARCH**

APPLICATION NUMBER:

22-315

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

04 May 2009

NDA: 22-315/N-000

Drug Product Name

Proprietary: Posurdex®
Non-proprietary: Dexamethasone biodegradable
Intravitreal implant.

Drug Product Priority Classification: Priority.

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
27 AUG 2008	28 AUG 2008	06 JAN 2009	06 JAN 2009
19 MAR 2009	20 MAR 2009	N/A	N/A

Applicant/Sponsor

Name: Allergan, Inc.
Address: 2525 Dupont Dr.
Irvine, CA 92612
Representative: Ms. Elizabeth Bancroft
Telephone: 714-246-4391

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

Conclusion: Recommend approval.

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA.
 2. **SUBMISSION PROVIDES FOR:** A new drug product.
 3. **MANUFACTURING SITE:**
Allergan Pharmaceuticals Ireland
Castlebar Rd.
Westport
County Mayo
Ireland
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Intravitreal implant; degradable polymer.
 - 0.35 mg and 0.7 mg.
 5. **METHOD(S) OF STERILIZATION:** _____
 6. **PHARMACOLOGICAL CATEGORY:** Indicated for the treatment of patients with macular edema secondary to central retinal vein occlusion or branch retinal vein occlusion.
- B. **SUPPORTING/RELATED DOCUMENTS:** None.
- C. **REMARKS:**

The NDA is submitted electronically in the CTD format.

An Initial Quality Assessment has not been completed as of 12 February 2009.

This reviewer forwarded the following information request to the OND Project Manager on 18 February 2009 for distribution to the applicant:

A sterility assurance review of NDA 22-315 is on-going. Please provide the following information, or reference to its location in the subject submission:

- Data sets demonstrating the ability of the foil pouch to serve as a _____ . Sterility testing of stability samples is not a suitable substitute for container closure integrity testing.
- Reviewer's Comment
The subject submission states, "In addition to the dose mapping qualification, a VD_{max} study will be performed on three batches. This study will substantiate the choice of 25 kGy as the minimum sterilization dose and will use the VD_{max}^{25} method as described in ISO 11137-2 to substantiate 25 kGy as the minimum sterilization dose (Page 8 of Module 3.2.P.3.5 of the subject submission)." In

b(4)

contrast to this statement, Module 3.2.P.2.5-1 contains a Final Report (#797040244) that summarizes validation of a _____ process using a sterilization dose of _____ which provides an SAL of _____.

- Provide the critical process parameters to be used in the sterilization process.
- Provide validation that the sterilization process delivers an SAL of _____
- Reviewer's Comment
The subject submission states that bioburden testing is performed on 10 units prior to _____ sterilization.
- Provide the acceptance criterion for pre-sterilization bioburden testing.

b(4)

The application was amended with responses to each of the above requests on 19 March 2009.

This reviewer forwarded an additional request for information directly to Elizabeth Bancroft (applicant representative) via electronic mail on 06 April 2009. Following is the comment and request for information:

Reference is made to NDA 22-315 and to the 19 March 2009 amendment response to the Agency's request for studies demonstrating package integrity.

The package integrity studies provided in the 19 March 2009 amendment do not adequately demonstrate that the primary packaging system provides an effective _____ . The method sensitivity of the bubble leak test (ASTM F 2096-04; *Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)*) is _____ μm (with an _____ probability). Since microbes are much smaller than _____ μm , the test does not adequately demonstrate a _____

b(4)

Please perform a more sensitive container closure integrity test on product sterilized with worst case parameters to demonstrate the effectiveness of the _____ . Reference is made to Section 5.2; _____ Properties of ISO 11607-1: 2006; *Packaging for Terminally Sterilized Medical Devices*.

b(4)

The testing described in this information request needs to be performed only once, and does not need to be included in the 3 year aging study.

A response was received by this reviewer electronically on 17 April 2009 with a commitment from the applicant to amend the NDA with the response.

All of the applicant responses to these microbiology information requests are summarized and reviewed in appropriate sections of this review.

File Name: N022315R1.doc

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – NDA 22-315/N-000 is recommended for approval on the basis of product quality microbiology.
- B. **Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – Not applicable.

II. Summary of Microbiology Assessments

- A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – _____
_____ **b(4)**
- 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** _____
John W. Metcalfe, Ph.D.
- B. **Endorsement Block** _____
Stephen Langille, Ph.D.
- C. **CC Block**
N/A

8 Page(s) Withheld

Trade Secret / Confidential (b4)

Draft Labeling (b4)

Draft Labeling (b5)

Deliberative Process (b5)

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

/s/

John Metcalfe
5/4/2009 11:31:35 AM
MICROBIOLOGIST

Stephen Langille
5/4/2009 01:44:27 PM
MICROBIOLOGIST