

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-239

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

25 August 2008

NDA: 22-239

Drug Product Name

Proprietary: Sumavel™ DosePro™
Non-proprietary: Sumatriptan Injection,
6 mg/0.5 mL

Drug Product Priority Classification: N/A

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
28 DEC 2007	31 DEC 2007	23 JAN 2008	30 JAN 2008
16 JUN 2008	17 JUN 2008	N/A	N/A
28 JUL 2008	29 JUL 2008	N/A	N/A

Applicant/Sponsor

Name: Zogenix, Inc.
Address: 5858 Horton St, Suite 455
Emeryville, CA 94608
Representative: Edward F. Smith
Telephone: 510-550-8325

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:**
 Patheon UK, Limited
 Kingfisher Drive
 Covingham, Swindon
 Wiltshire, SN3-5BZ
 United Kingdom
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Solution in needle free injector.
 - Subcutaneous injection.
 - 6 mg/0.5 mL.
 - 5. METHOD(S) OF STERILIZATION:** (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** Indicated for:
 - The acute treatment of migraine attacks with or without aura.
 - The acute treatment of cluster headache episodes.

- B. SUPPORTING/RELATED DOCUMENTS:**
- Type V DMF (b) (4)
 - Type V DMF (b) (4)

C. REMARKS:
 The submission is electronic in the CTD format.

A request for information was forwarded to the division project manager for dissemination to the applicant on 28 May 2008. The following information was requested from the applicant:

Provide the Reports (or identify their location in the NDA) that contain the testing methodology, acceptance criteria and data in support of each of the following:

- *Validation of the ability of the sterilizing filter to retain a microbial challenge from the drug product.*
- *Validation of the Sterilization/Depyrogenation of Containers, Closures, Equipment and Components.*

The NDA was amended with a response to these questions in a submission dated 16 June 2008. The amended information is summarized and reviewed in relevant sections of this review.

A second request for information was forwarded to the division project manager for dissemination to the applicant on 03 July 2008. The following information was requested from the applicant:

1. Although holding periods are provided in Table 3.2.P.3.5.4-1 for the time between the (b) (4), there is no information provided regarding the holding period between the start of (b) (4)

Further, it is stated in Module 3.2.P.3.5.3 of the subject submission that holding times will be validated as part of the commercial process validation for the manufacture of the final dosage form.

➤ Provide the maximum holding period between the start of (b) (4)

➤ Have the holding periods been validated? If so, provide these data.

2. Module 3.2.P.3.3.2.4 states that routine monitoring for aerobic and anaerobic microbes is performed using (b) (4)

The narrative references a document (not identified) which defines the monitoring frequencies, locations of monitoring and media used for this monitoring.

➤ Provide the environmental monitoring document which contains this information.

3. It is stated on Page 12 of 32 of Module 3.2.P.3.3 that pistons, interface seals and stoppers are sterilized (b) (4)

. These operating parameters are inconsistent with those that are referenced in Protocol V/1935/023/PQ (Module 3.2.P.3.5).

➤ Provide the sterilization operating parameters for pistons, interface seals and stoppers.

➤ Provide the load pattern number in Protocol V/1935/023/PQ for both pistons and interface seals.

The NDA was amended with a response to these questions in a submission dated 28 July 2008. The amended information is summarized and reviewed in relevant sections of this review.

File Name: N022239R1.doc

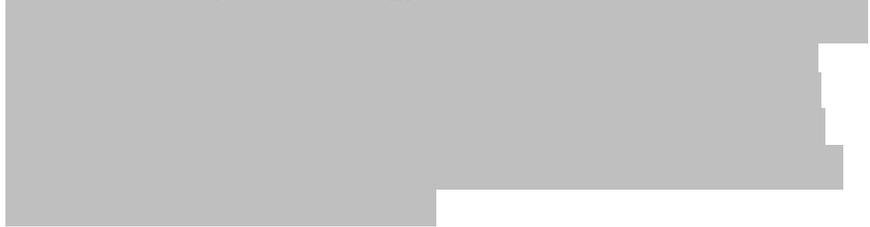
Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** – NDA 22-239 is recommended for approval on the basis of product quality microbiology.
- 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 -** (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

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this page is the manifestation of the electronic signature.**

/s/

John Metcalfe
8/27/2008 10:34:11 AM
MICROBIOLOGIST

Stephen Langille
8/27/2008 10:36:28 AM
MICROBIOLOGIST

MEMORANDUM



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

DATE: 3 July 2008

TO: Edward Smith, Zogenix

FROM: John W. Metcalfe, Ph.D.
Review Microbiologist
CDER/OPS/New Drug Microbiology Staff

THROUGH: Stephen Langille, Ph.D.
Senior Microbiology Reviewer
CDER/OPS/New Drug Microbiology Staff

SUBJECT: NDA 22-239: Request for Information.

1. Although holding periods are provided in Table 3.2.P.3.5.4-1 for the time between the start [REDACTED] (b) (4), there is no information provided regarding the holding period between the start of [REDACTED] (b) (4). Further, it is stated in Module 3.2.P.3.5.3 of the subject submission that holding times will be validated as part of the commercial process validation for the manufacture of the final dosage form.
 - Provide the maximum holding period between the start of [REDACTED] (b) (4).
 - Have the holding periods been validated? If so, provide these data.
2. Module 3.2.P.3.3.2.4 states that routine monitoring for aerobic and anaerobic microbes is performed using [REDACTED] (b) (4). The narrative references a document (not identified) which defines the monitoring frequencies, locations of monitoring and media used for this monitoring.
 - Provide the environmental monitoring document which contains this information.
3. It is stated on Page 12 of 32 of Module 3.2.P.3.3 that pistons, interface seals and stoppers are sterilized [REDACTED] (b) (4). These operating parameters are inconsistent with those that are referenced in Protocol V/1935/023/PQ (Module 3.2.P.3.5).
 - Provide the sterilization operating parameters for pistons, interface seals and stoppers.
 - Provide the load pattern number in Protocol V/1935/023/PQ for both pistons and interface seals.

MEMORANDUM

END

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/s/

John Metcalfe
7/7/2008 09:38:45 AM
MICROBIOLOGIST