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RESEARCH**

*APPLICATION NUMBER:*

**203340Orig1s000**

**MICROBIOLOGY REVIEW(S)**

# Product Quality Microbiology Review

June 28, 2012

**NDA: 203-340**

**Drug Product Name**

**Proprietary:** Nymalize

**Non-proprietary:** Nimodipine (-isopropyl 2-methoxyethyl 1,4-dihydro-2,6-dimethyl)

**Review Number: 1**

**Dates of Submission(s) Covered by this Review**

Submit	Received	Review Request	Assigned to Reviewer
18 NOV 2011	18 NOV 2011	8 MAR 2012	12 MAR 2012
20 MAR 2012	30 APR 2012	N/A	N/A
22 JUN 2012	22 JUN 2012	N/A	N/A

**Applicant/Sponsor**

**Name:** Arbor Pharmaceuticals

**Address:** 980 Hammond Drive, Suite 1250, Atlanta, GA 30328

**Representative:** Allison Lowry; Director, Quality and Regulatory Affairs

**Telephone:** 678-334-2428

**Name of Reviewer:** Erika Pfeiler, Ph.D.

**Conclusion:** Recommend approval

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## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** 505(b)(2)
  2. **SUBMISSION PROVIDES FOR:** New oral solution formulation, drug product has previously been marketed in gelcaps.
  3. **MANUFACTURING SITE:** Importfab  
50 Hymus Blvd.  
Pointe-Claire QC, Canada H9R 1C9
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
    - Oral solution (can be administered nasogastrically)
    - 60 mg/20 ml
    - Packaged in 16 oz. HDPE bottles with (b) (4) caps (b) (4) HDPE unit-dose cups with (b) (4) lids.
  5. **METHOD(S) OF STERILIZATION:** Non-sterile drug product
  6. **PHARMACOLOGICAL CATEGORY:** Treatment of subarachnoid hemorrhage
- B. **SUPPORTING/RELATED DOCUMENTS:** N/A
- C. **REMARKS:** This submission was in the eCTD format.

The following comments were included in an information request sent to the applicant on March 20, 2012. Responses were received on April 30, 2012 and June 27, 2012 and were incorporated into the relevant sections of the review.

- Section 3.2.P.2.5, Microbiological Attributes, states that an antimicrobial effectiveness testing report for the proposed formulation is provided in the application, but the report is not present. Please provide the report. Additionally, the sponsor should validate antimicrobial effectiveness on a batch containing at or below the lowest specified methylparaben concentration and provide the data for review.
- The application should provide test methods and acceptance criteria to demonstrate the product is free of the objectionable microorganism *Burkholderia cepacia*. We recommend that potential sources are examined and sampled as process controls, and these may include raw materials and the manufacturing environment. A risk assessment for this species in the product and raw materials is recommended to develop sampling procedures and acceptance criteria. Your test method should be validated and a discussion of those methods should be provided. Test methods validation should address multiple strains of the species

and cells that are acclimated to the environments (e.g., warm or cold water) that may be tested.

- The application should include specifications for the (b) (4) ml cup presentation of the drug product. Please provide these specifications.

**filename:** N203340R1.doc

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## **Executive Summary**

### **I. Recommendations**

- A. Recommendation on Approvability** – Recommend approval on the basis of product quality microbiology
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – N/A

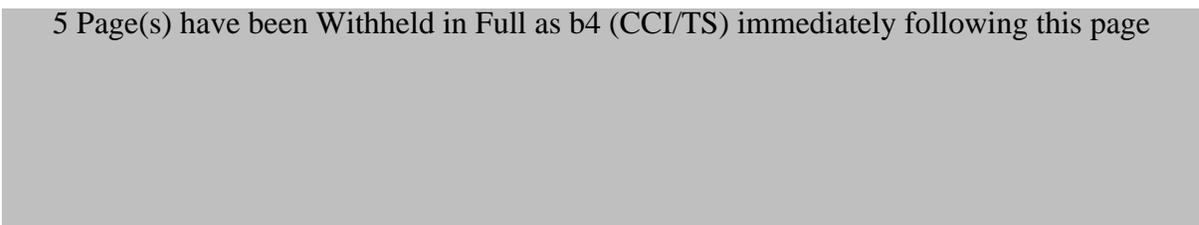
### **II. Summary of Microbiology Assessments**

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – Product is a (b) (4) oral solution (b) (4)
- B. Brief Description of Microbiology Deficiencies** – N/A
- C. Assessment of Risk Due to Microbiology Deficiencies** – N/A

### **III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Erika Pfeiler, Ph.D.
- B. Endorsement Block** \_\_\_\_\_  
Bryan Riley, Ph.D.  
Microbiology Team Leader
- C. CC Block**  
N/A

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ERIKA A PFEILER  
06/28/2012

BRYAN S RILEY  
06/28/2012  
I concur.