

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-159**

**MICROBIOLOGY REVIEW**

# Product Quality Microbiology Review

30-January-2008

**NDA:**

22-159-BZ

22-159-AI

**Drug Product Name**

**Proprietary:** NV-101 Injection 0.4 mg

**Non-proprietary:** Phenyltolamine mesylate

**Drug Product Priority Classification:** Standard

**Review Number:** 2

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

NDA	Letter	Stamp	Review Request	Assigned to Reviewer
22-159-BZ	12/20/07	12/20/07	N/A	N/A
22-159-AI	1/23/08	1/23/08	?	?

## Submission History (for amendments only):

Submission Date(s)	Microbiology Review #	Review Date(s)
4/9/07	1	11/19/07

## Applicant/Sponsor

**Name:** Novalar Pharmaceuticals, Inc.

**Address:** 12555 High Bluff Dr,  
Suite 300  
San Diego, CA

**Representative:** Laura A. Navalta

**Telephone:** (856) 436-1130

**Name of Reviewer:** Stephen E. Langille, Ph.D.

**Conclusion:** Recommended for approval

---

## Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Amendment to an original NDA
2. **SUBMISSION PROVIDES FOR:** Sterility assurance package for a New Drug Application
3. **MANUFACTURING SITE:** Novocol Pharmaceuticals of Canada, Inc.  
36 Wolseley Court  
Cambridge, Ontario  
Canada
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
- Sterile solution
  - Intraoral submucosal injection
  - 0.4 mg/1.7 mL
  - Glass dental cartridges
5. **METHOD(S) OF STERILIZATION:** \_\_\_\_\_ **b(4)**
6. **PHARMACOLOGICAL CATEGORY:** Reversal of dental anesthetic
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** The first review of NDA 22-159 was completed on November 19, 2007. The applicant provided additional information in the form of electronic amendments on December 20, 2007. A teleconference was held with the applicant on January 18, 2008 to clarify the information requirements of the Agency and additional information was provided by the applicant on January 23, 2008. The NDA was submitted in eCTD format.

filename: N022159R2.doc

---

**Executive Summary**

**I. Recommendations**

- A. Recommendation on Approvability -**  
NDA 22-159 is recommended for approval from the standpoint 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 -**  
The drug product will be \_\_\_\_\_ processed and packaged in sterile glass dental cartridges with rubber stoppers and tip caps.
- B. Brief Description of Microbiology Deficiencies -**  
No deficiencies were identified based upon the information provided.
- C. Assessment of Risk Due to Microbiology Deficiencies -**  
Not applicable

**b(4)**

**III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Stephen E. Langille, Ph.D.
- B. Endorsement Block** \_\_\_\_\_  
James McVey  
Microbiology Team Leader
- C. CC Block**  
N/A

9   Page(s) Withheld

  X   Trade Secret / Confidential (b4)

       Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)



---

## Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original NDA
  2. **SUBMISSION PROVIDES FOR:** Sterility assurance package for a New Drug Application
  3. **MANUFACTURING SITE:** Novocol Pharmaceuticals of Canada, Inc.  
36 Wolseley Court  
Cambridge, Ontario  
Canada
  4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
    - Sterile solution
    - Intraoral submucosal injection
    - 0.4 mg/1.7 mL
    - Glass dental cartridges
  5. **METHOD(S) OF STERILIZATION:** — fill b(4)
  6. **PHARMACOLOGICAL CATEGORY:** Reversal of dental anesthetic
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** The submission was submitted electronically and arranged in CTD format. An initial quality assessment was entered into DFS on May 25, 2007.

**filename:** N022159R1.doc

# Product Quality Microbiology Review

13-November-2007

**NDA:** 22-159

**Drug Product Name**

**Proprietary:** NV-101 Injection 0.4 mg

**Non-proprietary:** Phenyltolamine mesylate

**Drug Product Priority Classification:** Standard

**Review Number:** 1

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

Letter	Stamp	Review Request	Assigned to Reviewer
4/9/07	4/9/07	5/29/07	5/29/07

**Submission History (for amendments only):** Not applicable

**Applicant/Sponsor**

**Name:** Novalar Pharmaceuticals, Inc.

**Address:** 12555 High Bluff Dr,  
Suite 300  
San Diego, CA

**Representative:** Laura A. Navalta

**Telephone:** (856) 436-1130

**Name of Reviewer:** Stephen E. Langille, Ph.D.

**Conclusion:** Approvable pending revision

---

**Executive Summary**

**I. Recommendations**

- A. Recommendation on Approvability -**  
NDA 22-159 is approvable pending the resolution of microbiology deficiencies.
- 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 -**  
The drug product will be \_\_\_\_\_ processed and packaged in sterile glass dental cartridges with rubber stoppers and tip caps. b(4)
- B. Brief Description of Microbiology Deficiencies -**  
The applicant failed to provide adequate information regarding:
  - Environmental monitoring
  - Hold times
  - Sterilization \_\_\_\_\_ of equipment and components
  - Media fills
  - Endotoxin limits
- C. Assessment of Risk Due to Microbiology Deficiencies -**  
Failure to address the microbiology deficiencies could result in an increased risk of microbial and/or endotoxin contamination of the drug product.

**III. Administrative**

- A. Reviewer's Signature** \_\_\_\_\_  
Stephen E. Langille, Ph.D.
- B. Endorsement Block** \_\_\_\_\_  
David Hussong, Ph.D.  
Associate Directory for New Drug Microbiology
- C. CC Block**  
N/A

14 Page(s) Withheld

X 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/

-----  
Stephen Langille

11/19/2007 11:25:08 AM

MICROBIOLOGIST

Review of NV-101 - Novalar Pharmaceuticals. \_\_\_\_\_ dental  
cartridge.

b(4)

David Hussong

11/19/2007 11:27:49 AM

MICROBIOLOGIST

I concur with the reviewer's conclusions.