CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-010

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

11 JANUARY 2006

NDA: 22-010

Drug Product Name
Proprietary: Septocaine ——
Non-proprietary: Articaine hydrochloride 4%, Epinephrine ——— mg/mL
Drug Product Priority Classification: S

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
9/29/2005	9/30/2005	12/8/2005	12/12/2005

Submission History (for amendments only): N/A

Applicant/Sponsor
Name: Deproco Inc.
Address: 245-C Quigley Blvd, New Castle DE 19720
Representative: Wayne H. Matelski (US Agent for Deproco)
Telephone: 202-857-6340

Name of Reviewer: Bryan S. Riley, Ph.D.

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** NDA Resubmission

2. **SUBMISSION PROVIDES FOR:** New formulation of an approved drug product.

3. **MANUFACTURING SITE:** Novocol Pharmaceutical
25 Wolseley Court
Cambridge, Ontario
Canada N1R 6X3

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile aqueous solution (1.7 mL) in a glass cartridge for dental injection, Articaine HCl 40 mg/mL and Epinephrine — mg/mL.

5. **METHOD(S) OF STERILIZATION:** —

6. **PHARMACOLOGICAL CATEGORY:** Dental Anesthetic

B. **SUPPORTING/RELATED DOCUMENTS:** Product Quality Microbiology Review of NDA 20-971/SCM-005 (dated 27 April 2004).

C. **REMARKS:** This submission proposes a new strength of an approved drug product (NDA 20-971). The drug product composition in this submission was part of the original submission (along with the approved drug Septocaine —), but was withdrawn prior to approval. This submission was originally submitted as a supplement to the approved NDA, but it was changed to a new NDA for administrative reasons. The manufacturing process (including the terminal moist heat sterilization process) is identical to the approved process for Septocaine — at the same manufacturing site. The difference between Septocaine — and Septocaine — is the concentration of epinephrine in the drug product.

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Executive Summary

I. Recommendations

A. Recommendation on Approvability – This submission 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 – The drug product is terminally sterilized using moist heat.

B. Brief Description of Microbiology Deficiencies – N/A

C. Assessment of Risk Due to Microbiology Deficiencies – N/A

III. Administrative

A. Reviewer's Signature _____
Bryan S. Riley, Ph.D.

B. Endorsement Block _____
Stephen Langille, Ph.D.

C. CC Block
N/A

Appears This Way
On Original

Product Quality Microbiology Assessment

A. ——————— STERILIZATION

[redacted]

B. **OTHER —— STERILIZATION PROCESSES** – N/A

C. —— **MANUFACTURING PROCESS** – N/A

D. MISCELLANEOUS

D.1. Container Closure Integrity Validation – The container closure integrity was validated as part of NDA 20-971.

D.2. Preservative Effectiveness – N/A

D.3. Evidence of Formal Written Procedures – SOPs for the procedures used for the manufacture and testing of the drug product were referenced in the submission.

ADEQUATE

E. MAINTENANCE OF MICROBIOLOGICAL CONTROL AND QUALITY: STABILITY CONSIDERATIONS

E.1. Container Closure Integrity – Sterility testing is performed at ——

E.2. Pyrogen/Endotoxin Testing – Endotoxin testing is performed at ——

E.3. Microbial Limits Testing – N/A

ADEQUATE

F. RELEASE TESTS

F.1. Pyrogen/Endotoxin Testing – Endotoxin testing is performed on the drug product using a —— method. The endotoxin limit is NMT — EU/mg Articaine HCl (no change from NDA 20-971). — units are tested from each batch.

F.2. Sterility Test – A ———— method is used for sterility testing of the drug product (no change from NDA 20-971). — units are tested from each ——

F.3. Microbial Limits Testing – N/A

ADEQUATE

G. LABELING – N/A

H. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS – N/A