

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-028

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

15 JAN 2008

NDA: 22-028/N-000(AC)
22-028/N-000 (BI)

Drug Product Name

Proprietary:

Cosyntropin Injection 0.25mg/ml

Non-proprietary:

Cosyntropin Injection 0.25mg/ml

Drug Product Priority Classification: S

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
(AC) 20 AUG 2007	21 AUG 2007	04 SEP 2007	29 AUG 2007
(BI) 06 DEC 2007	07 DEC 2007	11 DEC 2007	14 DEC 2007

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
03 FEB 2006	1	04 DEC 2006

Applicant/Sponsor

Name:

SANDOZ CANADA INC.

Address:

145 Jules Leger Street

Boucherville (QC)

CANADA J4B 7K8

Representative:

Beth Brannan

Director, Regulatory Affairs

(U.S. Representative)

Telephone:

303-438-4237

Name of Reviewer:

Robert J. Mello, Ph.D.

Conclusion:

The application is recommended
for approval from microbiology
product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUBMISSION:** Amendment, New Drug Application (505b2)

2. **SUBMISSION PROVIDES FOR:** Request to market a new drug.

3. **MANUFACTURING SITE:** Sandoz Canada Inc

145 Jules-Leger Street
Boucherville (Quebec)
CANADA

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile injectable, intravenous, 0.25mg/ml, 1ml in 10ml vials **b(4)**

5. **METHOD(S) OF STERILIZATION:** **b(4)**

6. **PHARMACOLOGICAL CATEGORY:** Adrenal/ACTH Diagnostic agent for adrenocortical insufficiency.

B. **SUPPORTING/RELATED DOCUMENTS:** N/A

C. **REMARKS:**

- The (AC) submission is an NDA re-submission response to the Agency "AE" letter dated 06 DEC 2006.
- The (BI) submission is a response to this reviewer's information request dated 12 OCT 2007.
- The submissions (AC; 1 volume, brown binder. BI; 1 volume white binder) are paper desk copies not in CTD format. The (BI) amendment was also transmitted electronically to this reviewer as a PDF file.

filename: N022028N000R2.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability – Recommend Approval**
- 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 - None**
- C. Assessment of Risk Due to Microbiology Deficiencies – N/A**

III. Administrative

- A. Reviewer's Signature** _____
Robert J. Mello, Ph.D.

- B. Endorsement Block** _____
Bryan S. Riley, Ph.D.

- C. CC Block**
In DFS

6 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

 Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

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

/s/

Robert Mello
1/16/2008 03:05:45 PM
MICROBIOLOGIST

Recommend Approval

Bryan Riley
1/17/2008 08:06:47 AM
MICROBIOLOGIST
I concur with this review.

Product Quality Microbiology Review

04 DEC 2006

NDA:

22-028/N-000

Drug Product Name

Proprietary:

Injection 0.25mg/ml

Non-proprietary:

Cosyntropin Injection

Drug Product Priority Classification: S

b(4)

Review Number:

1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
03 FEB 2006	06 FEB 2006	24 FEB 2006	27 FEB 2006

Submission History (for amendments only): N/A

Applicant/Sponsor

Name:

SANDOZ CANADA INC.

Address:

145 Jules Leger Street

Boucherville (QC)

CANADA J4B 7K8

Representative:

Beth Brannan

Director, Regulatory Affairs

(U.S. Representative)

Telephone:

303-438-4237

Name of Reviewer:

Robert J. Mello, Ph.D.

Conclusion:

The application is approvable from a microbiology product quality standpoint pending receipt of additional information.

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** New Drug Application (505b2)
2. **SUBMISSION PROVIDES FOR:** Request to market a new drug
3. **MANUFACTURING SITE:** Sandoz Canada Inc
145 Jules-Leger Street
Boucherville (Quebec)
CANADA
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile injectable, intravenous, 0.25mg/ml, 1ml in a 1ml vial **b(4)**
5. **METHOD(S) OF STERILIZATION:** _____ **b(4)**
6. **PHARMACOLOGICAL CATEGORY:** Adrenal/ACTH Diagnostic agent for adrenocortical insufficiency.

B. **SUPPORTING/RELATED DOCUMENTS:** N/A

C. **REMARKS:** This was a paper submission consisting of six (6) white "Microbiology Section" jackets labeled as follows:

- Module 3, Volume 1.3
- Module 3, Volume 1.4
- Module 3, Volume 1.5
- Module 3, Volume 1.6
- Module 3, Volume 1.7
- Module 3, Volume 1.8

Filename: N022028N000R1.doc

Executive Summary

I. Recommendations

- A. **Recommendation on Approvability** - The application is approvable from a microbiology product quality standpoint pending receipt of additional information.
- 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** -

- Information provided on equipment identification and use in the manufacture of the drug product was inconsistent with the process performance testing submitted
- Data on _____ reduction from stoppers was not provided
- Container/closure studies did not include all cappers
- Duration of filling was not clearly specified
- Sterilization cycle parameters were inconsistently stated
- No justification was provided for the worst case sterilization/_____ loads used in revalidation studies
- Media fill validations may not reflect actual production operations

b(4)

- C. **Assessment of Risk Due to Microbiology Deficiencies** - Product _____ may be compromised by inadequate or flawed process validation studies and data.

b(4)

III. Administrative

- A. **Reviewer's Signature** _____
Robert J. Mello, Ph.D.
- B. **Endorsement Block** _____
Bryan S. Riley, Ph.D.
- C. **CC Block**
In DFS

24 Page(s) Withheld

☒ Trade Secret / Confidential (b4)

☐ Draft Labeling (b4)

☐ Draft Labeling (b5)

☐ Deliberative Process (b5)

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/s/

Robert Mello
12/4/2006 01:28:47 PM
MICROBIOLOGIST

Approvable pending receipt of additional information

Bryan Riley
12/4/2006 01:37:29 PM
MICROBIOLOGIST