# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPROVAL PACKAGE FOR:

## APPLICATION NUMBER

## 21-256

# Microbiology Review(s)

# Product Quality Microbiology Review
## Review for HFD 180
### 8-April-2004

| | |
|---|---|
| **NDA:** | 21-256/N-000-BI |
| **Drug Product Name:** | [redacted] (formerly [redacted]) |
| **Non-proprietary Drug Product Classification:** | Human Secretin |
| **Review Number:** | 4 |
| **Subject of this Review** | |
| **Submission Date:** | April 7, 2004 |
| **Receipt Date:** | April 7, 2004 |
| **Consult Date:** | April 7, 2004 |
| **Date Assigned for Review:** | April 7, 2004 |
| **Submission History (for amendments only)** | |
| **Date(s) of Previous Submission(s):** | October 10, 2003 (21-256/N-000-AZ)<br>March 26, 2004 (21-256/N-000-BI) |
| **Date(s) of Previous Micro Review(s):** | March 11, 2004 (21-256/N-000-AZ)<br>April 2, 2004 (21-256/N-000-BI) |
| **Applicant/Sponsor** | |
| **Name:** | ChiRhoClin, Inc. |
| **Address:** | 4000 Blackburn Lane,<br>Suite 270<br>Burtonsville, MD 20866-6129 |
| **Representative:** | Edward D. Purich |
| **Telephone:** | 301-476-8388 |

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

**Conclusion:** Recommended for approval. The comment on p. 9 of this review should be provided to the Sponsor.

# Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** NDA

2. **SUPPLEMENTS PROVIDE FOR:** Not applicable

3. **MANUFACTURING SITE:** Bell-More Labs, Inc.
4030 Gill Ave.
Hampstead, MD 21074-0179

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

- Intravenous Injection
- Lyophilized powder
- 16 ug

5. **METHOD(S) OF STERILIZATION:** —

6. **PHARMACOLOGICAL CATEGORY:** Diagnosis of pancreatic disease

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** NDA 21-256 was originally submitted on 3/16/00 and was judged to be non-fileable. The NDA was resubmitted on 6/14/01. The Microbiology Review was done by Dr. Neal Sweeney and the NDA was recommended for approval from the standpoint of product quality microbiology. NDA 21-256/N-000 AZ was submitted on Oct. 10, 2003 in response to the CMC action letter and to report a change in the manufacturing site (Bell-More Labs, Inc.) for —. The first microbiology review for production at Bell-More Labs was completed on March 11, 2004. A response to the deficiencies listed in the March 11 review was provided to the Agency on March 26, 2004. The second microbiology review was completed on April 2, 2004. Dr. Edward D. Purich of ChiRhoClin and — Bell-More Labs were contacted on April 8, 2004 regarding CMC issues at the Bell-More Labs manufacturing facility.

**filename:** c:\reviews\21-256r3.doc

# Executive Summary

## I. Recommendations

**A. Recommendation on Approvability -**
NDA 21-256/N-000-BI is recommended for approval. The comment on p. 9 of this review should be provided to the Sponsor.

**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 -**
— will be — at Bell-More Labs, Inc. in Hampstead, Maryland. The manufacturing site for the previous application was —.

**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

## III. Administrative

**A. Reviewer's Signature** /S/

**B. Endorsement Block**
Stephen E. Langille, Ph.D.
Peter Cooney, Ph.D.

**C. CC Block**
In DFS

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/s/

Stephen Langille
4/8/04 02:09:59 PM
MICROBIOLOGIST

Peter Cooney
4/8/04 02:32:26 PM
MICROBIOLOGIST

# Product Quality Microbiology Review
## Review for HFD 180
### 26-March-2004

| | |
|---|---|
| **NDA:** | 21-256/N-000-BI |
| **Drug Product Name:** | — (formerly — ) |
| **Non-proprietary Drug Product Classification:** | Human Secretin |
| **Review Number:** | 3 |
| **Subject of this Review** | |
| **Submission Date:** | March 17, 2004 |
| **Receipt Date:** | March 17, 2004 |
| **Consult Date:** | March 22, 2004 |
| **Date Assigned for Review:** | March 22, 2004 |
| **Submission History (for amendments only)** | |
| **Date(s) of Previous Submission(s):** | October 10, 2003 |
| **Date(s) of Previous Micro Review(s):** | March 11, 2004 |
| **Applicant/Sponsor** | |
| **Name:** | ChiRhoClin, Inc. |
| **Address:** | 4000 Blackburn Lane,<br>Suite 270<br>Burtonsville, MD 20866-6129 |
| **Representative:** | Edward D. Purich |
| **Telephone:** | 301-476-8388 |
| **Name of Reviewer:** | Stephen E. Langille, Ph.D. |
| **Conclusion:** | Approvable pending revision |

# Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** NDA

2. **SUPPLEMENTS PROVIDE FOR:** Not applicable

3. **MANUFACTURING SITE:** Bell-More Labs, Inc.
4030 Gill Ave.
Hampstead, MD 21074-0179

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

- Intravenous Injection
- Lyophilized powder
- 16 ug

5. **METHOD(S) OF STERILIZATION:** —

6. **PHARMACOLOGICAL CATEGORY:** Diagnosis of pancreatic disease

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** NDA 21-256 was originally submitted on 3/16/00 and was judged to be non-fileable. The NDA was resubmitted on 6/14/01. The Microbiology Review was done by Dr. Neal Sweeney and the NDA was recommended for approval from the standpoint of product quality microbiology. NDA 21-256/N-000 AZ was submitted on Oct. 10, 2003 in response to the CMC action letter and to report a change in the manufacturing site (Bell-More Labs, Inc.) for —. The Applicant has sought approval for the production of a related product, SecreFlo, (21-136, ). The first microbiology review was completed on March 11, 2004.

**filename:** c:\reviews\21-256r2.doc

# Executive Summary

## I. Recommendations

**A. Recommendation on Approvability -**
NDA 21-256/N-000-BI is approvable pending the resolution of microbiological 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 -**
— will be — at Bell-More Labs, Inc. in Hampstead, Maryland. The manufacturing site for the previous application was —

**B. Brief Description of Microbiology Deficiencies -**
The Applicant failed to provide adequate information regarding:

- —
- —
- —

**C. Assessment of Risk Due to Microbiology Deficiencies -**
Failure to address the microbiology deficiencies could result in the contamination of the drug product —

## III. Administrative

/S/

**A. Reviewer's Signature** _____

**B. Endorsement Block**
Stephen E. Langille, Ph.D.
Peter Cooney, Ph.D.

**C. CC Block**
In DFS

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/s/

Stephen Langille
4/2/04 12:32:57 PM
MICROBIOLOGIST

Peter Cooney
4/2/04 04:18:14 PM
MICROBIOLOGIST

# Product Quality Microbiology Review
## Review for HFD 180
### 1-March-2004

| | |
|---|---|
| **NDA:** | 21-256/N-000AZ |
| **Drug Product Name:** | — |
| **Non-proprietary Drug Product Classification:** | Human Secretin |
| **Review Number:** | 2 |
| **Subject of this Review** | |
| **Submission Date:** | October 10, 2003 |
| **Receipt Date:** | October 11, 2003 |
| **Consult Date:** | November 13, 2003 |
| **Date Assigned for Review:** | January 12, 2004 |
| **Submission History (for amendments only)** | |
| **Date(s) of Previous Submission(s):** | June 14, 2001 |
| **Date(s) of Previous Micro Review(s):** | November 6, 2001 |
| **Applicant/Sponsor** | |
| **Name:** | ChiRhoClin, Inc. |
| **Address:** | 4000 Blackburn Lane,<br>Suite 270<br>Burtonsville, MD 20866-6129 |
| **Representative:** | Edward D. Purch |
| **Telephone:** | 301-476-8388 |
| **Name of Reviewer:** | Stephen E. Langille, Ph.D. |
| **Conclusion:** | Approvable pending revision |

# Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** NDA

2. **SUPPLEMENTS PROVIDE FOR:** Not applicable

3. **MANUFACTURING SITE:** Bell-More Labs, Inc.
4030 Gill Ave.
Hampstead, MD 21074-0179

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**

- Intravenous Injection
- Lyophilized powder
- 16 ug

5. **METHOD(S) OF STERILIZATION:** —

6. **PHARMACOLOGICAL CATEGORY:** Diagnosis of pancreatic disease

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** NDA 21-256 was originally submitted on 3/16/00 and was determined to be non-fileable. The NDA was resubmitted on 6/14/01. The Microbiology Review was done by Dr. Neal Sweeney and the NDA was recommended for approval from the standpoint of product quality microbiology. NDA 21-256/N-000 AZ was submitted on Oct. 10, 2003 in response to the CMC action letter and to report a change in the manufacturing site (Bell-More Labs, Inc.) for — The Applicant has sought approval for the production of a related product, SecreFlo, (21-136)

**filename:** c:\reviews\21-256r1.doc

# Executive Summary

## I. Recommendations

### A. Recommendation on Approvability -

NDA 21-256/N-000 AZ is approvable pending the revision of microbiological 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 -

will be at Bell-More Labs, Inc. in Hampstead, Maryland. The manufacturing site for the previous application was

### B. Brief Description of Microbiology Deficiencies -

The Applicant failed to provide:

- 
- 
- 
- 
- 

### C. Assessment of Risk Due to Microbiology Deficiencies -

Failure to address the microbiology deficiencies will result in a high risk of drug product contamination

## III. Administrative

/S/

**A. Reviewer's Signature** _____

**B. Endorsement Block**

Stephen E. Langille, Ph.D.
Peter Cooney, Ph.D.

**C. CC Block**

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/s/
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Stephen Langille
3/11/04 08:10:30 AM
MICROBIOLOGIST

Peter Cooney
3/12/04 10:15:27 AM
MICROBIOLOGIST

**REVIEW FOR HFD-180**

**OFFICE OF NEW DRUG CHEMISTRY**
**MICROBIOLOGY STAFF HFD-805**
**Microbiologist's Review #1 of NDA 21-256**

**October 19, 2001**

**A. 1. APPLICATION NUMBER:** 21-256

**APPLICANT:** ChiRhoClin, Inc.
15500 Gallaudet Avenue
Silver Spring, MD 20905-4176
(Tel) 301-384-1554
(Fax) 301-384-1565

**2. PRODUCT NAME:** Synthetic Human Secretin

**3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:** Sterile, lyophilized synthetic human secretin (16 µg/vial) in 10 mL — vials. For intravenous administration.

**4. METHODS OF STERILIZATION:** —

**5. PHARMALOGICAL CATAGORY and/or PRINCIPLE INDICATION:** Gastrointestinal peptide hormone indicated (proposed) for diagnosis of pancreatic exocrine — diagnosis of gastrinoma, and facilitation of — during ERCP.

**6. DRUG PRIORITY CLASSIFICATION:** P

**B. 1. DATE OF INITIAL SUBMISSION:** 6/14/01 (Resubmission)

**2. DATE OF CONSULT:** 6/20/01

**3. ASSIGNED FOR REVIEW:** 7/26/01

**4. RELATED DOCUMENTS:** NDA 21-136, NDA 21-209, and DMF [redacted] (DMF submitted Sept. 1999 and amended Feb. 14, 2000 and May 8, 2000)

**E. REMARKS:** NDA 21-256 was originally submitted 3/16/00 and was determined to be non-fileable, and a Refuse to File letter was issued 5/11/00. The NDA was resubmitted 6/14/01.

## D. CONCLUSIONS:

The submission is recommended for approval for microbiology issues concerning sterility assurance. Specific comments are provided in section "E. REVIEW NOTES".

/S/

Neal Sweeney, Ph.D.

cc: NDA 21-256
HFM-180/Division File
HFM-180/A. Shaw/ M. McNeil
HFD-805/Consult File/N. Sweeney

Drafted by: N. Sweeney, October 19, 2001
R/D initialed by P. Cooney, October 19, 2001

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/s/
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Neal Sweeney
11/6/01 02:32:44 PM
MICROBIOLOGIST

Peter Cooney
11/6/01 02:48:46 PM
MICROBIOLOGIST

**See CMC review dated 3/18/04, pg. 19**

APPEARS THIS WAY
ON ORIGINAL

**See CMC review dated 3/18/04**

APPEARS THIS WAY
ON ORIGINAL

**A Statistical Review (stability) was not necessary for this application.**

RB 6/6/04

APPEARS THIS WAY
ON ORIGINAL