CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

021746Orig1s000

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

06 February 2012

NDA: **21-746/N-000**

Drug Product Name
Proprietary: **Surfaxin®**
Non-proprietary: lucinactant

Review Number: 5

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
September 02, 2011	September 06, 2011	November 02, 2011	November 03, 2011

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
April 13, 2004	1	January 18, 2005
October 5, 2005	2	March 6, 2006
October 31, 2007	3	April 21, 2008
October 17, 2008	4	March 09, 2009

Applicant/Sponsor
Name: Discovery Laboratories, Inc.
Address: Warrington, PA
Representative: Marjorie Hurley, Pharm D.
Telephone: 215-488-9360

Name of Reviewer: Denise A. Miller

Conclusion: The NDA is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Resubmitted New Drug Application

2. SUBMISSION PROVIDES FOR: The formulation and filling

3. MANUFACTURING SITE: Totowa, NJ

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

- Dosage Form: Sterile liquid
- Route of Administration: intra-tracheal
- Strength/Potency: 30mg/mL, 8.5mL/vial

5. METHOD (S) OF STERILIZATION: Sterile filtration (b) (4) (b) (4)

6. PHARMACOLOGICAL CATEGORY: Treatment of Respiratory Distress Syndrome

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: The consult requests a review of the fifth submission of NDA 21-746 for the drug product Surfaxin®.

filename: N021746N000R5.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The application is recommended for approval.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug product is manufactured (b) (4)

B. Brief Description of Microbiology Deficiencies – None

C. Assessment of Risk Due to Microbiology Deficiencies – NA

III. Administrative

A. Reviewer's Signature _____

Denise A. Miller
Reviewer, OPS/NDMS

B. Endorsement Block _____

Stephen E. Langille, Ph.D.
Senior Microbiologist, OPS/NDMS

C. CC Block

NA

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/s/

DENISE A MILLER
02/07/2012

STEPHEN E LANGILLE
02/07/2012

Product Quality Microbiology Review

March 09, 2009

NDA: **21-746 AZ**

Drug Product Name
Proprietary: **Surfaxin®**
Non-proprietary: lucinactant

Review Number: 4

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
October 17, 2008	October 18, 2008	November 5, 2008	November 6, 2008

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
April 13, 2004	1	January 18, 2005
October 5, 2005	2	March 6, 2006
October 31, 2007	3	April 21, 2008

Applicant/Sponsor
Name: Discovery Laboratories, Inc.
Address: Warrington, PA
Representative: Marjorie Hurley, Pharm D.
Telephone: 215-488-9360

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: The NDA is recommended for approval from microbiology product quality standpoint.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: NA

2. APPLICATION PROVIDES FOR: Resubmitted New Drug Application

3. MANUFACTURING SITE: Totowa, NJ

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 30mg/mL, 8.5mL/vial, intratracheal

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

6. PHARMACOLOGICAL CATEGORY: Treatment of Respiratory Distress Syndrome

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: The consult requests a review of the fourth submission of NDA 21-746 for the drug product Surfaxin®. Three volumes of the application containing the responses to deficiencies cited in Review # 3 were submitted for review. Since Discovery assumed direct control of Laureate Pharma, during the last review cycle, it no longer maintains DMF (b) (4). No IQA was posted for the resubmission.

filename: **C:\my documents\review\NDA\N021746R4**

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The application is recommended for approval.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug product is manufactured (b) (4)

B. Brief Description of Microbiology Deficiencies – See section H.

C. Assessment of Risk Due to Microbiology Deficiencies – See section H.

III. Administrative

A. Reviewer's Signature _____

Vinayak B. Pawar, Ph.D.
Reviewer, CDER/OPS/NDMS

B. Endorsement Block _____

David Hussong, Ph.D.
Assoc. Director., CDER/OPS/NDMS

C. CC Block
NA

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/s/

Vinayak Pawar
3/24/2009 04:38:22 PM
MICROBIOLOGIST

The NDA is recommended for approval.

David Hussong
3/24/2009 05:17:16 PM
MICROBIOLOGIST
I concur with the reviewer's recommendation for approval of this new drug application.

Product Quality Microbiology Review

21 April 2008

NDA: **21-746 Resubmission**

Drug Product Name
Proprietary: **Surfaxin®**
Non-proprietary: lucinactant
Drug Product Priority Classification: S1

Review Number: 3

Dates of Submission(s) Covered by this Review

Letter	Stamp	Review Request	Assigned to Reviewer
October 31, 2007	November 2, 2007	December 4, 2007	December 11, 2007

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
April 13, 2004	1	January 18, 2005
October 5, 2005	2	March 6, 2006

Applicant/Sponsor

Name:	Discovery Laboratories, Inc.
Address:	Warrington, PA
Representative:	Marjorie Hurley, Pharm D.
Telephone:	215-488-9360

Name of Reviewer: Vinayak B. Pawar, Ph.D.

Conclusion: The application is approvable from microbiology standpoint pending resolution of the issues cited in Section H of this review.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: NA

2. APPLICATION PROVIDES FOR: Resubmitted New Drug Application

3. MANUFACTURING SITE: Totowa, NJ

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 30mg/mL, intratracheal

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

6. PHARMACOLOGICAL CATEGORY: Treatment of Respiratory Distress Syndrome

B. SUPPORTING/RELATED DOCUMENTS: DMF (b) (4)

C. REMARKS: The consult requests a review of a resubmitted NDA 21-746 for the drug product Surfaxin®. The resubmission contained several volumes of the application. For the past review cycles, Discovery Laboratories manufactured the drug product at Laureate Pharma Inc., a contract manufacturing site. However, in an official letter dated January 2006 from Laureate Pharma Inc. (the DMF (b) (4) holder) acknowledged the transfer of ownership of this facility to Discovery Laboratories. Thereafter, Discovery Laboratory resubmitted the NDA (letter dated October 31, 2007) as the manufacturer of Surfaxin®. The firm claims that this resubmission is a complete response to the deficiencies cited in the Agency's action letter dated 31 March 2006. When Discovery was asked how the deficiencies cited in the DMF will be addressed, the firm responded in a letter [dated February 21, 2008 addressed to the reviewer] as follows: "Since Discovery assumed direct control of Laureate Pharma, it is no longer necessary to maintain DMF (b) (4). Accordingly, cross reference to DMF (b) (4) was removed from NDA 21-746. Discovery believes that complete information supporting the CMC for Surfaxin including clarification requested by the Agency is now included in the NDA 21-746". No IQA was posted for the resubmission.

filename: **C:\my documents\review\NDA\N021746R3**

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The application is approvable upon resolution of the issues cited in review section H of this document.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug product is

(b) (4)

[redacted]

B. Brief Description of Microbiology Deficiencies – See section H.

C. Assessment of Risk Due to Microbiology Deficiencies – See section H.

III. Administrative

A. Reviewer's Signature _____
Vinayak B. Pawar, Ph.D.

B. Endorsement Block _____
David Hussong, Ph.D.

C. CC Block
NA

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/s/

Vinayak Pawar
4/30/2008 02:33:11 PM
MICROBIOLOGIST

The NDA 21-746 is approvable pending resolution of the issues cited in section H of this review.

David Hussong
4/30/2008 02:44:16 PM
MICROBIOLOGIST
I concur with the reviewer's recommendation of Approvable, and the deficiency questions to be provided to the applicant.

Product Quality Microbiology Review
Review for HFD-570

6 March 2006

NDA:	21-746 N000 AZ
Drug Product Name	
Proprietary:	**Surfaxin®**
Non-proprietary:	lucinactant
Drug Product Classification:	1S
Review Number:	2
Subject of this Review	
Submission Date:	October 5, 2005
Receipt Date:	
Consult Date:	October 31, 2005
Date Assigned for Review:	November 2, 2005
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	NA
Date(s) of Previous Micro Review(s):	NA
Applicant/Sponsor	
Name:	Discovery Laboratories, Inc.
Address:	Warrington, PA
Representative:	Christopher J. Schaber, Ph.D.
Telephone:	215-488-9494
Name of Reviewer:	Vinayak B. Pawar
Conclusion:	The application is approvable from microbiology standpoint pending resolution of issues cited here and in DMF review document.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: NA

2. APPLICATION PROVIDES FOR: Amended New Drug Application

3. MANUFACTURING SITE: Totowa, NJ

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 30mg/mL, intratracheal

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

6. PHARMACOLOGICAL CATEGORY: Treatment of Respiratory Distress Syndrome

B. SUPPORTING/RELATED DOCUMENTS: DMF (b) (4)

C. REMARKS: The consult requests review of amended NDA 21-746 [N000 AZ] for the drug product Surfaxin®. Nine volumes of the amended application were submitted for review. Discovery Laboratories has purchased Laureate Pharma Inc., the manufacturing site for the drug product. An official letter dated January 2006 from Laureate Pharma Inc. (The DMF (b) (4) holder) acknowledges the transfer of ownership of this facility. Therefore, for issues pertinent to this review, cross reference may be made between DMF (b) (4) and NDA 21-746 findings.

filename: C:\my documents\review\NDA\N021746R2

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The application is approvable upon resolution of the issues cited in review section H of this document and in review section H of DMF (b) (4).

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug product is

(b) (4)

B. Brief Description of Microbiology Deficiencies – See section H.

C. Assessment of Risk Due to Microbiology Deficiencies – See section H.

III. Administrative

A. Reviewer's Signature _____
Vinayak B. Pawar, Ph.D.

B. Endorsement Block _____
James McVey

C. CC Block
NA

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/s/

Vinayak Pawar
3/7/2006 11:55:48 AM
MICROBIOLOGIST

Approvable pending resolution of deficiencies cited in section H of this review.

James McVey
3/7/2006 01:10:56 PM
MICROBIOLOGIST

Product Quality Microbiology Review
Review for HFD-570

18 January 2005

NDA:	21-746
Drug Product Name	
Proprietary:	**Surfaxin®**
Non-proprietary:	lucinactant
Drug Product Classification:	1S
Review Number:	1
Subject of this Review	
Submission Date:	April 13, 2004
Receipt Date:	
Consult Date:	July 16, 2004
Date Assigned for Review:	August 3, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): NA
Date(s) of Previous Micro Review(s): NA

Applicant/Sponsor	
Name:	Discovery Laboratory, Inc.
Address:	Warrington, PA
Representative:	Christopher J. Schaber, Ph.D.
Telephone:	215-488-9494
Name of Reviewer:	Vinayak B. Pawar
Conclusion:	The application is approvable from microbiology standpoint pending resolution of issues cited in DMF review document.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUPPLEMENT: NA

2. SUPPLEMENT PROVIDES FOR: NA

3. MANUFACTURING SITE: Totowa, NJ

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: 30mg/mL, intratracheal

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

6. PHARMACOLOGICAL CATEGORY: Treatment of Respiratory Distress Syndrome

B. SUPPORTING/RELATED DOCUMENTS: DMF (b) (4)

C. REMARKS: The consult requests review of NDA 21-746 for the drug product Surfaxin®. Two volumes designated as Module 1 and Module 3 were submitted for review. Originally DMF (b) (4) was referenced as the document supporting the NDA. This DMF did not contain the (b) (4) validation data including the (b) (4) When the sponsor was contacted DMF (b) (4) was instead updated and submitted for review of the above processes.

filename: **C:\my documents\review\NDA\N021746R1**

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The application is approvable upon resolution of the issues cited in the DMF (b) (4) review document.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - NA

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The drug product is (b) (4)

B. Brief Description of Microbiology Deficiencies – See section H.

C. Assessment of Risk Due to Microbiology Deficiencies – See section H.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Vinayak B. Pawar, Ph.D.
David Hussong, Ph.D., Microbiology Supervisor

C. CC Block

cc:
Original NDA 21-746
HFD- 570/Division File/Christine Yu

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/s/

Vinayak Pawar
1/19/05 02:07:02 PM
MICROBIOLOGIST

David Hussong
1/19/05 02:12:12 PM
MICROBIOLOGIST
Deficiencies were found in the NDA and the referenced DMF