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APPLICATION NUMBER:

021746Orig1s000

**CLINICAL PHARMACOLOGY AND
BIOPHARMACEUTICS REVIEW(S)**

CLINICAL PHARMACOLOGY REVIEW

NDA	21-746
Submission Date	Oct 31, 2007
Brand Name	Surfaxin®
Generic Name	Lucinactant Intratracheal Suspension
Reviewer	Wei Qiu, Ph.D.
Secondary Reviewer	Chandra Sahajwalla, Ph.D.
OCP Division	Clinical Pharmacology 2
OND Division	Pulmonary and Allergy Products
Sponsor	Discovery Labs
Submission Type	Resubmission: Complete Response to Action Letter dated March 31, 2006
Dosage Form	Intratracheal Suspension
Proposed Indications	Prevention of Respiratory Distress Syndrome (RDS) in premature infants and reduction of the incidence of RDS at 24 hours and mortality due to RDS.

1 EXECUTIVE SUMMARY

NDA 21-746, Surfaxin® (lucinactant) Intratracheal Suspension, has not been approved. Approvable letters were issued on February 11, 2005 and March 31, 2006, respectively. A Clarification meeting was held on December 21, 2006. This complete response intends to address the CMC deficiencies with regards to data variability, controls in manufacturing and analytical methodology, and justification of specified limits identified during the previous review cycles. No human PK study has been conducted and this submission does not contain any PK information.

Surfaxin is a peptide-containing, synthetic formulation consisting of phospholipids, a fatty acid, and sinapultide (KL₄ peptide), a 21-amino acid peptide that mimics the activity of human pulmonary surfactant proteins. Surfaxin is intended for intratracheal use only. The proposed indications are for the prevention of RDS in premature infants, and reduction of the incidence of RDS at 24 hours and mortality due to RDS.

Clinical Pharmacology review for this application is mainly focused on the proposed labeling.

1.1 Recommendation

From a Clinical Pharmacology perspective, the application is acceptable provided that a mutually satisfactory agreement can be reached between the Sponsor and the Agency regarding the language in the package insert. Recommendation and labeling comments should be conveyed to the sponsor as appropriate.

2 LABELING COMMENTS

The labeling comments from a clinical pharmacology perspective are shown below (deletion is ~~double strikethrough~~ and addition is underlined).

Under **CLINICAL PHARMACOLOGY** section **Pharmacokinetics** subsection:

Pharmacokinetics

SURFAXIN is administered directly to the (b) (4) the lung, where biophysical effects occur at the terminal airways and alveolar surface. No human pharmacokinetic studies have been performed to characterize the absorption, (b) (4) distribution, metabolism, or elimination of SURFAXIN.

3 SPONSOR'S PROPOSED LABELING

13 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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

/s/

Wei Qiu
4/18/2008 12:36:53 PM
BIOPHARMACEUTICS

Chandra Sahajwalla
4/18/2008 02:02:20 PM
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