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APPLICATION NUMBER: 20-744

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

DEC 1 2 1996

Clinical Pharmacology & Biopharmaceutics Review

CUROSURF®
Intratracheal Suspension
(Poractant)

NDA 20-744

Dey Laboratories
2751 Napa Valley Corporate Drive
Napa, CA 94558

Type of Submission:
NDA, NME, 1S

Submission Date:
July 3, 1996

Reviewer:
Brad Gillespie, PharmD

BACKGROUND CUROSURF is proposed to be used intratracheally for the treatment (rescue) of Respiratory Distress Syndrome (RDS) in premature infants. Clinical data has been submitted from six controlled (four rescue and two trials enrolling approximately 3400 subjects.

PHARMACOKINETICS Conventional bioavailability/pharmacokinetic studies were not performed with CUROSURF. The sponsor requests a waiver of the requirement for evidence of *in vivo* bioavailability under 21 CFR 320.22 (e) based on the medical fragility of premature infants. They reason that it would not be medically feasible to obtain the necessary blood specimens to determine bioavailability from a premature neonate.

DISCUSSION Two neonatal pulmonary surfactants have received FDA approval for marketing:

(a) EXOSURF® (Colfosceril, Burroughs Wellcome Company), a totally synthetic, protein-free product approved in August, 1990.

(b) SURVANTA® (Beractant, Ross Laboratories), a bovine extract approved in July, 1991.

Neither sponsor was required to perform human bioavailability/pharmacokinetic studies (see Dr Pradheep Sathe's Biopharmaceutics review of the colfosceril bio-waiver request of October, 1990).

CFR 320.22 (e) states that FDA may for good cause waive a requirement for the submission of evidence of *in vivo* bioavailability if that waiver is compatible with the protection of the public health.

CONCLUSION The product described in this submission appears to fit the criteria used to waive human bioavailability requirements in earlier pulmonary surfactant submissions.

RECOMMENDATION The Office of Clinical Pharmacology & Biopharmaceutics has reviewed the sponsor's request to waive the requirement for submitting evidence of *in vivo* bioavailability (21 CFR 320.22 (e)) and agree that this waiver should be granted.

/S/ 12/5/96

Bradley K. Gillespie, PharmD
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FT /S/ 12/5/96

Dale P. Conner, PharmD, Team Leader

cc:
HFD-570 (NDA20-744, Divisional File, Kuzmik, Pina)
HFD-870 (Conner, ChenM, Hunt, Gillespie, Chron, Drug, Reviewer)
HFD-850 (Lesko)
HFD-340 (Viswanthan)