FRESENIUS KABI

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Joseph G. Toerner, MD, MPH, Director
Division of Hepatology and Nutrition (DHN)
Office of Immunology and Inflammation
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Road
Beltsville MD 20705-1266

RE: NDA 207648 SMOFLIPID 20%, LIPID INJECTABLE EMULSION (SEQ 0087)
IND 102137
RESPONSE TO PREA NON-COMPLIANCE LETTER

Dear Dr. Toerner:

Reference is made to the 505(b)(1) New Drug Application (NDA) 207648 for Smoflipid 20%, Lipid Injectable Emulsion held by Fresenius Kabi USA, LLC.

Further reference is made to **NOTIFICATION OF NON-COMPLIANCE WITH PREA** letter received on 24 May 2021 to Postmarketing Requirement (PMR) # 3002-1 related to the following post-marketing required study.

3002-1: A prospective, randomized, controlled, double-blind, parallel-group study to compare the safety and efficacy of Smoflipid to standard- of- care soybean oil-based lipid emulsion in hospitalized neonates including low birth weight and very low birth weight neonates.

In response to the non-compliance letter, Fresenius Kabi is providing below the details on communications that have been ongoing with the Division prior to the issuance of this non-compliance letter. The communications summarized below relate to the referenced PREA PMR 3002-1 (b) (4) These include agreement received from the Division on submitting the Final Clinical Study Report (FSR) for pediatric assessment 3002-1 by the April 2021 deadline, (b) (4)

Summary of Discussions with the FDA between August 2019 and April 2021

A. Deferral Extensions for PMR 3002-1

Unanticipated delays were experienced in the timely completion of this clinical study in neonates per the original committed timelines related mainly to:

- slow recruitment rates in the required neonate patients at 15 enrolled sites over the course of the study, and subsequently,
- need for additional time to prepare the study report due to unexpected delays caused by the COVID-19 pandemic restricting site access for completion of source data verification.

These issues had been previously communicated to the FDA and 2 Deferral Extensions (DE) were granted in August 2019 and October 2020. The second **Deferral Extension Granted** letter provided agreement to extend the Final Report Submission date for PMR 3002-1 to April 2021.

Fresenius Kabi has continued to work diligently on completing the final data collection and verification for this study to target submission of the final pediatric study report by April 2021.

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(b) (4)

However, FDA responded with a **Deferral Extension Letter**, (b) (4) to allow for the review of (b) (4) (PREA PMR 3002-1). This decision was subsequently clarified in telephone discussion between Thao Vu, Regulatory Project Manager, DHN and Aparna Dagar, Sr Director, Fresenius Kabi, on 10 March 2021. The change in approach by FDA was acknowledged and Dr. Vu clarified that this was to allow FDA to evaluate the study data from PMR 3002-1 (b) (4)

C. Submission date confirmation for PMR 3002-1 Clinical Study Report (b) (4)

(b) (4)

(b) (4) PMR 3002-1 was discussed between the Division and Fresenius Kabi while clarifying the FDA's approach to evaluate (b) (4) he approach and timing of submission of the FSR (b) (4) was confirmed with an **email communication** between Thao Vu and Aparna Dagar. Specifically, it was stated via email the FSR should be submitted by 4/30/2021 to the NDA (b) (4)

The FSR for PMR 3002-1 was submitted to NDA 207648 on 30 April 2021 (b) (4)

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(b) (4)

Fresenius Kabi has been working closely over the past several years with the Division (DGIEP) to develop this study design and has now completed this challenging neonate study with the submission of the FSR by the due date. We are currently working diligently towards fulfilling the postmarketing requirement PMR 3002-1 for NDA 207648.

DEFERRAL EXTENSION REQUESTED:

Fresenius Kabi is hereby requesting a deferral extension of 2 months for the (b) (4) from the FSR to PMR 3002-1 (submitted 30 April 2021). This additional time is in order to (b) (4)

As the final study report for the PREA PMR clinical study had been submitted within the milestone deadline (b) (4) we respectfully request that the non-compliance letter and the response not be posted at this time by FDA. (b) (4)

This electronic submission contains a file size of approximately 3 MB and is submitted through Electronic Submission Gateway (ESG).

Should you have any questions or require any further information please contact the undersigned.

Sincerely,

Aparna Dagar

Digitally signed by Aparna Dagar
DN: c=US, st=Illinois, l=Lake Zurich, o=Fresenius Netcare, ou=IT, cn=Aparna Dagar, email=aparna.dagar@fresenius-kabi.com
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