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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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MAY 13 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: EPA ID # 006836: Registrant's Response to Agency Review of MEH (5-methyl-5-ethylhydantoin) General Metabolism Study

P.C. Code: 006315
Tox. Chem No.: 114A
DP Number: D197501
MRID Number: 430204-02
Submission Number: S454984

From: Paul Chin, Ph.D. Paul Chin 4/22/94
Section 2
Toxicology Branch I
Health Effects Division (H7509C)

To: Ruth Douglas/Barbara Pringle PM 32
Registration Division (H7505C)

Thru: Joycelyn Stewart, Ph.D. 4/27/94
Section Head, Section 2,
Toxicology Branch I
Health Effects Division (H7509C)

Registrant: Lonza Inc.

EXECUTIVE SUMMARY:

The Toxicology Branch I has reviewed the Registrant's Response to Agency Review of MEH General Metabolism Study (MRID Number: 430204-02).

The Toxicology Branch I concludes that the above metabolism study in rats with MEH has been adequately conducted. Thus, the Toxicology Branch I is upgrading this study from core-supplementary to core-minimum. This study satisfies the guideline requirement No. 85-1 for a metabolism data in the rat. This memorandum will serve as a supplement to the original DER (HED Document No. 009394, MRID No. 421239-02/421739-02).

TOXICOLOGY BRANCH EVAJUATION OF SUMITOMO'S COMMENTS:

Questions raised by the Toxicology Branch and Lonza's comments are listed below.

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Toxicology Branch Request

The sponsor needs to supply analytical data to demonstrate that the HPLC methodology was validated to confirm the identity of the metabolites in the urine samples.

Lonza's Comments

The urine samples were analyzed by two separate HPLC gradient systems and copies of the chromatograms from these analyses are attached. The retention times of the major radioactive peak in the urine samples matched that of an analytical standard of $^{14}C$-MEH when analyzed by both gradient systems. The principal radioactive component found in the urine samples was parent compound (MEH), accounting for 96.38 to 97.61% of the radioactivity in urine.

Toxicology Branch Response

The analytical data supplied by Lonza adequately demonstrated that the HPLC methodology was validated to confirm the identity of the major radioactive peak in the urine samples. Thus, we are upgrading the study [MRID No. 421238-02 (Addendum to 421739-02)] from supplementary to core-minimum. This study satisfies the guideline requirement No. 85-1 for a metabolism data in rats.

REQUESTED ACTION:

The Registration Division requested that the Toxicology Branch review Registrant's Response to Agency Review of MEH General Metabolism Study (MRID Number: 430204-02).

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cc: Tox. Chem. No.: 306
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