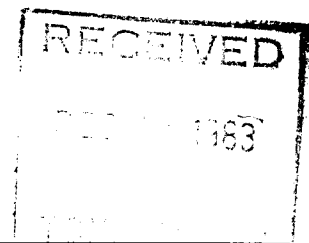


JEFFERSON MEDICAL COLLEGE
of
THOMAS JEFFERSON UNIVERSITY



Daniel Baugh Institute
Department of Anatomy
Office of the
Director and Chairman



AR 226-0015

Philadelphia, 19107
(215) 928-7820

December 7, 1983

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Mr. William C. McCormick, III
Toxicology Services, Medical Department
220-2E 3M Center
St. Paul, MN 55101

Dear Mr. McCormick:

I have received the draft report of T3351 from Dr. Wetzel and after careful review find it to be a clearly explained study. It is a state-of-the-art safety evaluation for developmental toxicity.

The data demonstrate severe maternal toxicity is evident both during and after treatment at both 5 and 10 mg T3351/kg/da and that the higher dosed group was the more severely affected. Their food intake was reduced and, not only did the dams not gain weight normally, actual maternal weight losses occurred in both these treatment groups. Numerous clinical signs of maternal distress and even hair loss were observed. There were directly related reductions in fetal body weights from these ill dams. However, for such ill mothers and small fetuses, the 5 mg group showed fewer skeletal delays than one might expect in such severely stressed mothers. No signs of either maternal or developmental toxicity occurred in the low dose group. In short, at dose levels severely maternally toxic and even lethal, T3351 exerts only a relative few of the adverse effects on the conceptus one would expect. At a dose level below that producing maternal death, but numerous other signs of maternal toxicity, there were only minor effects on the rate of fetal development and, at the all important maternally nontoxic dose level, embryonic and fetal development were absolutely normal.

This study clearly illustrates the safety of the test substance for the conceptus. The mother appears more vulnerable to T3351 than the conceptus and one would conclude that as long as exposures are kept below adult toxic levels, embryonic development would also not be affected.

This study of T3351 makes a clear statement of a no effect level and fetal safety. You have gone the extra mile and are to be congratulated for your

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high motivation. I cannot envision a customer or a regulatory agency being confused by, or having reservations regarding, this data base clearly establishing T3351 to not represent a developmental hazard to the conceptus.

Sincerely,

A handwritten signature in dark ink, appearing to read "E Marshall Johnson", with a long horizontal flourish extending to the right.

E. Marshall Johnson, Ph.D.
Professor and Chairman
Director, Daniel Baugh Institute

EMJ:amf
cc Dr. Lawrence T. Wetzel, Ph.D.
Department of Toxicology
Hazleton Laboratories America, Inc.
9200 Leesburg Turnpike
Vienna, VA 22180

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