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

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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Re-evaluation of "Teratogenic studies with Technical CGA 72662 in Rabbits".

TO: Herb Harrison, Chief
Insecticide and Rodenticide Branch
Registration Division (TS-767)

FROM: Quang Q. Bui, Ph.D. Quang Bui
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6/29/84

BACKGROUND:

The teratogenic potential of CGA 72662 in rabbits has been tested in three (3) studies by International Research and Development Corporation (IRDC), Mattawan, Michigan :

1. Pilot study - IRDC # 382-071, 11/14/79
2. Teratology study in rabbits - IRDC # 382-072, 5/7/81 *
3. Teratology study in rabbits - IRDC # 382-072 a, 5/7/81*

* Data from the two teratology studies are combined and presented in the same final report submitted to this Agency.

These studies were previously reviewed by Toxicology Branch/HED on 04/26/83.

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RECOMMENDATION:

These studies are inadequate to evaluate the teratogenicity of the test chemical due to the following points:

I. Conduct of the study:

1. Unsatisfactory state of health (suitability of animals)

a) Congested lungs, pitted kidneys, foci on lungs, and high incidences of "hydroceles on oviduct" were found in both control and treated groups and may indicate unhealthy animals prior to as well as during the experiment. The necropsy findings of congested lungs and pitted kidneys may be suggestive of, respectively, pasteurellosis and nosematosis. Sulfa treatment may not be effective for these infections (Experiment II)

b) The low conception rate observed in Experiment I may be related to the overall poor health status of the females inseminated. This index is comparable to historical control data in Experiment II.

c) Insignificant maternal weight gain in control animals (8 grams, Experiment I) during the dosing period which may be correlated with the poor health of the animals used.

d) Coccidial infection in animals found in Experiment II during the acclimation period but all animals were apparently treated with Sulfa.

e) Zero incidence of malformation findings were noted in the control group of both experiments.

f) Erratic maternal weight ~~gain~~ between the two control groups during the dosing period (8 grams vs. 112 grams).

2. Data suggest technical errors :

a) Faulty dosing period which may lead to decrease in implantation (Pilot study), decrease in conception rate and increase in preimplantation loss (experiment I).

b) Mishandling of the animals which may be characterized by the presence of esophageal perforation in one animal (experiment II) and congested lungs which may be due to gavage error as well to other factors (i.e. infections).

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II. Final Report Deficiencies - Data to be requested from the registrant.

1. Incomplete necropsy observations : No attempt was apparently made to assess the reproductive status (implantation, resorptions,...) of most animals that aborted, aborted prior to death, or died in late gestation period. These data should be made available

2. Incomplete daily clinical observations: Clinical observations were not tabulated per group and were either inadequate (Experiment I) or missing (Experiment II).

3. No litter variation data were available.

4. Undefined variations (i.e. major vessel variations) etc.

5. The historical control data are inadequate:

   a) Data collecting time is unknown.
   b) Study identification is unknown.
   c) Maternal body weight gain data are unavailable.

The historical control data should be presented in a format (by individual study) covering a period of 2 years prior to and 2 years subsequent to the initiation of the study.

CONCLUSION:

Primarily due to the questionable animal suitability (i.e. health), the teratogenic potential of CGA-72662 could not be ascertained in these studies. Some increased incidences of malformations were noted in the treated groups but not in a clear dose related manor. Fetotoxicity was suggested at all dose levels tested.

In conclusion, to adequately assess the teratogenic potential of CGA-72662, a new teratology study in rabbits is requested (with meaningful historical control data).