June 16, 1977

Safety Factors for Teratogens: Carbaryl

Chief
Toxicology Branch (WH-567)

Kyle R. Barbehenn
Project Manager, OSPR

THRU: Acting Director
Registration Division (WH-567)

THRU: Director
OSPR

It is very difficult to formulate a helpful reply to your memo of 6/13/77 because I do not have a specific safety factor for teratology. I have tried to present my views on this subject in my recent memo (I can't find my copy and therefore can't give you a date).

Specific response to your 5 listed items.

1. We agree that we are dealing with educated guesses and not a precise scientific determination. This is a major frustration that all toxicologists know very well. Because of this I have no difficulty understanding Dr. Durrough's position on the metabolism studies used to support the alleged difference between man and dog as far as Carbaryl is concerned. If this study is inadequate for your purposes you might consider asking the manufacturer to provide a better one as part of his rebuttle.

2. I have not reviewed the guinea pig study and therefor will accept Dr. Courtney's opinion. A reasonably clear cut NOEL is essential to teratological hazard evaluation. In the past we have used the rat study as the basis of our Carbaryl teratological deliberations. If new or other evidence is more compelling we will want to change this position ASAP. I wish I knew of a way to quantitate the uncertainties in this particular case. If I can help you within the limits of my own responsibilities I will do what I can.

3. I would agree that the particular monkey studies are debatable as to their ultimate relevance to solution of the problem since they seem to produce both positive and negative responses.

4. The TOX Branch can not help you in the calculation of potential exposure quantities for the applicator regardless of sex. You might follow the examples given in the preamble of the Sec. 3 Reg. for acute exposures to applicators.

   One way to resolve the concern for single acute exposure effects during critical periods of question is to request the manufacturer to perform the type of teratology test used by FDA in their drug evaluation program. (See The Testing of Chemicals for CarcinogMuta-Teratogenicity, Health and Welfare Canada, p. 172).

5. I am very pleased with your expression of confidence in the TOX Branch. It is most welcome at this time. Please rest assured we will do whatever we can to be of help to you and to continue to deserve your trust. Thanks.

Orville E. Paynter, Ph.D.

Attachment

OEPaynter/ccw 6/16/77