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

JUN 29 1992

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM:

SUBJECT: Report on the SECOND RfD/Peer Review of Nitrapyrin
CAS No. 1929-82-4
EPA Chem. No. 069203
Caswell File No. 217
Reg. Group: List A (6B)

FROM: George Z. Ghali, PhD G. Ghali 6.10.92
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

TO: Walter Waldrop, PM 71
Special Review and Reregistration Division
and
Joanne Miller, PM 23
Fungicide - Herbicide Branch
Registration Division (H7505C)

The Health Effects Division RfD/Peer Review Committee met on January 24, 1992 to evaluate data submitted in support of Nitrapyrin registration with particular emphasis on long term toxicity in rodent and non-rodent species, and developmental and reproductive toxicity.

Since the carcinogenicity issue of this chemical has been already referred to the HED Cancer Peer Review Committee by the respective Toxicology Branch for a weight of the evidence evaluation, the RfD/Peer Review Committee felt that there was no need to discuss any material related to the carcinogenicity issue. Therefore, the carcinogenic potential of this chemical was not classified.

In the meeting of January 24, 1992, the following conclusions and recommendations were made:

1) The chronic toxicity phase of the rat long term feeding study and the chronic toxicity study in dogs were considered to be acceptable and their data evaluation records to be adequate.

2) The Committee recommended a reevaluation of the rabbit developmental toxicity study and a repeat of the rat developmental toxicity study along with an appropriate range finding study. The Committee considered that the

multigeneration reproduction study in the rat and the data evaluation record of this study to be acceptable. However, the Committee determined that there was no reproductive/ developmental toxicity concern, at least at that time, to warrant referral of this chemical to the HED Developmental Toxicity Peer Review Committee for weight of the evidence determination.

3) The Committee recommended that the RfD for Nitrapyrin should be established on the basis of a NOEL of 3 mg/kg/day for increased levels of cholesterol and alkaline phosphatase activity observed in a one-year feeding study in beagle dogs at or higher than 15 mg/kg/day using an uncertainty factor of 100 to account for intra- and interspecies differences. The RfD was calculated to be 0.03 mg/kg/day.

However, since another RfD value had been established for nitrapyrin by the HED RfD Committee and verified by the Agency RfD Work Group in September 1986 based on 6-chloropicolinic acid (6-CPA), a nitrapyrin major plant metabolite and/or degradation product, the Committee was confronted with the question of whether two RfD values would then be required for the regulation of this chemical, i. e. one based on the metabolite/breakdown product 6-CPA and one based on the parent compound nitrapyrin, or whether an RfD based on nitrapyrin would be sufficiently protective. To resolve this problem, the Committee requested the following:

a) data on the nature and magnitude of plant residues,

b) animal metabolism data, and

c) comparative toxicity evaluation of the parent and its metabolite/breakdown product 6-CPA.

* Nitrapyrin is a soil microbiocide with food tolerances established under 40 CFR 180.350 for the combined residues of the parent compound and its metabolite 6-chloropicolinic acid.

A. Individuals in Attendance

1. Peer Review Committee Members and Associates (signature indicates concurrence with the peer review unless otherwise stated).

Reto Engler

Karl Baetcke

Henry Spencer

Marcia Van Gemert

Stephen Dapson

Roger Gardner

Gary Burin

George Ghali

Rick Whiting

2. Peer Review Members in Absentia (committee members or associates who were unable to attend the discussion; signatures indicate concurrence with the overall conclusions of the committee).

William L. Burnam

Laurence Chitlik

Esther Rinde

3. Scientific Reviewer (committee or non-committee members responsible for data presentation; signatures indicate technical accuracy of panel report).

Marion Copley

Linnea Hansen

B. Material Reviewed

The material available for review consisted of an RfD summary document and data evaluation records (DER's) requested by the Committee in the previous meeting.

a) data on the nature and magnitude of plant residues,

b) animal metabolism data, and

c) comparative toxicity data of the parent and its metabolite/breakdown product 6-CPA.

C. Conclusions and Recommendations

1. Limited metabolism data available indicated that the parent compound is rapidly converted to the metabolite 6-CPA and that this metabolite was present along with the parent compound. Limited comparative toxicity data available indicated also that the metabolite 6-CPA was not more toxic than the parent compound itself. It was therefore concluded that the RfD should be established on the basis of the parent compound, and that this RfD would be adequately protective against both the parent and its breakdown product, 6-CPA.

2. The Committee agreed with the reviewer interpretation and conclusions, and considered the updated version of the data evaluation records for the rabbit developmental toxicity study [Berdasco, N. M., Lomax, L. G. and Hanlley, T. R. Jr. (1985), MRID No. 470092-036, HED Doc. No. 008447] to be adequate. The study is acceptable as Core Guideline and therefore satisfies data requirement 83-4 of Subdivision F of the Pesticide Assessment Guideline.

3. The Committee reiterated its previous position that there was no need to refer the chemical for a full weight of the evidence evaluation by the HED Developmental Toxicity Peer Review Committee until the new developmental toxicity study in the rat is submitted to replace the existing rat study (MRID No. 00163792).

CC. P. Fenner/Crisp
R. Schmitt
K. Dearfield