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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: June 6, 2003

MEMORANDUM

SUBJECT: DIMETHOATE: Response to Rebuttal to EPA's Dermal Penetration Factor
(MRID No. 45922601)

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INTRODUCTION:

The registrant, Cheminova, submitted a "Rebuttal to EPA's Dermal Penetration Factor for Dimethoate" (from Cheminova to Pat Dobak, SRRD dated May 2, 2003, MRID No. 45922601). The registrant's comments have been reviewed and addressed in detail below.

Registrant's comments:

Cheminova believes that the appropriate dermal penetration factor to be used for human risk assessment is 5.6% factor. Cheminova reached this conclusion based on the following information:

Comment I

The dermal penetration factor (28%) was determined by EPA from the results of the rat dermal penetration study using a formulation (1:200 aqueous dilution) that is not sold in the U.S.

Comment II

Results from *in vitro* studies using human and rat epidermis indicate that dermal penetration is conservatively at least 5-fold greater in rat skin than in human skin.

Comment III

Therefore, dividing 28% by 5 gives a dermal penetration factor of 5.6%.

HED's response:

Comment I.

The dermal penetration factor (28%) was determined by EPA from the results of the 2nd rat dermal penetration study (newer study; MRID 45530501) using a formulation (1:200 aqueous dilution) that is not sold in the U.S. The Agency chose the 2nd study for the dermal absorption factor (28%) for the following reasons:

1. The 2nd study was conducted with a formulation concentrate of the most widely used formulation. Agency guidelines recommend that the vehicle/solvent be the material used in the commercial formulation. Dilutions for the dermal penetration study should be made with the field vehicle to produce a solution or suspension.

2. The dose levels in the 1st study do not readily span the range of anticipated dermal residues. For example, the lowest dose (0.2 mg/cm^2) in the 1st study is not low enough compared to the 2nd study (0.02 mg/cm^2). In addition, the duration of exposure in the 1st study (6 hours) is not long enough compared to the 2nd study (10 hours).

3. The 2nd study shows more clearly the release over time of skin bound residues.

4. The 1st (older) study (MRID 43964001) used carboxymethyl cellulose, which may impedes (retards) absorption, and therefore is a poor reflection of dimethoate's absorption characteristics.

Comment II

The registrant stated that results from *in vitro* studies (MRID 45922602) using human and rat epidermis indicate that dermal penetration is 5-fold greater in rat skin than in human skin. However, the Agency has determined that the *in vitro* preparation does not accurately model *in vivo* dermal

absorption based on sufficient comparative dermal absorption data on chemicals tested *in vivo* in the rat and *in vitro* with this preparation of rat epidermis (for details see memo from Robert P Zendzian, HED to Pat Dobak, SRRD, TXR # 0051898 dated May 16, 2003). Errors range from 2 to 6 fold. They usually overestimate penetration but may underestimate and appear to be random. In addition, this study employed heat processing during preparation of human skin. However, the heat processing can be expected to denature the protein matrix of the epidermis (of the stratum corneum) resulting in an unpredictable decrease in permeability.

Comment III

As stated in Comment II above, the Agency has sufficient experimental information to show that this *in vitro* methodology does not accurately predict human or rat *in vivo* dermal absorption. Therefore, the Agency cannot support this *in vitro* methodology which was used to derive a dermal penetration factor of 5.6% by dividing 28% by 5.