7-20-88

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

JUL 20 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDOM

SUBJECT: Bifenthrin, Protocol for Dermal Absorption

TO: George LaRocca PM-15
Registration Division (TS-767)

FROM: Robert P. Zendzian PhD
Senior Pharmacologist
Toxicology Branch
HED (TS-769)

THROUGH: William Burnam
Deputy Chief
Toxicology Branch

Compound; Bifenthrin

Tox Chem #463F

Registration #79-3055

Registrant; FMC

Accession #N/A

Tox Project #8-0945

Action requested

Review the following protocol;

Dermal penetration and distribution of ^{14}C-Bifenthrin (FMC 54800) in skin of male rats, Hazleton Laboratories America, Protocol TP7479, Jan 6, 1988

Discussion and recommendations

A 1986 study of the dermal absorption of Bifenthrin showed that significant quantities of the compound remained on the skin after washing and were potentially available for absorption. This study is designed to determine if and to what extent that residue is absorbable.

A dermal absorption study in rats with ^{14}C-FMC 54800; Craine, E.M. WIL Laboratories iNc; Study number 1825AT M06; Aug 15, 1986.

The standard dermal absorption study is designed to determine, 1. The quantity of test material that can be washed

off of the skin at the end of the exposure period, 2. The quantity of test material that remains on/in the washed skin and 3. The quantity of test material that actually penetrates and skin and enters the body. The quantity that actually penetrates the skin is available to produce toxic effects but the quantity that cannot be washed off of the skin may also penetrate with time. For regulatory purposes a risk assesment is made on the quantity absorbed and on the quantity absorbed plus the quantity in the washed skin. This is a worst case assesment and the truth of the risk should lie somewere between these two values.

In the WIL study a very small portion of the applied dose was found to actually penetrate the skin but approximately half of the dose remained on the washed skin. At this time we cannot predict what will happen to this residual material. We have two studies, in other compounds, that indicate absorption of at least some of this material. One study actually tested for absorption of the retained material by washing the application site and finding absorption for up to two weeks following the wash. For the second compound, a dermal teratology study indicated that the systemic dose had to be more than the dose indicated solely by absorption but was probably less than the total of absorbed and skin residue. On the other hand, recent information indicates that the method used to wash the skin in the WIL study may have artifactually increased the skin residue. In the WIL study, the animals were sacrificed, the skin was removed and then it was washed. In the study to determine absorption of retained material mentioned above, some rats were sacrificed at 10 hours, the skin removed and washed and some rats were washed at 10 hours and carried for extended periods. At each of three doses, two to three times as much material could be waahed off of the skin of the living rats as off of the skin of the sacrificed rats. Further information on yet another compound indicates that this may not be a function of life or death but rather an artifact of the way the skin removed from the rat is washed. In this case when the wash fluid came into contact with the cut edge and/or the underside of the skin additional test material became bound.

In general the protocol is acceptable with the following modifications/additions.

1. The protocol proposes to use one dose, 50 ug per rat, as this is the best value to be used for field exposure. The WIL study also used 50 ug/rat (49 ug actual), as the low dose. However, in that study the dose was applied to a skin area of 10 cm^2 and in the protocol is appears that the dose will be applied to 12 cm^2. Since dermal absorption is a function of dose per unit area, it is important for comparative purposes that the dose per cm^2 in the proposed study be as close as technically possible to the dose per cm^2 in the WIL study.

2. Considering the questionable the skin washing procedure, it is recommended that an additional 4 animals be treated. These animals should be exposed for only 10 hours and all samples collected as per the protocol. This will provide a bridge to the WIL study by a commonly treated group which will enable us to determine if that skin residue data was artifactually high.

cc
Backus