INFORMATION WHICH MAY REVEAL INERT INGREDIENTS IS NOT INCLUDED

INFORMATION WHICH MAY REVEAL FORMULATION IMPURITIES IS NOT INCLUDED

IRB/TSS Precautionary Labeling Review 11/24/86

TO: PM-16 2

SUBJECT: 707-ENG
Kelthane Technical
Rohm and Haas Company
Philadelphia, PA 19105

In TSS: 11-10-86
Record #: 183673
Action #: 160

FORMULATION: Technical Kelthane.

Active Ingredient:
Dicofol.....89%
Inert Ingredients.....11%
(Impurities in this technical dicofol contain [redacted]

BACKGROUND: This is an application for a new registration. Product is proposed to replace already registered Technical Kelthane (Registration Number 707-107). The new technical has been purified to reduce amount of the DDTr impurities [redacted] Registrant has referenced data from the old technical (Accession No. 256589) to support this registration.

COMMENTS:

1. Data in Accession Number 256589 consist of a lot of studies that the company had submitted to fill data gaps that were identified for various Kelthane products in dicofol registration standard. Five studies were referenced to support registration of old Kelthane Technical. Three of these were submitted for TSS review. We have the following comments about these studies:

(a). Acute Inhalation LC50: Rohm and Haas Technical report Number 80R-27. Test substance was Kelthane EC, an 18.5% a.i. emulsifiable concentrate [redacted] Study was reviewed by Byron Backus on 6-10-82 and was classified as core minimum data. Acute inhalation LC50 was considered to be greater than 1.62mg/l. Concentration of test chamber was measured gravimetrically and expressed for the product. This study would place the test substance in toxicity category III for acute inhalation exposure.

(b). Acute Inhalation LC50: Rohm and Haas Technical Report number 82R-134, dated 8-24-82, accession number 248306. Test substance was Kelthane MF (42% a.i. and [redacted] Study was reviewed by Phil Hutton on 11-4-82 and was classified as core minimum data. Acute inhalation LC50 was considered to be > 1.51 mg/l. Concentration was measured gravimetrically and expressed for the product. This study would place test substance in toxicity category III for acute inhalation exposure.

(C). Dermal Sensitization: Rohm and Haas Technical Report number 85R-15. Test substance was described as Kelthane MF 417. Study was reviewed by Carolyn Gregorio of Toxicology Branch on 6-28-85 and classified as supplementary data because composition of test substance was not given. According to this study, test substance was a sensitizer in guinea pig.

(d). Referenced primary eye irritation and primary dermal irritation studies were not submitted for TSS review.

2. According to dicofol registration standard, sufficient data are on file to address acute oral and acute dermal toxicity of Kelthane Technical. Existing data suggest toxicity category III for acute oral and acute dermal routes of exposure.

3. The acute inhalation LC50 studies summarized above cannot be used to support registration of Technical Kelthane for reasons listed below:

(a). Registrant should explain why testing was not done on Technical Kelthane. Guidelines require that the technical grade of an active ingredient should be tested to support registration of a manufacturing use product.

(b). Guidelines also state that, when needed, test substance may be dissolved or suspended in a suitable vehicle, but the toxic characteristics of the vehicle should be determined before the test. If it is to use a vehicle, Technical Kelthane should be mixed with it to highest attainable concentration of dicofol attainable concentration. A vehicle should be selected that will not significantly alter toxicity of the test substance, and dose/concentration should be expressed in terms of the technical.

4. Composition of test substance used for dermal sensitization study was not given, so we don't know what was tested and how it will compare with Technical Kelthane.

5. New formulation of Technical Kelthane, which contains fewer DDTr impurities [redacted] and higher percentage of dicofol (89% vs 82%), is substantially similar to the old formulation from an acute toxicity standpoint. Acute toxicity profile on the old technical, when complete, will adequately support registration of the new technical.

6. Bill Burnam, Deputy Chief, Toxicology Branch, is in agreement with comments 3 and 5.

Rita Kumar
IRB/TSS