from the RED
file for case # 3148 Case # 3148

PHASE FOUR REVIEW

(**NOTE:** This only contains additions and changes from the phase 2 response.)

Pesticide: 3-(Trimethoxysilyl)- propyldimethyl-octadecyl ammonium chloride

Transmitted to HED on: 12/03/92 Chemical#/Case#: 107401/819411

Tox. Chem #: 892B Sponsor: DOW CORNING CORP. 107401

Submission No.: S430115

CRM: Bruce Sidwell Phone #: 308-8078

Branch: Toxicology Branch I Reviewer: John C. Redden

Completed: 02/23/93 Concurrence: 2/25/93

Division Director's Concurrence: P.A. Jennings 2/26/93

Are there any changes from the reviews in phase 2? ____ NO X YES (see below)

Summary:

Tier 1 Data Gaps:

The following missing studies or data are needed to complete this package:

1) Guideline 83-3 Teratogenicity (1st species: rat or rabbit) An upgradable study with Dow Corning 5700 Hydrolysate exists (missing purity).

Note: **we are currently not requiring Tier 2 and 3 studies. However, they may be triggered depending on Tier 1 results, and the Agency reserves the right to require the below listed studies.**

Tier 2 Studies (not Data Gaps but may be required):

1) Guideline 82-1 90-day feeding/rodent
2) Guideline 83-3 Teratogenicity (2nd species)
3) Guideline 85-2 Dermal Penetration; upgradable study present

Tier 3 Studies (not Data Gaps but may be required):

1) Guideline 83-1 Chronic feeding (2 species); only if it is determined that the margin of safety is less than 1000 based on the subchronic data, and exposure cannot be reduced.

2) Guideline 83-2 Oncogenicity (2 species); required if the Agency determines from the mutagenicity test battery that the AI may pose an oncogenic risk, or based on dermal exposure times the Q* of unity the calculated risk is unacceptable.

3) Guideline 83-4 Metabolism; only if the metabolism of the chemical is necessary to clarify unusual effects observed in chronic or reproduction studies to clarify issues concerning structure activity relationships.

Response, by Guideline

Guideline #: 81-1 Acute oral/rat

1. MRID #:93218011, 93218010 (Dup of -11), 40385201 **Study #:**AD-0003

Discussion/Recommendation:

Summary of MRID 40385201 submitted to the Agency, the study was previously reviewed, and core graded Minimum (HED Document#006796, 002486). The following deviations were noted: 1) individual observations done on day 1, 7 and 14; and 2) gross necropsy not done. However, due to the high LD_{50} (12.27 g/kg) it is not necessary to repeat the study and it remains core graded Minimum. **Requirement satisfied.**

2. MRID #:93218049, 42456511 **Study #:**

Discussion/Recommendation:

DOW CORNING 5772; this study is tentatively accepted for review.

Guideline #: 81-2 Acute dermal/rabbit

1. MRID #:93218024, 42456512, 41339402

Study #:

Discussion/Recommendation:

New submission; the Registrant submitted a 14-day range finding dermal study in rats for Guideline 81-2. The following deviations from 81-2 exist: 1) 2 animals/sex/group (5 animals/sex/group); 2) animals dosed for five consecutive days a week for fourteen days (Dosing, single dermal); and 3) material left in contact for a period of 6 hours/day, 5 days per week. The highest dose group tested was 1,000 mg/kg/day. The material was suspended in propylene glycol. Quoting the study: "No overt signs of toxicology or mortality were seen in any of the groups. No significant differences in mean body weights or food consumption were observed between treated and control animals. Also, no treatment-related effects were noted at gross necropsy."

2. MRID #:

Study #:

Discussion/Recommendation:

The registrant submitted by vax an acceptable for review study (summary) with the 72% formulation (tested to limit dose). This study is acceptable for review. Note: Once Registrant submits study a MRID NO will be assigned.

Guideline #: 81-3 Acute inhalation/rat

1. MRID #:93218008, 9318025, 40385219 **Study #:**
Discussion/Recommendation
Reformat of MRID No. 40385219 previously submitted to the Agency. However, this study does not appear in the Tox One-Liners. Study to determine respirable particle size. This study is unacceptable for review.

2. MRID #:93218014, 41157803 **Study #:** Dow Corning Corp 1312
Discussion/Recommendation:
Summary of MRID 41157803 previously submitted and reviewed by the Agency. The study was core graded Supplementary (HED Document#007667), and was upgradable if purity was supplied. This summary states purity to be 72.1% The Registrant supplied additional information by vax that allows this study to be upgraded to **Minimum.**

Guideline #: 81-4 Primary eye irritation/rabbit

1. MRID #:93218017, 40385201 **Study #:** AD-0003
Discussion/Recommendation
Summary of MRID 40385201 previously submitted and reviewed by the Agency, and core graded Minimum (HED Document#006796, 002486). The following minor deviation was noted: left eye washed within 30 seconds of dosing and right eye washed 1 hour post dosing (24 hours required in guideline). **Requirement satisfied.**

2. MRID #:93218015; 41157801 **Study #:**
Discussion/Recommendation
Summary of MRID 41157801 previously submitted to the Agency. However, this study does not appear in the TOX ONELINERS. The following deviations were noted: 1) only 1 rabbit used (guideline requires 6); and 2) left eye washed within 30 seconds of dosing and right eye washed 1 hour post dosing (24 hours required in guideline). The study is Core Supplemental and not upgradable.

3. **MRID #:**93218016, 41157802 **Study #:**
Discussion/Recommendation
Summary of MRID 41157802 previously submitted to the Agency. However, this study does not appear in the TOX ONELINERS. The following deviations were noted: 1) only 1 rabbit used (guideline requires 6); and 2) left eye washed within 30 seconds of dosing and right eye washed 1 1/2 hours post dosing (24 hours required in guideline). The study is Core Supplemental and not upgradable.

Guideline #: 81-5 Primary dermal irritation/rabbit

from the RED file for case # 3148

Chemical/Case Number	Company Number / Name
107401 / 3148	034292 DOW CORNING CORP.

GDLN #	DESCRIPTION	REGISTRANT'S COMPLIANCE/MRID	EPA DECISION

MRID Comments Continued:
toxicity in rats.
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The following deviations exist:
1) 2 animals/sex/group (5 animals/sex/group);
2) animals dosed for five consecutive days a week for fourteen days (Dosing, single dermal); and
3) material left in contact for a period of 6 hours/day, 5 days per week. The highest dose group tested was 1,000 mg/kg/day. The material was suspended in propylene glycol.

81-2 Acute dermal tox. rabbit/rat 42456512-St

Comments: This submission was reviewed with MRID 41339402. Please see the comments for MRID 41339402.

81-3 Acute inhal. tox rat 40385219-St Denied/Def.

Comments: This study is unacceptable for review

81-3 Acute inhal. tox rat 93218038-Re Accept

81-3 Acute inhal. tox rat 41157803-St Accept

Comments: Summary of MRID 41157803 previously submitted and reviewed by the Agency. The study was graded core Suplimentary, and was upgradable if the purity was supplied. This summary states the purity to be 72.1%. The Registrant supplied additional information by FAX that allows this study to be upgraded to core Minimum.

81-4 Primary eye irration-rabbit 40385201-St Accept

Comments: Summary of MRID 40385201 previously submitted and