

12-22-92

PHASE FOUR REVIEW

H. E. D.

PESTICIDE: Thidiazuron (Dropp 50WP)

Chemical #/Case #: 4092      Tox. Chem. #: 120301

Sponsors: NOR-AM CHEMICAL COMPANY      Use: Cotton defoliant

CR Manager: Tom Myers      Phone: 308-8074

Reviewer: Deborah McCall      Signed: DMcCall 12/10/92

Phone: 308-2718      Completed: 12/10/92      Branch: TOX II

Concurrence:

Section Head: James N. Rowe      Date: 12/10/92

Branch Chief: Muan Jensen      Date: 12/14/92

HED Director: Penelope A. Jenner - Cusp      Date: 12/22/92

Sponsor: NOR-AM CHEMICAL COMPANY

Use: Terrestrial food/non-food

**SUMMARY:** Thidiazuron is used as a wettable powder (50% A.I.) to be used as a cotton defoliant in Arizona. The registrants have submitted 17 summaries for review and 7 have already been reviewed by the Agency. Four of the toxicity studies were performed at IBT in 1976 or 1980, but these have been validated by the contractors and also by the Agency for acceptance. The remaining toxicity studies were performed during 1981 & 1986.

There are several data gaps present in the current database due to "Supplementary" studies, they are: 90-day feeding - rats, 90-day feeding - dogs, combined chronic and oncogenicity - rats, chronic - dogs, and developmental study in rats. The submitted summary for a teratology study in rats (77127) will probably be "supplementary" data due to the examination methods which were used for the skeletal and soft tissue exams. However, there was another teratology study (070129) which was classified as a Minimum study in the oneliners and could be used to fulfill this data requirement.

Additionally, because these studies were conducted prior to GLP's and our current guidelines, I also recommend that the 1) Oncogenicity - mouse (050936), 2) teratology - rat (070129), 3) teratology - rabbit (77129), and 4) multi-generation reproduction (8533-096300 studies be re-reviewed by the Agency.

**PHASE FOUR REVIEW  
Response, by Guideline**

Guideline #: 81-1 Description: Acute oral/rat  
MRID 64726 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study is acceptable for review.

Guideline #: 81-2 Description: Acute dermal/rabbit  
MRID 414269-01 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study is acceptable for review.

Guideline #: 81-3 Description: Acute inhalation/rat  
MRID 38137 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study is acceptable for review.

Guideline #: 81-4 Description: Primary eye irritation/rabbit  
MRID 420996-01 Study # \_\_\_\_\_  
Recommendation: This study has been reviewed by the Agency and found to be a Guideline study.

Guideline #: 81-5 Description: Primary dermal irritation/rabbit  
MRID 420996-02 Study # \_\_\_\_\_  
Recommendation: This study has been reviewed by the Agency and  
found to be a Guideline study.

Guideline #: 81-6 Description: Dermal sensitization/Guinea Pig  
MRID 64737 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study  
is acceptable for review.

Guideline #: 82-1a Description: 90-day feeding/rodent  
MRID 38147 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency (and Dynamac) and determined to be Supplementary. IBT Study  
- 1976 (lab ID # 8560-08337). [If the chronic data (§83-1a or 83-5)  
gap is fulfilled this would also fulfill this data requirement.]

Guideline #: 82-1b Description: 90-day feeding/nonrodent  
MRID 38148 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency (and Dynamac) and determined to be Supplementary. IBT Study  
- 1976 (lab ID # 8531-08338). [If the chronic data gap (§83-1b or  
83-5) is fulfilled this would also fulfill this data requirement.]

Guideline #: 82-2 Description: 21 Day dermal/rabbit  
MRID 64724 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study  
is acceptable for review.

83-1(a)  
Guideline #: 83-5 Description: Combined Chronic/Carcinogenicity/rodent  
MRID 159346, 407983-02, 407983-03 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency and found to be Supplementary for both chronic and  
carcinogenicity endpoints and should be **repeated**. The reviewer  
indicated the study did not achieved a MTD nor a chronic NOEL.

Guideline #: 83-1b Description: Chronic toxicity/nonrodent  
MRID 159344, 409085-01, 407983-01 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency and found to be Supplementary. The reviewer indicated the  
study could be upgraded with additional information to clarify the  
possible immunotoxicity effects.

Guideline #: 83-2a Description: Carcinogenicity/rat  
MRID 159346, 407983-02, 407983-03 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study  
is acceptable for review.

Guideline #: 83-2b Description: Carcinogenicity/mouse  
MRID 050936 Study #

Recommendation: This study has been reviewed by the Agency and found to be a Minimum study. I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 83-3a Description: Teratology/rat  
MRID 77127 Study #

Recommendation: After an assessment of the summary, several of the acceptance criteria were either not fully satisfied or not performed which might compromise the results of the study. However, another rat study was listed in the oneliners which was a Minimum study (070129). I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 83-3b Description: Teratology/rabbit  
MRID 77129 Study #

Recommendation: This study has been reviewed by the Agency and found to be a Minimum study. I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 83-4 Description: 3-generation reproduction/rat  
MRID Study #

Recommendation: After a review of the oneliners, a Minimum reproduction study was performed by IBT (8533-09630). I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 84-2a Description: Mutagenicity/Ames  
MRID 70129 Study #

Recommendation: An Acceptable study exists (negative w & w/o S9).

Guideline #: 84-2b Description: Chromosomal aberr./human lymphocytes  
MRID 407983-04 Study #

Recommendation: The study was reviewed by the Agency and found to be Acceptable (negative) for the activated assay, but Unacceptable for the non-activated assay. There is an additional study (dominant lethal study in mice), which is acceptable and is suggestive of a weak positive response.

84-2a

Guideline #: 84-2b Description: Chinese hamster V79  
MRID 417611-02 Study #

Recommendation: Based on the assessment of the summary, the study is acceptable for review.

Guideline #: 84-4

Description: UDS

MRID 417611-03 Study #

Recommendation: Based on the assessment of the summary, the study is acceptable for review.

Guideline #: 85-1

Description: Metabolism

MRID 425290-01 Study #

Recommendation: Based on the assessment of the summary, the study is acceptable for review.

Guideline #: 81-5 Description: Primary dermal irritation/rabbit  
MRID 420996-02 Study # \_\_\_\_\_  
Recommendation: This study has been reviewed by the Agency and  
found to be a Guideline study.

Guideline #: 81-6 Description: Dermal sensitization/Guinea Pig  
MRID 64737 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study  
is acceptable for review.

Guideline #: 82-1a Description: 90-day feeding/rodent  
MRID 38147 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency (and Dynamac) and determined to be Supplementary. IBT Study  
- 1976 (lab ID # 8560-08337). [If the chronic data (§83-1a or 83-5)  
gap is fulfilled this would also fulfill this data requirement.]

Guideline #: 82-1b Description: 90-day feeding/nonrodent  
MRID 38148 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency (and Dynamac) and determined to be Supplementary. IBT Study  
- 1976 (lab ID # 8531-08338). [If the chronic data gap (§83-1b or  
83-5) is fulfilled this would also fulfill this data requirement.]

Guideline #: 82-2 Description: 21 Day dermal/rabbit  
MRID 64724 Study # \_\_\_\_\_  
Recommendation: Based on the assessment of the summary, the study  
is acceptable for review.

Guideline #: 83-5 Description: Combined Chronic/Carcinogenicity/rodent  
MRID 159346, 407983-02, 407983-03 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency and found to be Supplementary for both chronic and  
carcinogenicity endpoints and should be repeated. The reviewer  
indicated the study did not achieved a MTD nor a chronic NOEL.

Guideline #: 83-1b Description: Chronic toxicity/nonrodent  
MRID 159344, 409085-01, 407983-01 Study # \_\_\_\_\_  
Recommendation: DATA GAP. This study has been reviewed by the  
Agency and found to be Supplementary. The reviewer indicated the  
study could be upgraded with additional information to clarify the  
possible immunotoxicity effects.

Guideline #: 83-2a Description: Carcinogenicity/rat  
MRID 159346, 407983-02, 407983-03 Study # \_\_\_\_\_  
Recommendation: DATA GAP (see 83-5).

Guideline #: 83-2b

Description: Carcinogenicity/mouse

MRID 050936 Study #

Recommendation: This study has been reviewed by the Agency and found to be a Minimum study. I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 83-3a

Description: Teratology/rat

MRID 77127 Study #

Recommendation: After an assessment of the summary, several of the acceptance criteria were either not fully satisfied or not performed which might compromise the results of the study. However, another rat study was listed in the oneliners which was a Minimum study (070129). I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 83-3b

Description: Teratology/rabbit

MRID 77129 Study #

Recommendation: This study has been reviewed by the Agency and found to be a Minimum study. I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 83-4

Description: 3-generation reproduction/rat

MRID Study #

Recommendation: After a review of the oneliners, a Minimum reproduction study was performed by IBT (8533-09630). I recommend that this study be re-reviewed, because the study was not reviewed under our current guidelines or conducted under GLP's.

Guideline #: 84-2a

Description: Mutagenicity/Ames

MRID 70129 Study #

Recommendation: An Acceptable study exists (negative w & w/o S9).

Guideline #: 84-2b

Description: Chromosomal aberr./human lymphocytes

MRID 407983-04 Study #

Recommendation: The study was reviewed by the Agency and found to be Acceptable (negative) for the activated assay, but Unacceptable for the non-activated assay. There is an additional study (dominant lethal study in mice), which is acceptable and is suggestive of a weak positive response.

Guideline #: 84-2a

Description: Chinese hamster V79

MRID 417611-02 Study #

Recommendation: Based on the assessment of the summary, the study is acceptable for review.