

US EPA ARCHIVE DOCUMENT

12-22-92

PHASE FOUR REVIEW

H. E. D.

PESTICIDE: Thidiazuron (Dropp 50WP)

Chemical #/Case #: 4092

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

Guideline #: 84-2b Description: Chromosomal aberr./human lymphocytes
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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.