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

008589

SEP 13 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

Subject: Assure II Herbicide (DPX-Y6202-52 D+) Data review.
Tox Chem No 215 D
HED Project No 1-1520

From: Dan W. Hanke, Ph. D. Dan W Hanke September 6, 1991
Review Section III
Toxicology Branch II (HFASB)
Health Effects Division (H7509C)

To: Mr. Robert J. Taylor
Product Manager, Team 25
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: James N. Rowe, Ph. D. James N. Rowe 9/6/91
Head, Review Section III
Toxicology Branch II (HFASB)
Health Effects Division (H7505C)

and

Marcia van Gemert, Ph. D. Marcia van Gemert 9/6/91
Chief, Toxicology Branch II (HFASB)
Health Effects Division (H7505C)

ACTION:

E. I. duPont deNemours & Co Haskell Laboratory has submitted a revised primary dermal irritation study report (§81-5) in one volume entitled "Primary Dermal Irritation Study with DPX-Y6202-52 (9.7% EC) in Rabbits". The results of a review of the study are summarized below.

DISCUSSION:

Six young adult male New Zealand White rabbits were treated with 0.5 ml of undiluted test material on test patches for four hours. One hour post treatment as well as 24, 48, 72 hrs, and 4 days later the test sites were evaluated. There was essentially no edema formation, and none of the rabbits died. Based on a mean Primary Irritation Index score of 2.0 for erythema the test material is classified as a moderate dermal irritant. Ordinarily /

this study could appropriately be returned to the registrant to be repeated without evaluating it any further, once it was apparent that significant ocular effects occurred. However, this study has already been revised by the registrant to address data deficiencies as per an EPA DER dated October 27, 1989: need to include dermal examination within 60 min post exposure (primary irritation), a review of the primary dermal irritation index, and a discussion of the ocular involvement. In the present revised study the author speculates the reason for ocular involvement is accidental eye contamination during the experimental procedure. The report includes supplemental commentary (no supporting data are included with this revised study report) that strongly supports their speculation. Apparently an earlier eye irritation study established this test material as a severe eye irritant, and the test material also apparently caused severe skin lesions during an acute dermal absorption study without provoking ocular involvement- systemically or otherwise. Therefore, this test material will most likely produce dermal irritation to some degree as well. Hence, the presumed accidental ocular involvement may not fatally flaw this revised study.

Toxicity Category: III

A signed quality assurance statement was present.

Core Classification: Minimum.

This study satisfies the guideline requirements (§81-5) for a Primary Dermal Irritation study.



2

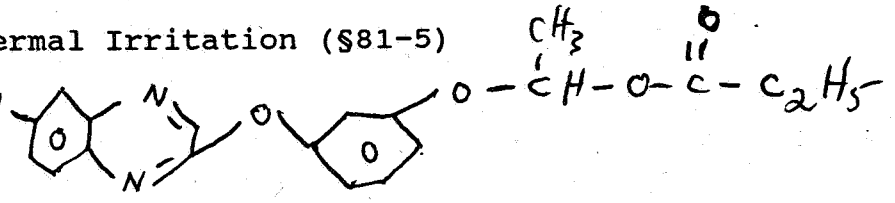
008589

Reviewed by: Dan W. Hanke, Ph. D. Dan W Hanke Sep-5, 1991
Section III, Tox. Branch II(H7509C)
Secondary reviewer: James N. Rowe, Ph. D. James N. Rowe 9/5/91
Section III, Tox. Branch II(H7509C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation (§81-5)

TOX. CHEM NO: 215 D



MRID NO.: 418646-01

TEST MATERIAL: DPX-Y6202-52 D+ (the active isomer); propanoic acid, 2-[4-((6-chloro-quinoxalinyl)2-oxy)phenoxy]-, ethyl ester

SYNONYMS: Assure II, Quizalofop-ethyl, Targa, Pilot

STUDY NUMBER: 52593-88; AG0079-138

SPONSOR: Du Pont Agricultural Products
E. I. du Pont de Nemours & Company
Wilmington, Delaware

TESTING FACILITY: E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and
Industrial Medicine
Elkton Road, P. O. Box 50
Newark, Delaware 19714

TITLE OF REPORT: Primary Dermal Irritation Study with DPX-Y6202-52 (9.7 % EC) in Rabbits

AUTHOR(S): John W. Sarver

REPORT ISSUED: Revised April 9, 1991; Study first completed February 22, 1989; In Life phase was initiated January 31, 1989 and completed February 6, 1989.

CONCLUSIONS: Six young adult male New Zealand White rabbits were treated with 0.5 ml of undiluted test material on test patches for four hours. One hour post treatment as well as 24, 48, 72 hrs, and 4 days later the test sites were evaluated. There was essentially no edema formation, and none of the rabbits died. Based on a mean Primary Irritation Index score of 2.0 for erythema the test material is classified as a moderate dermal irritant. Ordinarily this study could appropriately be returned to the registrant to be repeated without evaluating it any further, once it was apparent that significant ocular effects occurred. However, this study has already been revised by the registrant to address data deficiencies as per an EPA DER dated October 27, 1989: need to include dermal examination within 60 min post exposure (primary irritation), a review of the primary

dermal irritation index, and a discussion of the ocular involvement. In the present revised study the author speculates the reason for ocular involvement is accidental eye contamination during the experimental procedure. The report includes supplemental commentary (no supporting data are included with this revised study report) that strongly supports their speculation. Apparently an earlier eye irritation study established this test material as a severe eye irritant, and the test material also apparently caused severe skin lesions during an acute dermal absorption study without provoking ocular involvement- systemically or otherwise. Therefore, this test material will most likely produce dermal irritation to some degree as well. Hence, the presumed accidental ocular involvement may not fatally flaw this revised study.

Toxicity Category: III

A signed quality assurance statement was present.

Core Classification: Minimum.

This study satisfies the guideline requirements (§81-5) for a Primary Dermal Irritation study.

MATERIALS.

1. Test compound: DPX-Y6202-52 D+ technical. propanoic acid, 2-[4-((6-chloro-2-quinoxalinyl)oxy)phenoxy]-, ethyl ester. Description: Reddish-brown liquid. Batch #: None reported. Purity: 9.7 % active isomer, 89.8 % inert ingredients. Stability: No data were submitted with this report. They apparently assumed the test material to be stable under the experimental conditions based on visual inspection alone.

Under the Protocol section on p 11 of the revised study report, they say that three other test materials were evaluated along with DPX-Y6202-52 D+.

2. Test animals: Species: white rabbit. Strain: New Zealand. Age: young adults: six males. Weight: 1937 to 2803 grams on the day of treatment. Source: Hare Marland, Hewitt, New Jersey.

METHODS.

A copy of the Materials and Methods is attached as Appendix I.

It is important to note, that four test materials were evaluated on each of the six rabbits with adjacent areas of untreated skin serving as controls.

RESULTS.

None of the rabbits died. There was very mild edema (scored 1) in only two of the animals at the one hr observation period; otherwise there was no edema reported. The range of severity of the ensuing erythema was on average scored (according to Draize) as 3.3 (4 is the most severe) at one hr and 0.5 (or 1) at 72 hr. The grand score mean (or average of the means) from the six rabbits across time was 1.88 (or 2); within each time period the grand score mean was 1.85 (or 2), which makes DPX-Y6202-52 D+ a Class III or Moderate Irritant ($2 \leq$ Class III $\leq 5$). The mean irritation score (3.3) for the one hr evaluation of erythema was not incorporated into the table for mean scores as a distinct entry nor was this value included in the calculation of the Overall Average erythema score (see Appendix II of this DER taken from Table III, p 17 of the revised study report).

DISCUSSION.

The revised study appears to adequately address the concerns raised by the first DER of the original report from February 22, 1989. However, along with the present revised study report the registrant should also have supplied Haskell Laboratory Report No. 740-88 and Haskell Laboratory Report No. 54-89 as companion pieces in order to substantiate their claims, that accidental ocular involvement during the in life phase did not alter the outcome of this study. Furthermore, it is not abundantly clear whether this study is a repeat of the original study, which lacked the one hour post exposure data; or whether the one hour post exposure data were originally collected but failed to be included in the earlier report and have now been made a part of the present submission. Additionally, it would have been useful if their data analysis had also indicated, that the range of severity of the average erythema responses was 3.3 at one hr and 0.5 at 72 hr. Since three other test materials were evaluated along with DPX-Y6202-52 (p 11 of the revised study report under Protocol, which is included with the attached copy of Materials and Methods in this DER), it is impossible to ascertain which of the test materials evoked the ocular effects. The spirit of § 81-5 of the Subdivision F Toxicity Testing Guidelines of FIFRA 88 implies only one concentration of one test substance per animal be evaluated at a time with each animal serving as its own control. This study tested four materials per rabbit. This study, nevertheless, is judged Minimum, because the Guideline §81-5 does not expressly require only one test material per animal.



5

Appendix I follows

ASSURE 128711

Page_____ is not included in this copy.

Pages 7 through 14 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

X FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.