

US EPA ARCHIVE DOCUMENT



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

10-1-91  
009276

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 2792-AU  
Decco Saet NO 35-

FROM: Lucy D. Markarian 4/27/91 E 10/1/91  
Precautionary Review Section  
Registration Support Branch  
Registration Division (H75-05C)

TO: Susan Lewis/James Stone (PM)  
Fungicide - Herbicide  
Registration Division (H75-05C)

APPLICANT: Atochem - North America  
Decco Agrichemicals Division  
1713 California Ave.  
Menlo Park, Ca

FORMULATION FROM LABEL:

Active Ingredient(s):	3 by wt.
<u>2,6 Dichloro-4 nitroaniline</u>	<u>24.90</u>
<u>3, (3,5 dichlorophenyl) 1 (1-methyl-2,4-dioxo- imidazolidine carbonyl) imide</u>	<u>33.33</u>
Inert Ingredient(s):	<u>41.65</u>
Total	100.00

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## BACKGROUND:

Reviews dated 8/3/90 and 12/29/90 recommended submission of Dermal Toxicity, Inhalation Toxicity and Dermal Irritation Tests to support the registration of Decoalt 35 under EPA symbol 2792-AU. Atochem North America, Decco Agrochemicals Division has now submitted the required Tests.

## RECOMMENDATION:

The Dermal Toxicity study is accepted as guideline data. The Inhalation study is accepted as core minimum data for the following reasons:

1. The samplings for determination of chamber concentration were for 30 seconds. This is a shorter sampling time than the average.

2. The chamber concentration varied between 1.85 to 5.3 mg/L. Equilibration (99%) was supposed to have been reached at about 2 minutes the sampling was one hour after equilibration. The value of 1.85 is too low, and it is what explained why it is left out of the average, when the incidence would not have changed the toxicity category. So much variation in the chamber concentration signifies uneven exposure and the average concentration does not really mean very much.

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3. The MMAD extrapolated from the particle size analysis is somewhat higher than desirable. The distribution shows about 30% of the particles <sup>possibly</sup> inhalable by the test model. Therefore this higher MMAD value is considered acceptable.

The Sensitization study is considered supplementary data for the following reasons:

1. Buehler method uses a patch screening to define the induction and elicitation concentrations. He states "That the choice of concentrations and vehicles used during the induction and elicitation phases of testing is very critical to the meaningfulness of the results obtained"

The test used solid material, noritend, for induction with no attempt at defining these concentrations.

When some irritation was observed the induction was switched to a 50% solution. The change was not ever necessary, because according to Buehler the induction is made at the lowest irritating concentration, and the irritation observed was Grade 2 redness in one animal (the most prominent) This is hardly an in-depth injury to warrant the change of concentration. Some irritation is desirable during induction.

2. No indication is made of the concentration of the challenge concentration. It is not clear if challenge

-1 Ritz & Buehler - Planning, conduct, and interpretation of Guinea Pig Sensitization Patch tests. Current Concepts in Cutaneous Toxicity, 1980 Academic Press

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was made at 100% or 50% or at a lower concentration.

According to Buehler Challenge is made at the highest non irritating concentration. This was not defused at any time before or during the test.

3. There were no naive controls. Buehler<sup>2</sup> states that "The significance of reactions in the experimental group is based on intensity and incidence relative to the reactions in the two control groups" By the two control groups Buehler means naive controls and vehicle controls. Positive controls are not a base for comparison. They merely state that the laboratory has the ability to induce sensitization with a known sensitizer. Positive controls are not required with every test, a reference to a positive control test performed within a reasonable interval is considered adequate.

In summary the test does not decide if the formulation has any sensitization potential. It is recommended that a new sensitization study be presented.

### Label

Based on the present toxicity profile the signal word remains "Caution"

Oral Toxicity LD<sub>50</sub>

Dermal Toxicity LD<sub>50</sub>

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- 2. Buehler & Griffiths. Experimental Skin Sensitization in the Guinea pig and man - Animal Models in Dermatology (H. I. Maibach ed) Churchill Livingstone, Edinburgh, London, NY, 1975.

Inhalation Toxicity Category III

Eye irritation Category III

Dermal irritation Category IV

The Precautionary Statement must include

Harmful if swallowed, absorbed through skin or inhaled  
 Causes moderate eye irritation. Avoid contact with skin,  
 eyes and breathing dust, vapor or spray mist. Wash  
 Thoroughly with soap and water after handling. Remove  
 contaminated clothing and wash before reuse.

The statement of Practical Treatment must include:

If swallowed: call a physician or poison control center.

Drink 1 or 2 glasses of water and induce vomiting by  
 placing fingers in back of throat. Do not induce vomiting or  
 give anything by mouth to an unconscious person.

If on skin: wash with plenty of soap and water

If inhaled: Remove victim to fresh air, if not breathing  
 give artificial respiration, preferably mouth to mouth.

Get medical attention

If in eyes: Flush eyes with plenty of water. Call a physician if  
 irritation persists.

Depending upon the results of the requested sensitization  
 Test further additions to the precautionary statements  
 may have to be made

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: (21) Reviewer: L. Markarian  
 MRID No.: 417757-01 Report Date: 4/25/91  
 Testing Laboratory: North View Pacific Laboratories, Inc. Report No. YOK022G  
 Author(s): M. J. Deenihan  
 Species: Rabbit, New Zealand White (Elkhorn rabbitry, Waterville Co.)  
 Sex: 5♂ & 5♀ Wt.: 2.0 - 2.6 kg.  
 Test Material: Decosalt 35 Fine Yellow Powder  
 Quality Assurance (40 CFR §160.12): included

Summary:

1. LD50 (mq/kg): Males = \_\_\_\_\_; Females = \_\_\_\_\_; Combined = \_\_\_\_\_;
2. The estimated LD50 is 72000 mg/kg
3. Tox. Category: III. Classification: ... white

Procedure (Deviations From §81-2): Test material was applied to the shaved dorsum of rabbits moistened with few drops of deionized water, held in contact with skin with surgical gauze & tape. The trunks of the animals were wrapped in dental dam & gauze. At 24 hrs the wrappings were removed the sites rinsed with water. Animals were observed for 14 days. Body weights were recorded at initiation and on days 7 & 14. Necropsy was performed on all animals.

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
<u>2000</u>	<u>0/5</u>	<u>0/5</u>	<u>0/10</u>

Symptomology & Gross Necropsy Findings:

There was no mortality. Diarrhea observed in one male on day 7. At necropsy one animal showed gc in the intestines. There was no other sign of gross pathology.

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## DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: ( 21 ) Reviewer: L. Markarian  
 MPID No.: 417757-08 Report Date: 4/26/91  
 Testing Laboratory: Product Safety Labs Report No. T-513  
 Author(s): Ralph Shapiro  
 Species: Rat Sprague Dawley  
 Sex: 50♂ + 50♀ Weight: ♂ 225-240g, ♀ 220-242g  
 Source: Hilltop Lab Animals, Scottsdale Pa  
 Test Material: Deconox 35, NVP #UOK0026 (PO # NVP-026) Yell. p. c.  
 Quality Assurance (40 CFR §160.12): Included

## Summary:

- LC<sub>50</sub> (mg/kg): Males = \_\_\_\_\_; Females = \_\_\_\_\_; Combined = \_\_\_\_\_
- The estimated LC<sub>50</sub> is > 4.4 mg/L
- Mean Concentration: 4.4 mg/L
- Tox. Category: III. Classification: Low Inhalation

Procedure (Deviations From §81-2): Exposure was in a 100L rectangular Perspex chamber. The aerosol was generated by packing the test material in a DF183 weight dust container fitted with a stainless steel cutting blade driven with a Masterflex (Model 1520-30) adjustable Motor. Compressed air was supplied from a dust generator at 31psi. Approximately 6.71pm of filtered room air was applied to dilute the generated aerosol. The aerosol was fed directly into the chamber through the dust outlet assembly. Chamber concentrations were measured by sampling from the breathing zone using membrane filter at the sampling rate of 41pm for 0.5 minute. Particle size

## Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
4.4	0/5	0/5	0/10

Analysis & distribution was determined using an eight-stage Andersen Cascade impactor. MMAD and standard deviation were determined graphically. Chamber air flow was monitored throughout the exposure & recorded periodically. It varied 32.2 - 37.7 and averaged 35.71pm is measured by calibrated flow meters. The total exposure for the test was 4 1/2 hrs. Time of equilibration was 6.44 - 12.33 minutes for 50♂ + 50♀, respectively. At the end of 4 hrs the chamber was operated with clean air for 30 minutes. Observations were at 15 min intervals during the first hour of exposure, and at 30 min intervals to the end of exposure. Animals were observed individually at the end of the exposure. No indication of observation intervals after that. Body weights were recorded on days 1, 2, 4, 7, 10, & 14. Necropsy was performed on all animals.

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Results

The average chamber concentration was 4.1 mg/L. However there was variation from 1.75 to 5.8 mg/L during exposure. The 1.75 mg/L value was not used for the average concentration. MMAD was derived for two samples and was 4.5 + 4.3  $\mu$ m. The Standard Geometric Deviation of 2.0 + 2.1, respectively. The particle size distribution shows that about 3.3% of particles during the first sample and 3.7% of particles during the second sampling were 2.1  $\mu$ m or smaller.

In chamber observation of test animals includes closed eyes, fur coated with test material. Due to poor visibility in the chamber observations were limited. When removed from the chamber all animals showed facial staining, ocular discharge and tail matting in fur. Beginning on day 1 post exposure, lethargy, ocular discharge, facial & ano-genital staining were observed in some. Anogenital staining persisted in 2 females to termination. Weight gain was low among the females at termination. At necropsy slight to moderate redness of the lungs were noted in all animals. There were no other signs of gross pathology.

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DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (21 ) Reviewer: L. Markarian  
 MRID No.: 417767-01 Report Date: 4/25/91  
 Testing Laboratory: North Uraw Pacific Laboratories Report No. X0K0226  
 Author(s): M.J. Desnick  
 Species: Guinea Pig, Hartley  
 Sex: Not Specified Weight: 374.6 - 470.9 g  
 Source: Camm Research, Wayne, NJ  
 Test Material: Ducosalt 31, Fine Yellow Powder  
 Positive Control Material: DNCB  
 Quality Assurance (40 CFR §160.12): included  
 Method: Buehler Method

Summary:  
 1. This product is / is not a dermal sensitizer.  
 2. Classification: Supplementary

Procedure (Deviation From §81-5): There was no prescreening to define the induction and elicitation concentrations. The test material was applied at 100% moistened with five drops of deionized water in 0.5 sq portions in Hilltop chambers for the first three induction applications. Some irritation was observed after the third induction therefore the inductions were continued at 50% in deionized water. Inductions were three times a week for two weeks. Period of exposure was 6 hrs. after each application the exposure site was rinsed with water. Ten animals were induced with test material and five with 0.5 ml of 0.1% DNCB in 10% ethanol. Two weeks after the last induction challenge was made at naive sites with "the appropriate material". Exposure for challenge was 24 hrs. Induction and challenge sites were scored at 24 hrs after application and at 48 hrs only challenge sites were scored according to Buehler. Results. There were no positive reactions in the TTT group at any interval after challenge. The positive control group showed 5/6 Grade 2 positive responses at 24 hrs, and two at 48 hrs.

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