



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 2.792-AU

Decco Salt NO 35-

FROM:

Lucy D. Markarian 4/2/91
Precautionary Review Section
Registration Support Branch
Registration Division (H75-05C)

10/1/91

TO:

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

APPLICANT:

Atochem - North America

Decco Agrichemicals Division

1713 California Ave.

Marrovia, Ca

FORMULATION FROM LABEL:

Active Ingredient(s):

2,4 Dichloro-4-nitroaniline

3, (3,5 dichlorophenyl) 1 (1-methylethyl) 2,4 dioxo -

1 imidazolidine carbonyl

3 by wt.

24.94

38.33

Inert Ingredient(s):

41.64

Total 100.03

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10/9

BACKGROUND:

Reviews dated 8/3/90 and 12/29/90 recommended submittal of Dermal Toxicity, Inhalation Toxicity and Dermal Sensitization Tests to support the registration of Decosalt 35 under EPA symbol 2792-AU. Attochem North America, Deico 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 concentrations were for 30 seconds. This is a shorter sample 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 not explained why it is left out of the average, when the inclusion 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 ^{Possibly} 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. Buchler method uses a pretest 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, noritened, 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 even necessary, because according to Buchler 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 & Buchler - 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. Buehler² 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 LD₅₀

Dermal Toxicity LD₅₀

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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.

if

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: Northview Pacific Laboratories, Inc. Report No. YOKO-226
 Author(s): M.J. Deenhan
 Species: Rabbit, New Zealand White (Elkhorn rabbitry, Watsonville, Ca.)
 Sex: ♂ & ♀ Wt.: 2.0 - 2.6 kg.
 Test Material: Decosalt 35 Fine Yellow Powder
 Quality Assurance (40 CFR §160.12): included

Summary:

1. LD₅₀ (mg/kg): Males = _____; Females = _____
 2. The estimated LD₅₀ is 72000 mg/kg
 3. Tox. Category: III Classification: G.I. irritant

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 trunk of the animals was wrapped in dental dam & gauze. At 24 hrs the wrappings were removed and 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
2000	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

There was no mortality. Diarrhea was observed in one male on day 7. At necropsy one animal showed gas 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.: 4177 57-08

Report Date: 4/25/91

Testing Laboratory: Product Safety Labs

Report No. T-513

Author(s): Ralph Shapiro

Species: Ratt. Sprague Dawley

Sex : 5♂ + 5♀

Weight: ♂ 225-240, ♀ 220-242 g.

Source: Hilltop Lab Animals, Scottsdale Pa

Test Material: Demozest 35, NVP #UOK0026 (PO # NVP-076) Yellow p...

Quality Assurance (40 CFR §160.12): Included

Summary:

1. LC₅₀ (mg/kg): Males = _____; Females = _____
 2. The estimated LC₅₀ is > 4.4 mg/L
 3. Mean Concentration: 4.4 mg/L
 4. Tox. Category : III . Classification: Core Invertebrate

Procedure (Deviations From §81-2): Exposure was in a 100 L rectangular Perspex chamber. The aerosol was generated by passing the test material into a DF113 Wright dust classifier fitted with a stainless steel cutting blade driven with a Masterflex (Model 7520-3C) adjustable Motor. Compressed air was supplied from a dust generator at 31 psi. Approximately 6.7 lpm of filtered ~~com~~ air was supplied 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 filters at the sampling rate of 4 lpm 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-page Andersen Comable
calculator. Mean and Standard deviation were determined graphically. Chamber
air flow was monitored throughout the exposure & recorded periodically. It
varied 32.2 - 37.7 and averaged 35.7 lpm vs measured by calibrated flow
meter. The total exposure for the test was 4 1/2 hrs. Time of equilibration was
6.44 ± 12.38 mins for 90 & 99%, 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 4.4 mg/L . However there was variation from 1.85 to 5.8 mg/L during exposure. The 1.85 mg/L value was not used for the average concentration. MMAD was derived for two samples and was 4.5 & 4.3 in the Standard Geometric distribution of 2.0 & 2.1 , respectively. The particle size distribution shows that about 31.8% of particles during the first sample and 32.7% of particles during the second sample were 2.1μ or smaller.

In chamber observation of the 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 test material 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 uropyg was 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.: 417757-01 Report Date: 4/25/91
 Testing Laboratory: North Vassar Pacific Laboratories Report No. XOK0226
 Author(s): M.J. Deanehan
 Species: Guinea Pig, Hartley
 Sex: Not specified Weight: 374.6 - 470.9 g
 Source: Camm Research, Wayne, NJ
 Test Material: Dacco Salt 8.5, 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 §81-6): There was no prescreening to define

The induction and elicitation concentrations. The test material was
applied at 100% moistened with ten 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 test 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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