10-1-91
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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 2792-AU
Decco Salt NO 3-

FROM: Lucy D. Markarian 4/25/91 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.
Monrovia, Ca

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
2,6 Dichloro - 4 nitroaniline	24.9%
3,(3,5 dichlorophenyl)1(1-methylethyl)2,4 dioxo - 1 imidazolidine Carboxamide	33.33
Inert Ingredient(s):	41.6%
Total	100.0%

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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 Deccosalt 35 under EPA symbol 2792-AU. Atochem North American, Decco Agrichemicals Division has now submitted the rquired 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 5.8 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's not explained why it is left out of the average, when the inclusion would not have changed the toxicity catagory. So much variation in the chamber concentration signifies uneven exposure and the average concentration does not really mean very much.

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. However this higher MMAD value is considered acceptable.

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

1. Buehler method uses a pretest screening to define the induction and elicitation concentrations. He states[-1] 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, moistened, 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 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 inquiry 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

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 defined at any time before or during the test.

3. There were no naive controls. Buehler[2] 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 Cat III

Dermal Toxicity Cat III

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

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Inhalation Toxicity — Catagory III

Eye irritation — Catagory III

Dermal irritation — Catagory 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

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-2G
Author(s): M.T. Deenihan
Species: Rabbit, New Zealand White (Elkhorn rabbitry, Watsonville Ca.)
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. LD_{50} (mg/kg): Males = _____; Females = _____; Combined = _____;
2. The estimated LD_{50} is >2000 mg/kg
3. Tox. Category: III. Classification: (Guideline

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 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

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

Product Manager: (21)
MPID No.: 41757-03
Testing Laboratory: Product Safety Labs
Author(s): Ralph Shapiro
Species: Rat, Sprague Dawley
Sex : 50♂ & 5♀ Weight: ♂225-249g, ♀ 220-242 g
Source: Hilltop Lab Animals, Scottdale Pa
Test Material: Decozaat 35, NVP #40K0026 (PO # NVP-036) Yellow pa...
Quality Assurance (40 CFR §160.12): Included

Reviewer: L. Markarian
Report Date: 4/26/91
Report No. T-513

Summary:

1. LC_{50} (mg/kg): Males = _____; Females = _____; Combined = _____
2. The estimated LC_{50} is > 4.4mg/L
3. Mean Concentration: 4.4mg/L
4. Tox. Category : III . Classification: Core minimum

Procedure (Deviations From §81-2): Exposure was in a 100L rectangular perspex chamber. The aerosol was generated by packing the test material into DF183 Wright dust cartridge fitted with a Stainless Steel cutting blade driven with a Masterflex (Model 7520-35) adjustable Motor. Compressed air was supplied to the dust generator at 31psi. Approximately 6.7 lpm of filtered room 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 4lpm 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 35.7 lpm as measured by calibrated flow meter. The TOTAL exposure for the test was 4½ hr - Time of equilibration was 6.44 - 12.38 minutes for 90 & 99% respectively. At the end of 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 exposures. 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 1.85 to 5.8 mg/L daily exposure. The 1.85 mg/L value was not used for the average concentration. MMAD was derived for Two samplings and was 4.5 & 4.3 with Standard Geometric deviation of 2.0 & 2.1, respectively. The particle size distribution charts That about 31.8% of particles during the first sampling and 32.7% of particles during the second sampling were 2.1 μ 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 test material on 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.

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

Product Manager: (21)
Reviewer: L. Markarian
MRID No.: 417767-01
Report Date: 4/26/91
Testing Laboratory: North Crow Pacific Laboratories
Report No. XOKO22G
Author(s): M.J. Donahue
Species: Guinea Pig, Hartley
Sex: Not specified
Weight: 374.6 - 470.9 g
Source: Camm Research, Wayne NJ.
Test Material: Durosalt B.T. 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 few drops of deionized water in 0.5gm patches in Hilltop chambers for the first three inductions 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 inducted with test material and five with 0.5ml of 0.1% DNCB in 10% Ethanol.

Two weeks after the last induction challenge was made at native 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 site 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 5/5 Grade I positive responses at 24 hrs, and Two at 48 hrs