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

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#770

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: Toxicology Review for the Reregistration Eligibility Document on Sodium Fluoroacetate

To: Karen Whitby, Ph.D., Head, Reregistration Section
Chemical Coordination Branch
Health Effects Division (7509C)

From: Patricia McLaughlin, Ph.D. P M McLaughlin 11/29/94
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Chemical: Sodium fluoroacetate; Compound 1080
Case 3073; chemical number 075003 (PC code); CAS Reg No. 62-74-8

S469827, D206495

Products: Impregnated collar/tag on goats and sheep

Considerations: In phase 4 we stated that studies for guidelines 81-1, 81-2, 81-4, and 81-5 were acceptable. All other study requirements were waived due to the severe acute toxicity of the compound and the conditional use in a livestock protection collar.

1. Toxicology Data Base

The toxicological data base on sodium fluoroacetate is adequate and will support reregistration eligibility.

a. Acute Toxicity

ACUTE DATA

TEST	RESULTS	CATEGORY
Oral LD50--rat	LD_{50} 0.22 mg/kg	I
Dermal LD50--rabbit	LD_{50} 277.1 mg/kg M; 324.2 mg/kg F	II
Eye irritation--rabbit	slight irritation	III
Dermal irritation--rabbit	not irritating	IV

An acute oral toxicity study with rats used 90.0% sodium fluoroacetate. The LD_{50} was 0.22 mg/kg, which was toxicity category I (guideline 81-1; MRID 40016971). An acute oral toxicity study with coyotes used doses of sodium fluoroacetate diluted with water. The LD_{50} was 0.12 mg/kg sodium fluoroacetate, which was toxicity category I (guideline 81-1; acc 243665). Literature reports have indicated oral LD_{50}s of 100 ug/kg for rats, 500 ug/kg for mice, 66 ug/kg for dogs, and 340 ug/kg for rabbits. The human oral LD_{lo} has been reported as 714 ug/kg, and the dangerous dose for humans has been stated as 0.5-2.0 mg/kg (Sax and Lewis, 1989).

An acute dermal toxicity study with rabbits used technical sodium fluoroacetate. The LD_{50} was 277.1 mg/kg for males and 324.2 mg/kg for females. The animals showed lethargy, diarrhea, and convulsions preceding death, along with extensive hemorrhage of the thymus and congestion of the lungs. This was toxicity category II (guideline 81-2; MRID 152129).

A primary eye irritation study used a 1.0% aqueous solution of sodium fluoroacetate with rabbits. There was slight irritation and slight chemosis, which was toxicity category III (guideline 81-4; MRID 40402603). A primary dermal irritation study also used a 1.0% aqueous solution on rabbits. There was only transient slight edema on one rabbit and the compound was considered not irritating (guideline 81-5; MRID 40402604).

Requirements for acute inhalation toxicity and dermal sensitization studies were waived.

b. Subchronic Toxicity

Technical sodium fluoroacetate was administered by gavage for 13 weeks to Crl:CD(SD)Br rats. The doses were 0, 0.05, 0.20, and 0.50 mg/kg/day. The NOEL was 0.05 mg/kg/day. The LOEL was 0.20 mg/kg/day, based on dose-related findings in histopathology (hypospermatogenesis, fusion bodies, and immature or abnormal sperm) and decreased size and weight of testes and epididymides in males. Females had dose-related increases in absolute and relative heart weights at the mid and high doses (guideline 82-1; Wolfe, 1988).

In a study with male Sprague Dawley rats, the animals were dosed with 0, 0.07, 0.19, or 0.71 mg/kg/day of sodium fluoroacetate in their drinking water for seven days. This was followed by 21 days without the test compound. A group of rats from each dose level was killed each day of treatment and on days 3, 7, 14, and 21 after dosing. The testes, kidneys and liver were examined. Testicular atrophy and nonreversible tubular degeneration were found at the mid and high dose. Testicular atrophy with reversible

tubular degeneration was found at the low dose. No effects on liver or kidney were seen. The lowest dose was the LOEL (MRID 40016990).

c. Metabolism

Fluoroacetate in the mammalian body is converted to fluorocitrate. This compound inhibits the enzyme aconitase, thus blocking the citric acid cycle. This leads to accumulation of citric acid, which in turn causes convulsions and death from cardiac failure or respiratory arrest (Gribble, 1973).

Sodium fluoroacetate can be absorbed through the gastrointestinal tract, respiratory tract, or open wounds, but only slowly through intact skin (Sax and Lewis, 1989).

d. Reference Dose (RfD) for Chronic Oral Exposure

The RfD was determined to be 0.00002 mg/kg/day. This was based on the 13-week oral rat study, in which the NOEL was 0.05 mg/kg/day. An uncertainty factor of 3000 was used to account for interspecies extrapolation, intraspecies differences, lack of additional studies, and use of a subchronic study (Ghali, 1994).

REFERENCES

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