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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

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MAY -5 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: RfD/Peer Review Report of CADRE (AC 263,222)

CASRN. 81334-60-3
EPA Chem. Code: 128943
Caswell No.

FROM: George Z. Ghali, Ph.D. G. Ghali
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The Health Effects Division RfD/Peer Review Committee met on April 21, 1994 to discuss and evaluate the toxicology data submitted in support of an experimental use permit and a temporary tolerance for AC 263,222 and to assess the Reference Dose (RfD) for this chemical.

The Committee was also asked to address the following issues: 1) whether a new chronic feeding study in dogs would be required since the existing study did not establish a no-observable effect level for skeletal muscle degeneration, and 2) whether maternal toxicity effects observed at the lowest dose level in the developmental toxicity study in rabbits and thought to be treatment-related are biologically significant and, consequently, whether or not a new study would be required.

Material available for review included data evaluation records for a chronic toxicity study in dogs **(83-1b)**, a subchronic toxicity study in rats **(82-1a)**, developmental toxicity studies in rats and rabbits **(83-3a and -3b)** and a repeated-dose dermal toxicity study in rabbits **(82-2)**.

The Committee considered the chronic toxicity study in dogs (83-1b, MRID No. 42711421), the subchronic toxicity studies in rats (82-1a, MRID No. 42711419), the developmental toxicity study in rats and rabbits (83-3a and -3b, MRID No. 42711422; 42711423) and the data evaluation records (HED Doc. No. 00000; 00000; 00000; 00000) to be adequate.

Although the chronic toxicity study in dogs failed to establish a no-observable effect level (NOEL), the Committee determined that effects seen at the lowest dose level were minimal and therefore, the NOEL might not be much lower than the lowest dose tested. On this basis, the Committee did not recommend for a new study in dogs.

The Committee recommended to raise the lowest observable effect level (LOEL) for maternal toxicity in the rabbit developmental toxicity study from 175 mg/kg/day, the lowest dose tested, to 500 mg/kg/day based on decreased body weight gain and decreased food consumption. In this study, at dose levels equal to or lower than 500 mg/kg/day, mortality in most cases, appeared to be the result of dosing errors and not treatment-related. The increased mortality at 700 mg/kg/day, on the other hand, was considered to be treatment-related. Therefore, the NOEL for maternal toxicity was considered to be 350 mg/kg/day. The NOEL and LOEL for developmental toxicity were left unchanged at 500 mg/kg/day and > 500 mg/kg/day, respectively.

The Committee recommended that an RfD for this chemical be established on the basis of the chronic toxicity study in dogs with an LOEL of 137 mg/kg/day. A total uncertainty factor (UF) of 3,000 was used; a UF of 100 to account for the inter-species extrapolation and intra-species variability, an additional UF of 10 to account for the lack of chronic and reproductive toxicity data in rats, and an additional UF of 3 to account for the lack of a NOEL in the critical study. On this basis, the RfD was calculated to be 0.05 mg/kg/day.

It should be noted that this chemical is a new chemical and still in experimental stages and has not been reviewed by the World Health Organization (WHO) up to this date.