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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

January 5, 2000

MEMORANDUM

SUBJECT: ***CACODYLIC ACID:*** Report of the FQPA Safety Factor Committee.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chair
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Diana Locke, Risk Assessor
Registration Action Branch 2
Health Effects Division (7509C)

PC Code: ~~061402~~ 012501

The Health Effects Division (HED) FQPA Safety Factor Committee met on December 20, 1999 to evaluate the hazard and exposure data for cacodylic acid and recommended that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) is required when assessing the risks posed from the use of this pesticide.

I. HAZARD ASSESSMENT

(*Correspondence:* G. Reddy to B. Tarplee dated December 13, 1999)

1. Adequacy of Toxicity Database

The toxicology data base for cacodylic acid is adequate according to the Subdivision F Guidelines for a food-use chemical. However, the HIARC required a developmental neurotoxicity study in rats with cacodylic acid based on the observation of endocrine effects in the reproduction study (thyroid lesions) and other studies. The HIARC also recommended that acute and subchronic neurotoxicity studies be submitted due to concern for neurotoxic and neuropathological effects associated with other arsenical compounds.

2. Determination of Susceptibility

In the developmental toxicity study in rats, a qualitative increase in susceptibility was demonstrated following exposure to cacodylic acid. Developmental toxicity was observed as increased incidence of delayed/lack of ossification and suggestion of diaphragmatic hernia in the presence of minimal maternal toxicity (decreased body weight, body weight gain, food consumption, and gravid uterine weights).

The data provided no indication of increased susceptibility of rabbit fetuses following *in utero* exposure or of rat fetuses/pups following pre-/postnatal exposure to cacodylic acid. In these studies, developmental/offspring effects were observed only at or above treatment levels which produced maternal/parental toxicity.

II. EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

1. Dietary (Food) Exposure Considerations

(*Correspondence:* G. Reddy to B. Tarplee dated December 13, 1999)

Cacodylic acid (dimethylarsinic acid or DMAA) and its sodium salt are contact herbicides registered for use as defoliants on cotton.

Tolerances are currently established for residues of the defoliant cacodylic acid (dimethylarsinic acid), expressed as As_2O_3 in/on cottonseed at 2.8 ppm, in kidney and liver of cattle at 1.4 ppm, and in meat, fat, and meat byproducts (except kidney and liver) of cattle at 0.7 ppm [40 CFR §180.311]. There are no Codex MRLs for these compounds.

The HED Metabolism Committee concluded that the residue of concern is cacodylic acid *per se* (HED Metabolism Committee memo by C. Swartz and B. Cropp-Kohlligian dated 1/26/95). The tolerance expression will be cacodylic acid, calculated as As_2O_3.

No monitoring data are available. Field trial data are available, however, there are concerns about the adequacy of the analytical methods used to generate these data. In order to ensure that the residue levels will not be underestimated, radiovalidation data will be used to correct for the recoveries of the analytical method. Percent crop treated (%CT) information is also available for cacodylic acid.

The HED Dietary Exposure Evaluation Model (DEEM) is used to assess the risk from acute and chronic dietary exposure to cacodylic acid residues in food. The only food item of cotton consumed will be refined cottonseed oil. There is little or no consumption of cottonseed meal. Residues are expected to transfer to milk and meat through consumption of cotton gin trash bearing relatively high residues of cacodylic acid. At the time of this meeting, the DEEM analyses had not been completed. These analyses could be refined using anticipated residues calculated from field trial and radiovalidation data and the available %CT information which would result in a more realistic reflection of dietary food exposure resulting from the use of cacodylic acid.

2. Dietary (Drinking Water) Exposure Considerations
(*Correspondence:* D. Reider to B. Tarplee and Jean Holmes dated December 16, 1999)

The environmental fate database for cacodylic acid is adequate for the characterization of drinking water exposure. The data indicate that cacodylic acid is persistent under some conditions, with metabolic half-lives ranging from 20 days up to approximately one year. Cacodylic acid is not particularly mobile and is not expected to leach significantly, however, overland runoff may occur as cacodylic acid is transported with eroded soil and runoff.

Estimated Environmental Concentrations (EECs) for human health risk assessment will be based on a combination of modeling and monitoring:

> For surface water, PRZM EXAMS will be used to estimate exposure from cacodylic acid. SCIGROW will not be used for groundwater because it is not likely that cacodylic acid will leach under agricultural use conditions.
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> Monitoring sources include USGS (mostly ground water but with some surface water), BASINS STORET (surface water only), and published literature. In most cases, analysis was for total arsenic (unspeciated), however, limited surface and groundwater data exist for speciated arsenic (MSMA, Cacodylic acid, arsonite, and arsonate).

3. Residential Exposure Considerations
(*Correspondence:* G. Reddy to B. Tarplee dated December 13, 1999)

Cacodylic acid is used in residential settings for lawn renovation and weed control around evergreen, shrubs and deciduous ornamentals, buildings, fences, walls, flower beds, and gardens, brick and gravel walks, patios, curbs, gutters, sidewalks, and driveways. There are no label restrictions on the number of times cacodylic acid may be applied per year. For lawn renovation, it would probably be used only once. For spot weed control, it

could be used as often as necessary. Post-application exposure (dermal and ingestion) to infants and children could occur in the residential environment from contact with treated areas.

Since there are no chemical-specific data for post-application exposure resulting from the use of cacodylic acid in non-occupational settings, the *Draft Standard Operating Procedures for Residential Exposure Assessments* will be used as the basis for all calculations. No deviations from SOPs are expected.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The Committee recommended that the FQPA safety factor for protection of infants and children (as required by FQPA) should be retained.

2. Rationale for Requiring the FQPA Safety Factor

The FQPA SFC concluded that a safety factor is required because:

- a qualitative increase in susceptibility of fetuses (compared to dams) is demonstrated in the prenatal rat developmental toxicity study; and
- a developmental neurotoxicity study in rats is required for cacodylic acid based on concerns for endocrine effects observed in the reproduction and other studies.

3. Application of the Safety Factor - Population Subgroups / Risk Assessment Scenarios

Females 13-50 Population Subgroup: When assessing **Acute Dietary and Short-term Residential Exposures,** the safety factor should be **Retained at 10x** since there is concern for the qualitative increase in susceptibility observed in rat fetuses following *in utero* exposure to rats in the developmental study (which could potentially occur after a single dose); and since there is a data gap for the developmental neurotoxicity study in rats. The developmental neurotoxicity study may further define the neurotoxic potential observed in the developing fetus in the prenatal developmental study in rats.

All Population Subgroups: When assessing **Acute and Chronic Dietary and Residential Exposures of All Durations,** a safety factor is required since there is a data gap for the developmental neurotoxicity study. However, the safety factor can be **Reduced to 3x** since the concern for increased susceptibility seen after *in utero* exposure in the developmental study has no bearing on population subgroups other than females of child-bearing age.

4

FQPA SAFETY FACTOR COMMITTEE MEETING

20DEC1999

CACODYLIC ACID

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5