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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 13, 1999

MEMORANDUM

SUBJECT: *CARBARYL* - Reassessment Report of the FQPA Safety Factor Committee.

NOTE: THIS REPORT REPLACES THE PREVIOUS REPORT OF THE FQPA SAFETY FACTOR COMMITTEE DATED AUGUST 27, 1998 (HED Doc. No. 012834).

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

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

TO: Virginia Dobozy, Risk Assessor
Reregistration Action Branch 1
Health Effects Division (7509C)

PC Code: 056801

The Health Effects Division (HED) FQPA Safety Factor Committee (SFC) met on November 29, 1999 to re-evaluate the hazard and exposure data for carbaryl and maintained that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) should be retained at 10x when assessing the risks posed by the use of this pesticide. This report replaces the previous report of the FQPA Safety Factor Committee dated August 27, 1998 (HED Doc. No. 012834).

I. HAZARD ASSESSMENT

(*Memoranda:* V. Dobozy to V. Dobozy dated April 28, 1999 and November 15, 1999: HED Doc. Nos. 013333 and 013850.)

The toxicology data base for carbaryl was re-evaluated by the HED Hazard Identification Assessment Review Committee (HIARC) on April 6, 1999 and November 2, 1999 considering recently submitted developmental studies in rats and rabbits.

1. Adequacy of the Toxicology Database

The toxicology data base for carbaryl is incomplete. There is a data gap for the multi-generation reproduction study in rats. The registrant has stated that this study is in progress and that the estimated time of submission to the Agency is late 2000.

Since the last meeting of the FQPA SFC (August 17, 1998), acceptable guideline prenatal developmental studies in rats and rabbits have been submitted to the Agency. Additionally, there is an acceptable developmental neurotoxicity study for carbaryl, however, there is uncertainty about the developmental neurotoxicity NOAEL/LOAEL:

> Significant changes in some of the morphometric measurements of the brain were observed in the high-dose group; only the control and high dose groups were examined. EPA requested that measurements be done in the low- and mid-dose groups. The registrant has responded that the requested examinations are not possible because the tissues of the low- and mid-dose animals have been stored in a fixative for two years, which caused shrinkage. Therefore, comparison to the control group, which was not similarly stored, would not be valid. A re-examination of the control and high-dose groups was conducted. The re-assessment uncovered errors in some measures and confirmed some of the original findings. The additional statistical analyses, which attempted to account for multiple comparisons, rendered far fewer statistically significant findings, but some results, including data on pup cerebellar length, remained statistically significant. The decrease in the length of the cerebellum in 10 mg/kg/day female pups is still regarded as a treatment-related effect. The NOAEL/LOAEL for this study was originally regarded as tentative, awaiting information from the registrant. Since morphometric examinations of the mid-dose group are impossible, there remains some uncertainty about the NOAEL/LOAEL (HED Doc. No. 013850).

2. Determination of Susceptibility

The HIARC concluded that there is no evidence of increased fetal susceptibility in the prenatal developmental studies in rats and rabbits (for more information regarding developmental / reproductive toxicity of carbaryl, refer to HED Doc. No. 012731). Since there is a data gap for the multi-generation reproduction study in rats, susceptibility following pre-/post-natal exposure to carbaryl cannot be assessed. Likewise, an assessment of susceptibility in the developmental neurotoxicity study cannot be made since critical information is not available.

The FQPA SFC suggested that morphometric measurements such as those in question in the developmental neurotoxicity study be made in the multi-generation reproduction study in rats in an attempt to address the uncertainties associated with the effect of concern (i.e., morphometric changes observed in the high dose animals which cannot be assessed at the lower doses).

II. EXPOSURE ASSESSMENT

1. Dietary (Food) Exposure Considerations
(*Correspondence:* C. Olinger to V. Dobozy and B. Tarplee dated November 18, 1999)

Carbaryl is a broad spectrum insecticide registered for use on many foods and residential uses. Permanent tolerances are established for residues of carbaryl in/on many agricultural commodities ranging from 0.1 to 100 ppm (40CFR§80.169). Transfer of residues to meat and milk is possible and tolerances for these commodities are established. Codex MRLs have been established for numerous commodities including fruits, grains, forage/fodder, and livestock commodities.

Carbaryl is used on many foods which are highly consumed by infants and children, including bananas, citrus fruits, peaches, beans, carrots, milk, meats, cereal grains and soybeans (1993 NAS report, Pesticides in the Diets of Infants and Children). Residues of carbaryl, however, are primarily surface residues and are, therefore, likely to be significantly removed from raw fruits and vegetables during normal preparation such as washing and peeling. The HED Metabolism Assessment Review Committee (MARC) has determined that only parent carbaryl should be regulated for plants, however, for livestock commodities, free and conjugated forms of carbaryl, 5,6-dihydro-5,6-dihydroxy carbaryl, and 5-methoxy-6-hydroxy carbaryl should be regulated.

A variety of residue data sources are available for carbaryl, including field trial data, Pesticide Data Program (PDP) monitoring data, and FDA surveillance data. Information on percent of crop treated (%CT) has been requested from the Biological and Economic Analysis Division (BEAD) for this pesticide.

PDP monitoring data (1996) indicate quantifiable residues of Carbaryl (well below tolerance level) in approximately 7% of the samples tested (342 samples with detections in a total of 4832 samples) including apples, apple juice, grapes, green beans, oranges, peaches, spinach, and sweet peas. There were no detections in carrots, sweet potatoes, and tomatoes. The rate of detection was highest for apple juice (32%) but the maximum concentration detected was 0.1ppm. A task force is currently developing single-serving sample data for carbamates, but a full year of data will not be available at the time the risk assessment for carbaryl is due.

The HED Dietary Exposure Evaluation Model (DEEM) will be used to assess the risk from acute and chronic dietary exposure to carbaryl residues in food. At the time of this meeting, an acute analysis had not yet been conducted. Anticipated residues were calculated in 1990, but will be updated for the RED using monitoring data whenever possible. The result will be a less exaggerated representation of dietary food exposure resulting from the use of carbaryl.

2. Dietary (Drinking Water) Exposure Considerations
(*Correspondence:* J. Holmes to B. Tarplee dated December 1, 1999)

The environmental fate data base for carbaryl is adequate for the characterization of drinking water exposure, although some submitted studies do not meet Agency data requirements. Fate data indicate that carbaryl has slight to moderate leaching potential, however, aerobic aquatic metabolism half-life was measured at approximately 5 days indicating an overall low potential for water contamination.

Some field monitoring data are available for carbaryl and are currently under review by EFED. The drinking water exposure assessment for carbaryl will be based on modeling output. Estimated Environmental Concentrations (EECs) will been calculated for ground and surface water based on the current EFED first level screening models, SCI-GROW and GENEEC respectively.

3. Residential Exposure Considerations
(*Correspondence:* S. Hanley to B. Tarplee dated November 22, 1999)

Carbaryl is currently registered for many residential uses: vegetable garden, fruit tree, lawn, ornamental, perimeter and pet treatments. Each use site for carbaryl includes many formulations such as baits, dusts, granular, sprays, ready to use and concentrated forms. Carbaryl is also formulated as a crack and crevice treatment and an in-the-wall bee treatment. Based on the registered use patterns, exposure to children and infants is most likely to occur from pet and lawn/landscaping uses.

A number of residential exposure studies have been submitted for carbaryl product application using various equipment. These studies are of sufficient scientific quality to be used for occupational/residential exposure assessments. The resulting exposure calculations for carbaryl will be compared to calculations made using PHED and Standard Operating Procedures (SOPs) for Residential Exposure Assessments. In addition to these chemical-specific data, one surrogate study was submitted for calculation of post-application exposure from treated turf (Jazzercise® model).

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The FQPA SFC recommended that the safety factor for protection of infants and children (as required by FQPA) should be **Retained at 10x.**

Additionally, the FQPA SFC suggested that morphometric measurements such as those in question in the developmental neurotoxicity study be made in the multi-generation reproduction study in rats in an attempt to address the uncertainties associated with the effect of concern (i.e., morphometric changes observed in the high dose animals which cannot be assessed at the lower doses).

2. Rationale for Retaining the FQPA Safety Factor

The FQPA SFC concluded that the safety factor should be retained because:

- The toxicology data base for carbaryl is incomplete; there is a data gap for the multi-generation reproduction study in rats;
- an assessment of susceptibility following pre-/post-natal exposure to carbaryl could not be made due to the data gap for the multi-generation reproduction study in rats; and
- there is concern for the results of the developmental neurotoxicity study (uncertainty about NOAEL/LOAEL; see Section I.1. above).

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

When assessing **Acute and Chronic Dietary Exposures and Residential (Non-occupational) Exposures of All Durations,** the safety factor should be **Retained at 10x** for **All Population Subgroups** since there is concern for the results of the developmental neurotoxicity study; and since there is a data gap for the multi-generation reproduction study in rats which could provide information relevant to all population subgroups (regardless of age or gender).

FQPA SAFETY FACTOR COMMITTEE MEETING

29NOV1999

CARBARYL (Revisit)

Name	Division/Branch
Jess Rowe	HED/RRB3
Betty Shackelford	SRRD/PB-3
Virginia Dobozy	HED/RRB1
Susan Hanley	HED/RRB1
Mike Metzger	HED/RRB1
Laurence Libelo	EFED/ERB IV
Rick Keigwin	RD
Susan Makris	HED/RRB4
Ray Kent	HED/RRB4
Jean Holman	EFED/ERB2
Ed Zager	HED
[illegible]	HED/SAB

6