**HED DOC. NO. 014634**

**August 07, 2001**

**MEMORANDUM**

**SUBJECT:** ***ZINC OMADINE*** - 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:** Timothy McMahon, Risk Assessor
Risk Assessment and Science Support Branch
Antimicrobials Division (7510C)

**PC Code: 088002**

The Health Effects Division (HED) FQPA Safety Factor Committee met on June 25, 2001 to evaluate the hazard and exposure data for zinc omadine and recommended that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) be retained at 10x in assessing the risk posed by this chemical.

## I. HAZARD ASSESSMENT

(*Memorandum:* T. McMahon to E. Zager dated 06/07/01)

1. Adequacy of Toxicity Database

The toxicology data base for zinc omadine is incomplete. There is a data gap for the two-generation reproduction study in rats. Also, the HIARC required a developmental neurotoxicity study be conducted with zinc omadine (see I.3. below).

2. Determination of Susceptibility

There is **qualitative** evidence of increased susceptibility following *in utero* exposure to zinc omadine in the developmental toxicity studies in both rats and rabbits. In rats, fetal effects were manifested as increased incidence of fused ribs at the same dose that caused only minimal maternal toxicity (salivation). In the rabbit study, fetal effects were manifested as increased post-implantation loss and decreased viable fetuses at the same dose that caused only minimal maternal toxicity (resorptions).

Reproductive susceptibility could not be assessed following pre-/postnatal exposure to zinc omadine since there is a data gap for the 2-generation reproduction study in rats.

3. Requirement of a Developmental Neurotoxicity Study

The HIARC concluded that a developmental neurotoxicity study with zinc omadine is required due to the observance of neurotoxicity and the presence of neuropathology (axonal degeneration) in the toxicology data base.

4. Other Findings in Open Literature

Publications in the open literature indicate neurotoxicity in adult animals at doses of approximately 3 mg/kg/day and higher (HED Doc. No. 013318).

## II. EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

(*Memorandum:* T. McMahon to E. Zager dated 06/07/01)

1. Dietary (Food) Exposure Considerations

Dietary exposure to zinc omadine can occur indirectly from the incorporation of zinc omadine into sponges as well as in dishwashing detergent. Zinc omadine is also incorporated into plastics that are used in manufacture of food storage containers. Residues of zinc omadine are assumed to exist on dishware and food contact surfaces from these uses.

There are no agricultural uses for zinc omadine and no metabolites of zinc omadine that currently require regulation. FDA Models and worst-case assumptions were employed to estimate potential dietary exposure (Recommendations for Chemistry Data for Indirect Food Additive Petitions; June 1995, FDA).

2. Dietary (Drinking Water) Exposure Considerations

Drinking water exposures to zinc omadine were estimated using EPA methodologies. There were no monitoring data available for zinc omadine so worst case assumptions were made regarding exposure (i.e. drinking water exposure was assumed to be equal to the residue that was estimated to leach from sponges or that was contained in dishwashing liquid).

3. Residential Exposure Considerations

Zinc omadine is registered as a preservative for many home use products. Post-application exposure to infants and children could occur as a result of this use. No chemical-specific exposure data are available for zinc omadine. The *Draft Standard Operating Procedures for Residential Exposure Assessments* will be used as the basis for all post-application risk assessment scenarios.

## 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** at 10x for zinc omadine.

2. Rationale for Retaining the FQPA Safety Factor

The FQPA SFC concluded that the FQPA safety factor be **retained** at 10x for the following weight-of-evidence considerations:

- there is qualitative evidence of increased susceptibility following *in utero* exposure to zinc omadine in the developmental toxicity studies in rats and rabbits;
- there is a data gap for the 2-generation reproduction study in rats;
- susceptibility can not be assessed following pre-/postnatal exposure to zinc omadine since there is a data gap for the 2-generation reproduction study in rats; and

- a developmental neurotoxicity study with zinc omadine is triggered due to the observance of neurotoxicity and the presence of neuropathology (axonal degeneration) in the toxicology data base.

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

The safety factor is required for **All Population Subgroups** when assessing **Acute and Chronic Dietary Exposure and Residential Exposures of All Durations** due to the weight of the evidence stated above.