

surface water and groundwater due to the use of cyromazine.

3. *From non-dietary exposure.* The term "residential exposure" is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets).

Cyromazine is not registered for use on any sites that would result in residential exposure. There are no currently existing or proposed uses for cyromazine in residential or public sites and therefore no residential risk assessment was performed.

4. *Cumulative effects from substances with a common mechanism of toxicity.* Section 408(b)(2)(D)(v) of the FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity."

EPA does not have, at this time, available data to determine whether cyromazine has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to cyromazine and any other substances and cyromazine does not appear to produce a toxic metabolite produced by other substances. EPA has determined, however, that there is no known mechanism of toxicity that would support grouping cyromazine by a common mechanism with atrazine, simazine, and cyanazine. For the purposes of this tolerance action, therefore, EPA has not assumed that cyromazine has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

D. Safety Factor for Infants and Children

1. *In general.* Section 408 of the FFDCA provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal

and postnatal toxicity and the completeness of the data base on toxicity and exposure unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a MOE analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans.

2. *Prenatal and postnatal sensitivity.* There is no evidence of susceptibility and no residual uncertainties for pre- and post-natal toxicity resulting from exposure to cyromazine.

3. *Conclusion.* There is a complete toxicity data base for cyromazine and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. EPA determined that the 10X Safety factor to protect infants and children should be reduced to 1X because:

- There is no evidence of increased susceptibility (quantitative or qualitative) to rats or rabbits following in utero exposure or post-natal exposure to rats. In the prenatal developmental toxicity study in rats, the NOAEL for developmental toxicity was higher than the maternal NOAEL. In the developmental toxicity study in rabbits, no evidence of developmental toxicity was noted. For developmental toxicity, the NOAEL was > 60 mg/kg/day highest dose tested (HDT). In the two-generation reproduction study in rats no reproductive effects were observed. In this study, the reproductive NOAEL is ≥ 150 mg/kg/day (HDT). No neurotoxic effects were observed in the available data, and there is no requirement for a developmental neurotoxicity study. Further, exposure assessments have been conducted in a manner unlikely to underestimate exposure.

- The dietary drinking water assessment utilizes water concentration values generated by models and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.

- The dietary food exposure assessment is based on current and proposed registrations and is completely unrefined (i.e. tolerance level residues and 100% crop treated). The dietary exposure analysis will not underestimate exposure/risk.

- No residual uncertainties were identified in the exposure database.
- There are no residential uses for cyromazine.

E. Aggregate Risks and Determination of Safety

To estimate total aggregate exposure to a pesticide from food, drinking water, and residential uses, the Agency calculates DWLOCs which are used as a point of comparison against the model estimates of a pesticide's concentration in water (EECs). DWLOC values are not regulatory standards for drinking water. DWLOCs are theoretical upper limits on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food and residential uses. In calculating a DWLOC, the Agency determines how much of the acceptable exposure (i.e., the PAD) is available for exposure through drinking water [e.g., allowable chronic water exposure (mg/kg/day) = cPAD - (average food + residential exposure)]. This allowable exposure through drinking water is used to calculate a DWLOC.

A DWLOC will vary depending on the toxic endpoint, drinking water consumption, and body weights. Default body weights and consumption values as used by the USEPA Office of Water are used to calculate DWLOCs: 2 liter (L)/70 kg (adult male), 2L/60 kg (adult female), and 1L/10 kg (child). Default body weights and drinking water consumption values vary on an individual basis. This variation will be taken into account in more refined screening-level and quantitative drinking water exposure assessments. Different populations will have different DWLOCs. Generally, a DWLOC is calculated for each type of risk assessment used: Acute, short-term, intermediate-term, chronic, and cancer.

When EECs for surface water and groundwater are less than the calculated DWLOCs, OPP concludes with reasonable certainty that exposures to the pesticide in drinking water (when considered along with other sources of exposure for which OPP has reliable data) would not result in unacceptable levels of aggregate human health risk at this time. Because OPP considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of comparison in drinking water may vary as those uses change. If new uses are added in the future, OPP will reassess the potential impacts of residues of the pesticide in drinking water as a part of the aggregate risk assessment process.

1. *Acute risk.* An appropriate endpoint attributable to a single dose (exposure) of cyromazine was not observed in oral toxicity studies. Thus, an acute dietary endpoint was not chosen, and cyromazine is not expected to pose an acute risk.