

pesticides from the source water. The primary use of these models by the Agency at this stage is to provide a coarse screen for sorting out pesticides for which it is highly unlikely that drinking water concentrations would ever exceed human health levels of concern.

Since the models used are considered to be screening tools in the risk assessment process, the Agency does not use estimated environmental concentrations (EECs) from these models to quantify drinking water exposure and risk as a %RfD or %PAD. Instead drinking water levels of comparison (DWLOCs) are calculated and used as a point of comparison against the model estimates of a pesticide's concentration in 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 from residential uses. Since DWLOCs address total aggregate exposure to fenhexamid they are further discussed in the aggregate risk sections in Unit III.E.

Based on the FIRST and SCI-GROW models the estimated environmental concentrations (EECs) of fenhexamid for acute and chronic surface water exposures are estimated to be 28.7 parts per billion (ppb) and 1.14 ppb, respectively. The EECs for acute and chronic ground water exposure is estimated to be 0.0007 ppb.

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). Fenhexamid is not registered for use on any sites that would result in residential exposure.

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 fenhexamid 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 fenhexamid and any other substances and fenhexamid does not appear to

produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that fenhexamid 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.* In the rat and the rabbit developmental toxicity studies, neither quantitative nor qualitative evidence of increased susceptibility of fetuses to *in utero* exposure to fenhexamid was observed. In the rat reproduction study, qualitative susceptibility was evidenced as significantly decreased pup body weights in both generations during the lactation period (on lactation days 7, 14, and 21 in the F₂ generation and lactation days 14 and 21 in the F₁ generation offspring) in the presence of lesser maternal toxicity (alterations in clinical chemistry parameters and decreased organ weights without collaborative histopathology). Considering the overall toxicity profile and the doses and endpoints selected for risk assessment for fenhexamid, the degree of concern for the effects observed in this study was characterized as low, noting that there is a clear NOAEL and well-characterized dose response for the offspring effects observed and that these effects occurred in the presence of parental toxicity. No residual uncertainties were identified. The NOAEL of 17 mg/kg/day from the chronic dog study used to establish the

chronic Reference Dose (cRfD) for the General Population (no aRfD was established for any population subgroup) is lower than the NOAEL of 38.2 mg/kg/day in the reproduction study in which the offspring effects of concern were observed (LOAEL = 406 mg/kg/day).

3. *Conclusion.* There is a complete toxicity data base for fenhexamid 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 for the following reasons:

- There are no residual uncertainties for pre and/or post natal toxicities via the oral route since the doses selected for overall risk assessments would address the concerns for the developmental and offspring toxicities seen in the above mentioned studies.
- There are no residual uncertainties for pre and/or post natal toxicities via the dermal route since the dose/endpoint/study/species of concern was used for dermal-risk assessment.
- The toxicology data base is complete.
- Developmental neurotoxicity studies are not required for fenhexamid based on the following weight-of-the-evidence considerations:
 - Lack of evidence of abnormalities in the development of the fetal nervous system in the pre/post-natal studies.
 - Neither brain weight nor histopathological examination of the nervous system was affected in the subchronic and chronic studies.
 - Decreased body temperatures observed in male rats in the acute neurotoxicity study were not considered to be toxicologically significant.
- The dietary (food) exposure assessment utilizes existing and proposed tolerance level residues and assumes 100% of crops treated with fenhexamid. The assessment is based on reliable data and is not expected to underestimate exposure/risk.
- Conservative assumptions are used in the drinking water models. The drinking water exposure assessment is not expected to underestimate exposure/risk.
- Fenhexamid is not registered for use sites that would result in residential exposure.

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