

2. *Prenatal and postnatal sensitivity.* EPA concluded that there is low concern, and no residual uncertainty, for pre- and/or postnatal toxicity resulting from exposure to emamectin, based on the following:

i. There is no quantitative or qualitative evidence of increased susceptibility of rat and rabbit fetuses to *in utero* exposure in developmental studies. There is no quantitative evidence of increased susceptibility of rat offspring in the two generation reproduction study, however, an increase in qualitative susceptibility was determined. EPA determined that the concern is low because:

(a) There was a clear NOAEL for offspring toxicity.

(b) Effects unique to offspring (decreased fertility in F<sub>1</sub> adults, and clinical signs (tremors and hind limb extensions during and following lactation)) were seen at the same dose that caused parental systemic toxicity (decreased body weight gain and histopathological lesions in the brain and spinal cord).

(c) The decreased fertility seen in F<sub>1</sub> adults may have been due to histopathological lesions in the brain and central nervous system (seen in both F<sub>0</sub> and F<sub>1</sub> generations), rather than due to a direct effect on the reproductive system.

ii. There is evidence of increased qualitative and quantitative susceptibility in the rat developmental neurotoxicity study, but EPA determined that the concern is low because: Although multiple offspring effects (including decreased pup body weight, head and body tremors, hind limb extension and splay, changes in motor activity and auditory startle) were seen at the highest dose, and no maternal effects were seen at any dose, there was a clear NOAEL for offspring toxicity at the low dose, and the offspring LOAEL (at the mid dose) is based on a single effect seen on only one day (decreased motor activity on PND 17) and no other offspring toxicity was seen at the LOAEL.

3. *Conclusion.* EPA concluded that the toxicology database was complete for FQPA purposes and that there are no residual uncertainties for pre-/post-natal toxicity. Based on the quality of the data, EPA determined that the special

FQPA SF should be reduced to 1x. However, as explained in Unit III.3.B. of this preamble, EPA determined that an additional 3x or 10x modifying uncertainty factor should be used for short-term or intermediate-term exposure, respectively. The recommendation for the 1x FQPA SF is based on the following:

- The toxicological database is complete for FQPA assessment.
- The acute dietary food exposure assessment utilizes anticipated residue estimates based on carefully reviewed field trial data and PCT data verified by EPA for several commodities (100% crop treated was assumed for remaining commodities). By using the 99.9<sup>th</sup> percentile exposure values for comparison to the aPAD, actual risks are not likely to be underestimated.
- The chronic dietary food exposure assessment utilizes tolerance level residue estimates and PCT data verified by EPA for several commodities (100% crop treated was assumed for remaining commodities). This assessment is somewhat refined and based on reliable data that is not likely to underestimate exposure/risk.
- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- There are no proposed or existing residential uses for emamectin.

#### *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 ground water are less than the calculated DWLOCs, EPA concludes with reasonable certainty that exposures to the pesticide in drinking water (when considered along with other sources of exposure for which EPA has reliable data) would not result in unacceptable levels of aggregate human health risk at this time. Because EPA 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, EPA 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.* Using the exposure assumptions discussed in this unit for acute exposure, the acute dietary exposure (at the 99.9<sup>th</sup> percentile) from food to emamectin will occupy 29% of the aPAD for the U.S. population, 23% of the aPAD for females 13 years and older, 51% of the aPAD for all infants (<1 year old) and 58% of the aPAD for children 3–5 years old. In addition, there is potential for acute dietary exposure to emamectin in drinking water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in the following Table 3: