

than 1,000 mg/kg/day, the highest dose tested (HDT); a LOAEL was not reached.

iii. *Prenatal developmental toxicity study—Metolachlor—Rabbit.* The maternal toxicity LOAEL was 360 mg/kg/day based on an increased incidence of clinical observations (persistent anorexia) and decreased body weight gain. The NOAEL was 120 mg/kg/day. The developmental toxicity LOAEL was not established. The NOAEL was 360 mg/kg/day.

iv. *Prenatal developmental toxicity study—S-metolachlor—Rabbit.* The maternal toxicity NOAEL was 20 mg/kg/day with a LOAEL of 100 mg/kg/day based on clinical signs of toxicity.

No significant treatment related developmental toxicity was noted at the dose levels tested. The developmental toxicity NOAEL was equal to or greater than 500 mg/kg/day, HDT; a LOAEL was not reached.

3. *Reproductive toxicity study.* No reproduction studies with s-metolachlor are available, however, in the two-generation reproduction study with metolachlor in rats, there was no evidence of parental or reproductive toxicity at approximately 80 mg/kg/day, HDT. At this dose, there was a minor decrease in fetal body weight beginning at lactation day 4; the NOAEL was approximately 25 mg/kg/day. Since a similar body weight decrease was not seen on lactation day 0, the cause of the effect on later lactation days was most likely due to exposure of the pups to metolachlor in the diet and/or milk and therefore is not evidence of an increased quantitative susceptibility in post-natal animals.

The parental toxicity LOAEL was not established. The NOAEL was 1000 ppm (F0 males/females: 75.8/85.7 mg/kg/day; F1males/females: 76.6/84.5 mg/kg/day).

The reproductive toxicity LOAEL was not established. The NOAEL was 1000 ppm (F0 males/females: 75.8/85.7 mg/kg/day; F1males/females: 76.6/84.5 mg/kg/day).

The offspring LOAEL was conservatively established at 1000 ppm (F0 males/females: 75.8/85.7 mg/kg/day; F1males/females: 76.6/84.5 mg/kg/day) based on decreased body weight in F1 and F2 litters. The NOAEL is 300 ppm (F0 males/females: 23.5/ 26.0 mg/kg/day; F1males/females: 23.7/25.7 mg/kg/day).

4. *Prenatal and postnatal sensitivity.* The data bases for prenatal developmental toxicity for metolachlor and s-metolachlor are considered complete. The prenatal developmental studies in the rat and rabbit with both metolachlor and s-metolachlor revealed

no evidence of a qualitative or quantitative susceptibility in fetal animals. No significant developmental toxicity was observed in most studies even at the HDT.

The data base for reproductive toxicity of metolachlor is considered complete. No reproduction studies with s-metolachlor are available. In the two-generation reproduction study with metolachlor in rats, there was no evidence of parental or reproductive toxicity at approximately 80 mg/kg/day, HDT. At this dose, there was a minor decrease in fetal body weight beginning at lactation day 4; the NOAEL was approximately 25 mg/kg/day. Since a similar body weight decrease was not seen on lactation day 0, the cause of the effect on later lactation days was most likely due to exposure of the pups to metolachlor in the diet and/or milk and therefore is not evidence of an increased quantitative susceptibility in post-natal animals.

5. *Conclusion.* There is a complete toxicity data base for s-metolachlor when bridged with the database for metolachlor 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 removed. The FQPA factor is removed because:

- i. The toxicological database is complete for FQPA assessment;
- ii. There is no indication of quantitative or qualitative increased susceptibility of rats or rabbits to in utero and/or postnatal exposure;
- iii. A developmental neurotoxicity study is not required; and
- iv. The dietary (food and drinking water) and residential exposure assessments will not underestimate the potential exposures for infants and children.

D. 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 + chronic non-dietary, non-occupational 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 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 s-metolachlor 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 s-metolachlor on 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 from food to s-metolachlor will occupy <1 % of the aPAD for the U.S. population, <1 % of the aPAD for females 13 years and older, <1 % of the aPAD for all infant and children subpopulations. In addition, despite the potential for acute dietary exposure to s-metolachlor in drinking water, after calculating DWLOCs and comparing them to conservative model estimated environmental concentrations of s-metolachlor in surface and ground water, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in Table 2 of this unit: