

scientists considered several different potential common mechanism of toxicity groupings for these chemicals.

In reviewing this issue, EPA scientists were guided by several relevant Agency science policies, including Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity. Additionally, on March 19, 1997, the Agency presented to the FIFRA Scientific Advisory Panel (SAP) a draft case study illustrating the application of the Common Mechanism Guidance to the grouping of chloroacetanilide pesticides based on a common mechanism of toxicity. The SAP agreed with the Agency's conclusion that there is sufficient evidence to support the grouping of certain chloroacetanilides that cause nasal turbinate tumors by a common mechanism of toxicity.

Upon consideration of the SAP comments, EPA's own reviews and the data underlying these reviews, as well as additional information received by the Agency from registrants or presented in the open literature since the 1997 draft document, EPA has revised its science document discussing the potential grouping of chloroacetanilide pesticides, or a subgroup of them, based on a common mechanism of toxicity.

In the revised document entitled "The Grouping of a Series of Chloroacetanilide Pesticides Based on a Common Mechanism of Toxicity," EPA has concluded that only some of the pesticides that comprise the class of chloroacetanilides should be designated as a "Common Mechanism Group" based on the development of nasal turbinate tumors by metabolism to a highly, tissue reactive moiety, i.e., quinoneimine. Thus, only acetochlor, alachlor, and butachlor should be grouped based on a common mechanism of toxicity for nasal turbinate tumors. Although metolachlor does distribute to the nasal turbinates, and might produce a quinoneimine, it is

not apparent from currently available data that it shares the same target site in the nasal tissue as acetochlor, alachlor and butachlor. Although propachlor does produce a precursor of a quinoneimine, the available data do not support its tumorigenicity to the nasal turbinates.

In conclusion, it is the Agency's position, that only some chloroacetanilides, namely acetochlor, alachlor, and butachlor should be considered as a "Common Mechanism Group" due to their ability to cause nasal turbinate tumors. For purposes of a cumulative risk assessment as a part of the tolerance reassessment process for acetochlor, alachlor, and butachlor, these three pesticides will be considered as a Common Mechanism Group. Following the initiation of a cumulative risk assessment, further analyses of new or existing data may occur which could impact the Agency's evaluation of specific members of this group or the group as a whole.

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.* Prenatal developmental studies in the rat and rabbit revealed no evidence of a qualitative or quantitative susceptibility in fetal animals.

3. *Conclusion.* There is a complete toxicity data base for *S*-metolachlor and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. EPA determined that the 10X SF to protect infants and children should be removed. The FQPA Safety Factor Committee met on November 5, 2001 to evaluate the hazard and exposure data for metolachlor and *S*-metolachlor, and recommended that the FQPA Safety Factor for the protection of infants and children be reduced to 1x for the following reasons: (1) The toxicology database is complete for the FQPA assessment; (2) there is no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure to metolachlor in the available toxicity data; (3) a developmental neurotoxicity study is not required for metolachlor; and (4) the dietary (food and drinking water) and non-dietary exposure (residential) assessments will not underestimate the potential exposures for infants and children from the use of metolachlor.

E. Aggregate Risks and Determination of Safety

1. *Acute risk.* An acute aggregate risk assessment addresses potential exposure from combined residues of metolachlor/*S*-metolachlor on food and in drinking water (both surface and ground water). Potential residential exposures are not incorporated into an acute aggregate risk assessment. As shown in Table 5 below, the EECs are below the Agency's back-calculated DWLOC values for the parent compound, the ESA degradate, and the OA degradate. The combined value of the parent plus the degradates is also below the acute DWLOC value. The Agency concludes that acute aggregate risk estimates are not of concern for any population subgroup.

TABLE 5.—ACUTE DWLOC CALCULATIONS FOR METOLACHLOR/S-METOLACHLOR

Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (ppb)*	Ground Water EEC (ppb)*	Acute DWLOC (ppb)
U.S. Population	3.0	1	200.9	103	1.0 x 10 ⁵
Females 13–50	3.0	1	200.9	103	9.0 x 10 ⁴
Children 1–6	3.0	1	200.9	103	3.0 x 10 ⁴
Males 13–19	3.0	1	200.9	103	9.0 x 10 ⁴

* Represents the combined value of parent plus the ESA and OA degradates.

2. *Chronic risk.* A chronic aggregate risk assessment considers chronic

exposure from food, drinking water, and non-occupational (residential) pathways

of exposure. For metolachlor and *S*-metolachlor, there are no chronic