The Health Effects Division (HED) FQPA Safety Factor Committee (SFC) met on June 17, 2002 to evaluate the hazard and exposure data for Chlorsulfuron with regard to making a decision on the additional safety factor for the protection of infants and children. The committee members concurred electronically to revisions the HIARC made upon reevaluation of studies conducted with Chlorsulfuron on July 11, 2002. The SFC determined that reliable data demonstrate that the safety of infants and children will be protected by use of an additional traditional uncertainty factor of 3X.
I. HAZARD ASSESSMENT
(Correspondence: F. Fort to B. Tarplee dated June 10, 2002; responses prepared by L. Taylor)

1. Adequacy of the Toxicology Database

The toxicology database for Chlorsulfuron is not complete. There is a datagap for the 2-generation reproduction study in rats. On July 11, 2002, the HIARC concluded that a developmental neurotoxicity study is not required.

HIARC further concluded that an additional 3X database uncertainty factor is needed for the lack of an acceptable 2-generation reproduction study conducted with Chlorsulfuron. Although the existing 2-generation reproduction study does not satisfy the guideline requirement, the results of that study suggest that the repeated 2-generation reproduction study is unlikely to result in evidence of toxicity more than 3-fold lower than the existing endpoints. Therefore, a 3X database uncertainty factor is protective (HED No. 118601).

2. Determination of Susceptibility

The HIARC concluded that there is no indication of increased susceptibility (quantitative or qualitative) of rats or rabbits following in utero exposure to Chlorsulfuron. The HIARC could not assess susceptibility in the 2-generation reproduction study in rats.

3. Degree of Concern and Residual Uncertainties

The HIARC concluded that there are no residual uncertainties for prenatal toxicity in the acceptable guideline developmental studies with Chlorsulfuron. Although susceptibility could not be assessed in the unacceptable reproduction study, this uncertainty has been accounted for by the application of a database uncertainty factor. Therefore, the hazard-based special FQPA safety factor can be removed (1X) when assessing dietary and non-dietary residential exposure resulting from the uses of Chlorsulfuron.

II. EXPOSURE ASSESSMENT

1. Dietary (Food) Exposure Considerations
(Correspondence: F. Fort to B. Tarplee dated June 10, 2002)

Chlorsulfuron is a selective herbicide currently registered for use on barley, oats, and wheat at a maximum label use rate of 0.375 oz a.i./A. It is now proposed for use on range grasses at a maximum application rate of 1.0 oz ai/A. (one application is allowed). Tolerances are currently established for the combined residues of Chlorsulfuron, 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl]benzenesulfonamide and its
metabolite 2-chloro-5-hydroxy-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-ylaminocarboyl]benzenesulfonylamide, in/on barley, oats and wheat at levels ranging from 0.1 to 20 ppm [40 CFR 180.405(a)]. The HED Metabolism Committee has determined that the residue to be regulated is the parent only (CBRS 15318, 4/11/95, J. Abbotts). Tolerances are also established for residues of Chlorsulfuron in/on meat fat and meat byproducts at 0.3 ppm and milk at 0.1 ppm. Tolerances of 11 and 19 ppm have been proposed for grass (pasture and rangeland) forage and hay, respectively. There are currently no Codex MRLs established for Chlorsulfuron.

Adequate field trial data are available for Chlorsulfuron. The limit of quantification (LOQ) was determined to be 0.05 ppm (LOD = 0.02 ppm). No USDA or FDA monitoring data is available. BEAD percent crop treated information is available but will not be used in the dietary food exposure assessment at this time.

The HED Dietary Exposure Evaluation Model (DEEM) was used to estimate chronic dietary food exposure resulting from the use of Chlorsulfuron (no acute endpoint was identified by the HIARC). A conservative Tier 1 analysis was performed using tolerance level residues and assuming that 100% of crops were treated with Chlorsulfuron.

2. Dietary (Drinking Water) Exposure Considerations

(Correspondence: F. Fort to B. Tarplee dated June 10, 2002; responses prepared by L. Shanaman)

The environmental fate database for Chlorsulfuron is adequate to characterize drinking water exposure for the parent compound. However, if any of the degradation products become of toxicological concern, then more data will be required. Fate data indicate that Chlorsulfuron is very mobile but not persistent in the environment.

Since Chlorsulfuron has not yet been reviewed by the HED Metabolism Assessment Review Committee (MARC) to determine the degradates of concern for drinking water risk assessment, the HED risk assessment team is making the following conservative assumptions: 1) all degradates are of concern; 2) all degradates are of equal toxicity to the parent compound; and 3) parent and all degradates should be included in the drinking water risk assessment.

No USGS, NAWQA monitoring data are available for Chlorsulfuron. *Pesticides in Groundwater Database, A Compilation Of Monitoring Studies: 1971-1991 National Summary*, US EPA September 1992, entries indicate that of eight wells tested, there were no recorded detections of Chlorsulfuron.

EFED provided a very conservative approach for calculating surface water estimated environmental concentrations (EECs) and drinking water concentrations which includes all degradates based on a direct application to water. The dimensions of the index reservoir used in typical EFED modeling scenarios was chosen as a representative water body. The
metabolite 2-chloro-5-hydroxy-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-ylaminocarboyl)benzenesulfonamide, in/on barley, oats and wheat at levels ranging from 0.1 to 20 ppm [40 CFR 180.405(a)]. The HED Metabolism Committee has determined that the residue to be regulated is the parent only (CBRS 15318, 4/11/95, J. Abbotts). Tolerances are also established for residues of Chlorsulfuron in/on meat fat and meat byproducts at 0.3 ppm and milk at 0.1 ppm. Tolerances of 11 and 19 ppm have been proposed for grass (pasture and rangeland) forage and hay, respectively. There are currently no Codex MRLs established for Chlorsulfuron.

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2. Dietary (Drinking Water) Exposure Considerations

(Correspondence: F. Fort to B. Tarplee dated June 10, 2002; responses prepared by L. Shanaman)

The environmental fate database for Chlorsulfuron is adequate to characterize drinking water exposure for the parent compound. However, if any of the degradation products become of toxicological concern, then more data will be required. Fate data indicate that Chlorosulfuron is very mobile but not persistent in the environment.

Since Chlorosulfuron has not yet been reviewed by the HED Metabolism Assessment Review Committee (MARC) to determine the degradates of concern for drinking water risk assessment, the HED risk assessment team is making the following conservative assumptions: 1) all degradates are of concern; 2) all degradates are of equal toxicity to the parent compound; and 3) parent and all degradates should be included in the drinking water risk assessment.

No USGS, NAWQA monitoring data are available for Chlorsulfuron. Pesticides in Groundwater Database, A Compilation Of Monitoring Studies: 1971-1991 National Summary, US EPA September 1992, entries indicate that of eight wells tested, there were no recorded detections of Chlorsulfuron.

EFED provided a very conservative approach for calculating surface water estimated environmental concentrations (EECs) and drinking water concentrations which includes all degradates based on a direct application to water. The dimensions of the index reservoir used in typical EFED modeling scenarios was chosen as a representative water body. The
maximum label application rate for turf was used to calculate this worst-case concentration (resulting from direct application to water).

3. Residential Exposure Considerations
(Correspondence: F. Fort to B. Tarplee dated June 10, 2002; responses prepared by S. Hanley)

Chlorsulfuron is registered for use on residential lawns (spot applications). Postapplication dermal and incidental oral exposures to children and infants are possible from exposure to treated lawns. The revised Draft SOPs for Residential Exposure Assessment are used to assess post-application dermal exposure to adults and children as well as incidental oral exposure of toddlers. This assessment is considered to be very conservative since it assumes that the entire time spent on the lawn was on the ‘spot-treated’ area.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendations

For the reasons set forth below, the FQPA SFC recommends that a 3X traditional database uncertainty factor is needed to address data deficiencies and that no additional Special FQPA safety factor is necessary. This recommendation is based on reliable data supporting the findings set forth below.

A. Traditional Additional Uncertainty Factors (Addressing Data Deficiencies)

The FQPA Safety Factor Committee concurs with the HIARC conclusion that a 3X additional traditional database uncertainty factor is required to address data deficiencies in the toxicology database of Chlorsulfuron (Refer to § I.1.).

B. Special FQPA Safety Factors

Taking into account the HIARC’s recommendation regarding the data deficiencies, the FQPA SFC recommends that no Special FQPA Safety Factor is necessary to protect the safety of infants and children in assessing Chlorsulfuron exposure and risks.

2. Rationale and Findings Regarding Recommendation on Special FQPA Safety Factor

The Committee concluded that no Special FQPA safety factor was needed because:

The toxicology database for Chlorsulfuron contains acceptable guideline developmental studies which show no quantitative or qualitative evidence of increased susceptibility following in utero exposure. The HIARC concluded that there are no residual uncertainties
for prenatal toxicity in the acceptable guideline developmental studies with Chlorsulfuron. Although susceptibility could not be assessed in the unacceptable reproduction study, this uncertainty has been accounted for by the application of a database uncertainty factor. The chronic RfD and the toxicity endpoints established are protective of pre-pre/postnatal toxicity.

There are no residual uncertainties identified in the exposure databases. The dietary food exposure assessment includes tolerance level residues and assumes that 100% of crops were treated with Chlorsulfuron. Dietary drinking water exposure is based on a worst-case scenario (direct application to water) which includes all degradates. The residential post-application assessment is also considered to be very conservative since it uses the Residential SOPs and assumes that the entire time spent on the lawn was on the ‘spot-treated’ area. These exposure assessments will not underestimate the potential exposure to infants and children resulting from the use of Chlorsulfuron.

3. Application of the FQPA Safety Factors (Population Subgroups / Risk Assessment Scenarios)

The FQPA safety factor recommendation is for a 3X traditional database uncertainty factor to address data deficiencies and no additional Special FQPA safety factor. The 3X safety factor should be applied to all dietary and non-dietary residential exposure scenarios. No other FQPA safety factor would be appropriate for Chlorsulfuron.
### Summary of FQPA Safety Factors for Chlorsulfuron

<table>
<thead>
<tr>
<th>Magnitude of Factor</th>
<th>LOAEL to NOAEL (UF$_{LO}$)</th>
<th>Subchronic to Chronic (UF$_{SC}$)</th>
<th>Incomplete Database (UF$_{DB}$)</th>
<th>Special FQPA Safety Factor (Hazard and Exposure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IX</td>
<td>1X</td>
<td>1X</td>
<td>3X</td>
<td>1X</td>
</tr>
<tr>
<td>Rationale for the Factor</td>
<td>No LOAEL to NOAEL extrapolations performed</td>
<td>No subchronic to Chronic extrapolations performed</td>
<td>For lack of acceptable reproduction study</td>
<td>No residual uncertainties regarding pre- or post-natal toxicity or completeness of the toxicity or exposure databases.</td>
</tr>
<tr>
<td>Endpoints to which the Factor is Applied</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
<td>All dietary and non-dietary residential exposure assessments</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>