DRAFT

STANDARD OPERATING PROCEDURES FOR FQPA SAFETY FACTOR COMMITTEE

Chairperson:	Ed Zager
Members:	Bill Burnam, Ray Kent, Betsy Behl/Dan Rieder, Kathy Monk, Rick Keigwin/Debbie McCall, Jess Rowland
Executive Secretary:	Brenda Tarplee

I. BACKGROUND

FQPA requires that in the case of threshold effects "an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure be applied to infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children.....the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children". The FQPA Safety Factor Committee will make FQPA safety factor decisions on all chemical risk assessments generated by HED following the guidance in the policy paper, *FQPA Safety Factor for Infants and Children: General Guidance for Use*.

II. SCOPE

The Committee will consider: 1)The contribution of hazard and dose response evaluations in determining whether the FQPA safety factor can be removed or reduced; 2)The contribution of exposure assessment in evaluating whether application of the safety factor is appropriate; 3)The characterization of both the hazard and exposure data base.

III. PROCEDURES

For special procedures for Section 18 Emergency Exemptions, see Section VII below.

In order to assess the completeness of the data used in risk assessments and any potential effects on infants and children, the committee will have at its disposal the Hazard ID report (provided by the Hazard ID Committee chair) and written responses to a set of standard questions in the hazard and exposure areas (dietary, residential, water) prepared by the reviewers. The final decision on the retention, reduction, or removal of the safety factor will be made by consensus of the committee members. If no consensus can be reached, the committee will provide seek guidance from the HED, RD, and SRRD Division Directors. The final committee decision, supported by the documentation presented at the meeting, will be summarized in a short report. The committee will maintain a compilation of its decisions. The FQPA Safety Factor Committee expects to hold

meetings approximately four weeks after the Hazard ID meetings. This committee schedule will be included in the master schedule on the LAN.

IV. ATTENDEES

All chemical reviewers, risk assessor, designated HED branch chiefs, and appropriate risk managers representing RD or SRRD, will attend the meeting to answer any additional questions that may arise during the deliberations of the committee. Each of the hazard and exposure assessment areas should be represented (toxicology, dietary exposure, drinking water exposure, and occupational/residential exposure). If a reviewer, assessor, or risk manager is unable to attend, that reviewer, assessor, or risk manager will designate an appropriate person to attend in their absence.

V. SCHEDULING A MEETING

For Section 18 Emergency Exemptions, see Section VII below.

This Committee will work in conjunction with the Hazard Identification Assessment Review Committee (HIARC) in reviewing registration and reregistration chemicals (FQPA SFC meeting will be scheduled approximately four weeks after HIARC) and the schedule for the FQPA Safety Factor Committee meetings will be incorporated into the master SARC schedule on the LAN (T:\HED\SCHEDULE\HAZ_RISK).

For chemicals not currently listed on the master SARC schedule the lead reviewer for the chemical risk assessment will contact the Executive Secretary and/or Committee Chair to schedule a meeting date.

VI. STANDARD INFORMATION TO BE PROVIDED BY REVIEWERS

The decision to retain, reduce, or remove the FQPA safety factor will be based on the answers to the following questions. The committee seeks characterization of the uncertainties in the data used for the hazard and exposure assessment, as well as, of the susceptibilities of infants and children.

I. Toxicological Considerations for FQPA Safety Factor Selection

Your scientific judgment and qualitative description are just as important as quantitative data in characterizing the hazard in terms of the reliability of data, severity of the effects, populations exposed, and the likelihood of effects on infants and children. So please keep in mind the goal of these questions (i.e., characterization of hazard).

1. Has the scientific quality of the toxicology data base and the confidence in the hazard endpoints and dose-response assessments been completely characterized?

2. Do we have adequate hazard studies for evaluation of risk to infants and children? These include, but are not limited to, developmental studies in 2 species; multi generation reproduction studies; neurotoxicity and developmental neurotoxicity studies as required for chemicals which affect the nervous system. Are additional studies being required?

3. Do these studies show enhanced susceptibility to infants and children? That is, do the effects in the young occur at doses not causing effects in the adults? Are the effects in the young at the same level but more severe? Completely describe the spectrum of effects in both adult and young animals (include the shape of the dose response curve, the reversibility of effects if known, etc.).

4. Have other studies (e.g., literature reviews) been considered which might influence a FQPA safety factor finding? Are there mode of action studies which may provide information on precursor effects at lower doses? Are there comparative metabolism and pharmacokinetic studies evaluating the dose at the target site or the duration of effect?

ii. Dietary Exposure Considerations for FQPA Safety Factor Selection

Your scientific judgment and qualitative description are just as important as quantitative data in characterizing the exposure in terms of the reliability of data, magnitude (are we overestimating or underestimating the real exposure), and populations exposed. So please keep in mind the goal of these questions (i.e., characterization of exposure).

1. Describe (semi-quantitatively) the typical use rates and frequency of application. [There is no need to reproduce the labels. We are trying to determine whether there is a likelihood of quantifiable residues in the food.]
Are there Codex MRL's for the compound?

2. What metabolites require regulation? Are the residues systemic? That is, are they distributed throughout the plant or likely to be removed by preparation (washing, peeling, etc.)? Is information available about the dissipation or half-life of the pesticide?

3. State and characterize the available residue databases for each crop (i.e field study data, sources of available monitoring data such as PDP, FDA, etc.). What are the limits of quantitation used ? Describe semi-quantitatively the results of residue testing (ranges, frequency of positive findings, etc.).

4. Is there information available on % crop treated? If so, what is the source of the information and the uncertainties around the number? What is the likely maximum % crop treated for each crop (based on potential market)?

5. Based on the Consumption Database used by DRES, which crops contribute significantly to the human diet for adults? Which contribute significantly to the diet of infants and children? Is there likelihood of transfer of residues to meat and/or milk? Describe the degree of refinement of the DRES analyses for acute and chronic exposure.

iii. Drinking Water Exposure Considerations for FQPA Safety Factor Selection

Your scientific judgment and qualitative description are just as important as quantitative data in characterizing the exposure in terms of the reliability of data, magnitude (are we overestimating or underestimating the real exposure), and populations exposed. So please keep in mind the goal of these questions (i.e., characterization of exposure).

1. Is the environmental database complete ? Briefly summarize the environmental fate assessment for this compound and any metabolites that may be of concern. Is the compound a leacher?

2. Are ground water or surface water EECs based on modeling? (Answer separately for ground and surface water). Describe EECs and scenarios and discuss which models were used.

3. Were ground water prospective studies (or other appropriate and reliable targeted monitoring data) used to estimate EECs for this chemical? Were the studies conducted in vulnerable areas at maximum label rates?

4. Were appropriate and reliable targeted surface water studies conducted in highly vulnerable areas ?

5. Based on your understanding of how this pesticide is used, what is the size of the potential population exposed?

Consider the following questions to evaluate if the data are appropriate and reliable:

- # Were detection limits sensitive enough to detect residues at concentrations expected in the environment ?
- # Does monitoring represent current uses/ label rates ?
- # How frequently were samples collected throughout the year?
- # How many monitoring samples were used to derive the final number, and how robust is the database?

iv. Residential Exposure Considerations for FQPA Safety Factor Selection

Your scientific judgment and qualitative description are just as important as quantitative data in characterizing the exposure in terms of the reliability of data, magnitude (are we overestimating or underestimating the real exposure), and populations exposed. So please keep in mind the goal of these questions (i.e., characterization of exposure).

1. Is the compound used around the home in such a way that children and infants may be exposed? What is the frequency and rate of application ?

2. Have Pesticide Handler Exposure Database (PHED) data been used in estimating the exposure? How well does the PHED scenario reflect the actual use pattern? Rate the data used based on the PHED grading criteria (high quality, medium quality, or low quality). If chemical-specific or other non-PHED data have been used, describe the scope of the study, resulting exposure values, and general quality of the study.

3. For residential post application exposure scenarios, have the *Draft Standard Operating Procedures for Residential Exposure Assessments* been used as the basis for all calculations? Describe any deviations from SOP calculations and the impact on the assessment results (e.g., assessment reflects a less conservative approach by altering transfer coefficient value for dermal exposure).

4. Is chemical-specific product use information available through BEAD or some other source? Has the assessment been developed to reflect this information? Has this information been used as a basis for characterizing the populations considered in the assessment?

5. Are reliable biologically-based exposure data or epidemiology data available to support the results of the assessment (e.g., incident report, CDC monitoring data, etc.)?

6. Have models other than PHED or those presented in the Residential SOPs been used to calculate dose in any aspect of the assessment (e.g., CONSEXPO, TherDbase, etc)? Summarize how these are integrated into the assessment.

7. Is 100% dermal absorption assumed (when dermal endpoints are derived from oral studies)?

v. Other Factors for FQPA Safety Factor Selection

VII. SPECIAL PROCEDURE FOR SECTION 18 EMERGENCY EXEMPTIONS

1) A "Tier I" risk assessment for the Section 18 action is performed, assuming that the 10x factor for enhanced sensitivity to infants and children (as required by FQPA) is retained. If risk estimates do not exceed HED's level of concern under these circumstances, the Section 18 goes forward noting that the safety factor determination applies only to the Section 18 and is subject to change when the chemical undergoes full review by the FQPA Safety Factor Committee.

2) If risk estimates exceed HED's level of concern when the 10x is assumed to be retained, the Section 18 team will contact designated "adhoc" representatives [FQPA Safety Factor Committee members, Debbie McCall (for RABI) or Rick Keigwin (for RABII) and Bill Burnam *OR* Ray Kent] to make the safety factor determination for the Section 18. This will be a conservative decision since all the data and information needed may not be available. The Section 18 review team will document the recommendation by completing the Section 18 FQPA Safety Factor Determination form (found on the LAN at T:\HED\SARC\FQPA\S18FQPA). Reviewers will note in the risk assessment document that the safety factor determination applies only to the Section 18 and is subject to change when the chemical is reviewed by the FQPA Safety Factor Committee.