ENVIRONMENTAL PROTECTION AGENCY

[OPP–00610; FRL–6088–7]

Pesticides; Policy Issues Related to the Food Quality Protection Act

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of availability.

SUMMARY: To assure that EPA's policies related to implementing the Food Quality Protection Act (FQPA) are transparent and open to public participation, EPA is soliciting comments on four policy papers entitled ''Toxicology Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health,'' ''Exposure Data Requirement for Assessing Risks of Pesticide Exposure to Children,'' ''The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process,'' and ''Standard Operating Procedures (SOP) for Determining the Appropriate FQPA Safety Factor(s) for Use in Tolerance Assessment.'' This notice is the ninth in a series concerning science policy documents related to FQPA and developed through the Tolerance Reassessment Advisory Committee (TRAC).

DATES: Written comments for these policy papers, identified under one docket control number provided in Unit I. of this document, should be submitted by September 7, 1999.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I.C. of this document. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP–00610 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: Penelope A. Fenner-Crisp, Environmental Protection Agency (7501C), 401 M St., SW., Washington, DC 20460; telephone number: (703) 605–0654; fax: 703–305–4776; e-mail: fenner-crisp.penelope@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Notice Apply to Me?

You may be potentially affected by this notice if you manufacture or formulate pesticides. Potentially affected categories and entities may include, but are not limited to:

Categories	NAICS	Examples of Potentially Affected Entities
Pesticide Producers	32532	Pesticide manufacturers Pesticide formulators

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed could also be affected. If available, the North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether or not this notice affects certain entities. If you have any questions regarding the applicability of this announcement to you, consult the person listed in the ''FOR FURTHER INFORMATION CONTACT'' section.

B. How Can I Get Additional Information or Copies of This Document or Other Documents?

1. *Electronically*. You may obtain electronic copies of this document and the four science policy papers from the EPA Home Page under the Office of Pesticide Programs (OPP) at http://www.epa.gov/pesticides/. On the Office of Pesticide Program Home Page select ''TRAC'' and then look up the entry for this document. You can also go directly to the listings at the EPA Home Page at the Federal Register--Environmental Documents entry for this document under ''Laws and Regulations'' (http://www.epa.gov/fedrgstr/) to obtain this notice and the four science policy papers.

2. *In person or by phone*. If you have any questions or need additional information about this action, you may contact the person identified in the ''FOR FURTHER INFORMATION CONTACT'' section of this document. In addition, the official records for the science policy papers listed in the SUMMARY section of this document, including the public version, have been established under the docket control number OPP–00610 (including comments and data submitted electronically as described below). This record not only includes the documents that are physically located in the docket, but also includes all the documents that are referenced in those documents. Public versions of these records, including printed, paper versions of any electronic comments, which do not include any information claimed as Confidential Business Information (CBI), are available for inspection in Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Public Information and Records Integrity Branch telephone number is 703–305–5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP–00610 in the subject line on the first page of your response.

1. *By mail*. Submit written comments to: Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, 401 M St., SW., Washington, DC 20460.

2. *In person or by courier*. Deliver written comments to: Public Information and Records Integrity Branch, Information Resources and Services Division (7502C), Office of Pesticide Programs, Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA.

3. *Electronically*. Submit your comments and/or data electronically by e-mail to: opp-docket@epa.gov. Do not submit any information electronically that you consider to be CBI. Submit electronic comments as an ASCII file, avoiding the use of special characters and any form of encryption. Comments and data will also be accepted on standard computer disks in WordPerfect 5.1/6.1 or ASCII file format. All comments and data in electronic form must be identified by the docket control number. Electronic comments on this notice may also be filed online at many Federal Depository Libraries.

D. How Should I Handle CBI Information That I Want to Submit to the Agency?

You may claim information that you submit in response to this document as CBI by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. In addition to one complete version of the comment that includes any information claimed as CBI, a copy of the comment that does not contain CBI must be submitted for inclusion in the public record. Information not marked confidential

will be included in the public docket by EPA without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please call the Public Information and Records Integrity Branch; the telephone number is (703) 305–5805.

E. What Should I Consider As I Prepare My Comments for EPA?

EPA invites you to provide your views on the draft science policy papers, new approaches the Agency has not considered, the potential impacts of the various options (including possible unintended consequences), and any data or information that you would like the Agency to consider. You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible.
2. Describe any assumptions that you used.
3. Provide solid technical information and/or data to support your views.
4. If you estimate potential burden or costs, explain how you arrived at the estimate.
5. Indicate what you support, as well as what you disagree with.
6. Provide specific examples to illustrate your concerns.
7. Make sure to submit your comments by the deadline in this notice.
8. At the beginning of your comments (e.g., as part of the ''subject'' heading), be sure to properly identify the document you are commenting on. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP–00610 in the subject line on the first page of your response. You may also provide the name, date, and **Federal Register** citation.

II. Background for the Tolerance Reassessment Advisory Committee (TRAC)

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) was signed into law. Effective upon signature, the FQPA significantly amended the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA). Among other changes, FQPA established a stringent health-based standard (''a reasonable certainty of no harm'') for pesticide residues in foods to assure protection from unacceptable pesticide exposure; provided heightened health protections for infants and children from pesticide risks; required expedited review of new, safer pesticides; created incentives for the development and maintenance of effective crop protection tools for farmers; required reassessment of existing tolerances over a 10–year period; and required periodic re-evaluation of pesticide registrations and tolerances to ensure that scientific data supporting pesticide registrations will remain up-to-date in the future.

Subsequently, the Agency established the Food Safety Advisory Committee (FSAC) as a subcommittee of the National Advisory Council for Environmental Policy and Technology (NACEPT) to assist in soliciting input from stakeholders and to provide input to EPA on some of the broad policy choices facing the Agency and on strategic direction for the Office of Pesticide Programs. The Agency has used the interim approaches developed through discussions with the FSAC to make regulatory decisions that met FQPA's standard, but that could be revisited if additional information became available or as the science evolved. As EPA's approach to implementing the scientific provisions of FQPA has evolved, the Agency has sought independent review and public participation, often through presentation of many of the science policy issues to the FIFRA Scientific Advisory Panel (SAP), a group of independent, outside experts who provide peer review and scientific advice to OPP.

In addition, as directed by Vice President Albert Gore, EPA has been working with the U.S. Department of Agriculture (USDA) and another subcommittee of NACEPT, the Tolerance Reassessment Advisory Committee (TRAC), chaired by the EPA Deputy Administrator and the USDA Deputy Secretary, to address FQPA issues and implementation. TRAC comprises more than 50 representatives of affected user, producer, consumer, public health, environmental, states and other interested groups. The TRAC has met six times as a full committee from May 27, 1998 through April 29, 1999.

The Agency has been working with TRAC to ensure that its science policies, risk assessments of individual pesticides, and process for decision-making are transparent and open to public participation. An important product of these consultations with TRAC is the development of a framework for addressing key science policy issues.

The Agency decided that the FQPA implementation process and related policies would benefit from initiating notice and comment on the major science policy issues. TRAC identified nine science policy issue areas they believe were key to implementation of FQPA and tolerance reassessment. The framework calls for EPA to provide one or more documents for comment on each of the nine issues by announcing their availability in the **Federal Register**. In accordance with the framework described in a separate notice published in the **Federal Register** of October 29, 1998 (63 FR 58038) (FRL–6041–5), EPA has been issuing a series of draft documents concerning the nine science policy issues identified by the TRAC related to the implementation of FQPA. This notice announces the availability of the four documents identified in the SUMMARY section of this document.

III. Background on FQPA Safety Factor Papers

A. 1993 National Research Council (NRC) Study

In response to a request from the U.S. Congress, the National Research Council (NRC) conducted a study on the scientific and policy issues concerning pesticides in the diets of infants and children. In its 1993 report, ''Pesticides in the Diets of Infants and Children,'' the NRC concluded that although the uncertainty factors that are widely used to establish guidelines for human exposure on the basis of animal testing results generally provide adequate protection for infants and children, children may be uniquely susceptible to chemical exposures at particularly sensitive stages of development. The NRC further concluded, ''in the absence of data to the contrary, there should be a presumption of greater toxicity to infants and children.''

B. Applicable FQPA Requirements

The Food Quality Protection Act (FQPA) of 1996 (Public Law 104–170) was signed into law on August 3, 1996. FQPA establishes a new safety standard and new procedures for EPA's pesticide tolerance-setting activities. Under new section 408(b)(2)(A)(i) of FFDCA, EPA can establish, revise or leave in effect a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if it is determined to be ''safe.'' Section 408(b)(2)(A)(ii) defines ''safe'' to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.'' Section 408(b)(2)(C) requires EPA to give special consideration to infants and children by ensuring ''that there is a reasonable certainty that no harm will result to infants and children from aggregate

exposure to the pesticide chemical residue.''

FQPA instructs EPA, in making its ''reasonable certainty of no harm'' finding, that in ''the case of threshold effects, . . . an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of data with respect to exposure and toxicity to infants and children.'' Section 408(b)(2)(c) further states that ''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.''

C. EPA 10X Task Force

In March 1998, the U.S. Environmental Protection Agency (EPA) established an agency-wide ''10X Task Force'' to address the use of the ten-fold (10X) margin of safety for infants and children (otherwise known as the ''FQPA Safety Factor'') provided for in the Food Quality Protection Act (FQPA) of 1996. Task Force members included high-level scientists primarily from the Office of Children's Health Protection, the Office of Prevention, Pesticides and Toxic Substances, and the Office of Research and Development. This group was charged with developing recommendations regarding the implementation of the FQPA Safety Factor.

In response to this charge, the 10X Task Force formed two working groups--the Toxicology Working Group and the Exposure Working Group. These groups have each drafted a report ''Toxicology Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health'' and ''Exposure Data Requirements for Assessing Risks of Pesticide Exposure to Children,'' respectively, which are summarized in Units IV.A. and IV.B. of this document. These reports contain recommendations concerning the implementation of the FQPA Safety Factor.

D. Pesticide Program Guidance

The Office of Pesticide Programs (OPP) is responsible for implementing the requirements of FQPA in making its pesticide regulatory decisions daily. Accordingly, OPP has developed updated, interim guidance as to how it will comply with FQPA concerning the FQPA Safety Factor for protecting infants and children. In drafting this guidance, OPP has taken into account the recommendations of the 10X Task Force as embodied in the above-mentioned documents. OPP's guidance consists of two documents: ''The Office of Pesticide Programs' Guidance Document on the Determination of the Appropriate FQPA Safety Factor(s) for Use in the Setting of Tolerances'' and ''Standard Operating Procedures (SOP) for Determining the Appropriate FQPA Safety Factor(s) for Use in Tolerance Reassessment'' which are summarized in Units IV.C. and IV.D. of this document. The former paper explains the general policies that OPP proposes to follow in making determinations concerning the use of the FQPA Safety Factor, while the latter paper specifies the detailed procedures that OPP will use in following these policies.

E. Scientific Peer Review

Since the FQPA was promulgated, OPP has submitted all interim policy and guidance documents on the FQPA safety factor for independent scientific peer review, with concurrent requests for public comment. Responses and comments received from the independent scientific panels, other offices within the Agency, government agencies, and from the public sector, in response to each of these document releases and/or presentations, have been carefully considered throughout the process of developing interim policy. The first interim policy paper explaining the OPP position on the use of the ten-fold margin of safety, was presented to the FIFRA Scientific Advisory Panel (SAP) in October 1996. In March 1998, a second OPP interim policy paper on the application of the ten-fold safety factor to risk assessments entitled ''Presentation for FIFRA Scientific Advisory Panel by Office of Pesticide Programs Health Effects Division on FQPA Safety Factor for Infants and Children,'' was presented to the SAP. An update on the Agency's progress in addressing issues raised by the SAP was brought before a subsequent Panel in July 1998; however, the primary positions described in the March paper were not altered in that update.

F. Public Comments

Before and during the TRAC meetings, the Agency received comments on how to approach and improve its interim policies. Specifically, EPA received several petitions, including those from the National Food Processors Association, the Natural Resources Defense Council (NRDC) and others, a report from the Implementation Working Group (IWG), letters from the Environmental Working Group, and various correspondence from Congress and others. These documents will be considered as the Agency refines its science policies, and will also be made available through the public docket.

1. *NRDC petition*. On April 23, 1998, the NRDC and various individuals and other public interest organizations filed a petition requesting that EPA issue an interpretive rule/policy statement regarding EPA's implementation of the FQPA provision concerning the additional ten-fold safety factor to protect infants and children. The petition seeks three specific actions:

i. Issuance of a policy statement/interpretive rule providing that EPA maintain the ten-fold safety factor unless the Administrator has determined that there are reliable data on [evolving] prenatal and postnatal toxicity and exposure for fetuses, infants, and children. The petition sets forth a minimum set of data that petitioners believe constitutes ''reliable data'' and requests that the statement/rule direct EPA to apply the additional ten-fold factor if any of these data are absent.

ii. Convene a ''blue ribbon panel'' to assist EPA in determining when there are reliable data for prenatal and postnatal toxicity to fetuses, infants, and children. NRDC recommends that this panel be convened under the auspices of the Children's Health Protection Advisory Committee.

iii. Issuance of a policy statement/interpretive rule providing that, pending completion of the panel's report, EPA will apply the ten-fold safety factor.

2. *Grower group and trade association petition*. On May 26, 1998, EPA received a petition on rulemaking under the FQPA submitted on behalf of several grower groups and trade associations. The petition requested EPA to use notice and comment rulemaking to establish policies and procedures for implementing FQPA. The petitioners claimed that rules are needed to establish policies and procedures for determining when the FQPA ten-fold safety factor may be reduced or removed.

3. *IWG report.* The IWG, a coalition of farm, food, manufacturing, and pest management organizations, issued a ''road map'' report on June 18, 1998, which presents the IWG's views on how EPA can ensure what they regarded as a more balanced and workable implementation of FQPA. Their comments included the FQPA Safety Factor.

IV. Summary of FQPA Safety Factor Papers

A. Toxicology Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health

The Toxicology Working Group of the 10X Task Force has developed a report addressing the role of toxicology data requirements in assessing risks to children's health from pesticide exposure. Specifically, the report provides guidance on the use of toxicity data in hazard characterization and dose-response analysis relevant to decisions about the FQPA 10X Safety Factor.

First, the report expands on the definition of prenatal and postnatal toxicity (developmental toxicity) from the EPA Guidelines for Developmental Toxicity Risk Assessment (1991), and recommends a core toxicology data set for conventional, food-use pesticides. In particular, the report suggests that adult and developmental neurotoxicity testing and adult immunotoxicity testing be included as a routine part of the core test data set for food-use pesticides because the current weight-of-the-evidence triggers may not identify all pesticides that have the potential to produce developmental neurotoxicity and immunotoxicity.

The report then describes criteria for assessing the overall ''degree of concern'' for children's health effects that encompasses a review of all available toxicity information. The recommended approach, which includes an evaluation of the degree of concern for children's health, represents an evolution and further harmonization of the approaches previously taken by EPA. The criteria for this approach fall into four basic categories, each of which the report discusses in detail:

1. Human data on prenatal and postnatal toxicity.
2. Prenatal and postnatal toxicity in animal studies.
3. The dose-response nature of the experimental animal data.
4. The relevance of the experimental animal data for humans.

When a dose-response analysis is done for health effects of pesticides in general, the report recommends how a dose-response analysis should be performed for children's health effects. That is, the data on developmental toxicity should be evaluated along with the data on adult toxicity, and the No Observed Adverse Effect Level (NOAEL) for the more sensitive or critical effect levels should be based on consideration of all health effects observed. In doing so, children's health will be protected along with that of other sensitive populations.

The report indicates that the default intraspecies ten-fold uncertainty factor, which is applied to account for variations in toxicity among humans, will be adequate in the majority of cases for protecting children's health regarding toxicity concerns, if a complete developmental toxicity data base is available. The report suggests that when data specific to children's health are missing or inadequate for a particular pesticide, application of the data base uncertainty factor in addition to the ten-fold intraspecies variability factor would account for the possibility that children may be significantly more sensitive than adults.

Although the report asserts that there is no formal process for considering the degree of concern in the RfD determination, the report recognizes that some aspects of degree of concern are taken into account at this point in the risk assessment process, for example, when developmental effects are selected as the most sensitive endpoints. Nevertheless, the report recommends that this issue be further considered in the calculation of the RfD.

In addition to the recommendations described above, the report makes several recommendations concerning the development of new data requirements:

1. 40 CFR part 158.340 should be updated to include the adult and developmental neurotoxicity guidelines and the adult immunotoxicity guidelines and to refer to the newly revised two-generation reproduction and prenatal developmental toxicity testing guidelines.

2. Guidelines for pharmacokinetic studies should be developed that include considerations of exposure during pregnancy and lactation, and of infants and children. These data can be developed as part of a tiered approach to overall pharmacokinetic evaluations and should be required for assessment of effects of pesticides on infants and children in 40 CFR part 158.

3. Specific testing guidelines for other types of functional or latent effects (e.g., developmental immunotoxicity, developmentally-induced cancer) do not currently exist. As well, guidelines for direct dosing of neonates and appropriate interpretation and application of such data are not available. Efforts should be made to develop these guidelines as well as criteria for when such studies should be conducted.

B. Exposure Data Requirements for Assessing Risks to Children's Health from Pesticide Exposure

The Exposure Working Group of the 10X Task Force has developed a report addressing the role of exposure data requirements in assessing risks to children's health from pesticide exposure. The report gives information and describes general principles for conducting exposure assessments. It also discusses issues that are specific to conducting exposure assessments for children.

The report contains criteria by which OPP evaluates data sets used in an exposure assessment. If direct measurements of exposure are used for the assessment, then the available exposure data must be of suficient quality and quantity to provide high confidence that the assessment will be protective of infants and children. If models are used to estimate exposure, then the exposure assumptions in the models must be judged to be conservative. The greater the uncertainty in the data associated with the assumptions, the more conservative (i.e., unlikely to underestimate exposure) the assumptions should be.

Finally, the report describes the assessment procedures for estimating single pathway pesticide exposures from food, drinking water, and non-occupational sources. It also characterizes the types of data that are used in the assessments. For each pathway, the procedures and data are evaluated to determine if there is a high level of confidence that the assessment is protective of infants and children. The report lists a number of recommendations on how to improve the assessment procedures, mentions the ongoing work within EPA to improve the procedures, and addresses the issues associated with aggregating exposures from different sources.

C. The Office of Pesticide Programs' Guidance Document on the Determination of the Appropriate FQPA Safety Factor(s) for Use in the Setting of Tolerances

The OPP guidance document describes the OPP policies for determining the appropriate FQPA Safety Factor(s) to apply when establishing, modifying, leaving in effect, or revoking a tolerance or exemption for a food use pesticide. It presents the legal framework for the FQPA Safety Factor and key interpretations of that framework. It states that, while the legislative language incorporates the term ''safety factor'' instead of the term ''uncertainty

factor,'' OPP believes that Congress clearly intended the FQPA Safety Factor to address uncertainty resulting from incompleteness of data and, therefore, deems the statutory term to incorporate the ''uncertainty factor'' concept. The document offers the opinion that the FQPA Safety Factor is to be applied in addition to the two routine or baseline factors which account for: (1) Differences in sensitivity and variability between humans (the ''intraspecies'' uncertainty factor) and (2) differences in sensitivity between experimental animals and humans, if animal data have been used as the basis for deriving the hazard values (the ''interspecies'' uncertainty factor). Therefore, the FQPA Safety Factor would include other uncertainty or modifying factors used in the calculation of hazard values, for example, the data base uncertainty factor that is applied when one or more critical core studies are missing.

The document describes the set of pesticides for which FQPA Safety Factor determinations would be made primarily as food-use chemicals of ''conventional'' chemistry for which hazard values such as the acute or chronic reference doses (RfD) can be derived. OPP would expect to make FQPA Safety Factor decisions when assessing risk to infants and children up through the time of sexual maturation, women of child-bearing age, and on occasion, sexually mature males. FQPA Safety Factor recommendations will be made as the risk characterization is being developed; the final decision will be made during the risk management process.

The guidance describes the criteria by which OPP determines the completeness of the toxicology data base for conducting a high quality hazard characterization. OPP makes this determination employing a weight-of-the-evidence approach. The core toxicology data base for a specific chemical generally consists of studies which meet three criteria:

1. All studies in the core data base must have ''official'' testing guidelines or standard, well-documented protocols available.

2. The studies will have been required under FIFRA/ FFDCA as first tier requirements or will have been triggered by results of Tier 1 or other existing studies (see the regulations in 40 CFR 158.340, subpart F). Alternatively, studies are required under a well-established policy and practice for registration and reregistration/renewal (e.g., data call-ins) and this requirement has resulted in the generation and submission of the data with which the Agency has acquired experience in evaluating.

3. There is consensus in the scientific community that there is a body of evidence supporting the conclusion that the results of such studies significantly improve the understanding of the potential hazard of the pesticide to humans, including infants and children.

The document notes that OPP will, in the next few months, propose to revise the toxicology data requirements in part 158, to include several new studies as Tier 1 requirements (e.g., the acute and subchronic neurotoxicity studies in adult mammals, the developmental neurotoxicity study, two immunotoxicity studies, and the 21–day dermal study) plus others as Tier 2 (i.e., conditionally required). In addition, there is a description of the criteria and other bases by which OPP has concluded that it is appropriate to begin the process to issue data call-ins for the acute and subchronic neurotoxicity studies in adult mammals and the developmental neurotoxicity study for a subset of conventional chemistry pesticides which are known neurotoxins.

Separate from the question of what data will comprise a complete data base is the issue of what data base uncertainty factor should be applied when critical core studies are missing or inadequate. This document addresses this issue, including when the number of studies considered critical for a ''high confidence'' chronic RfD is expanded in the near term from five to six, and, then, after the studies are routinely required, received and understood, to eight. The data base uncertainty factor fulfills the same purpose as, and, in effect, becomes part of the FQPA Safety Factor. This guidance document incorporates the criteria and factors for assessing the degree of concern regarding the potential for prenatal and postnatal effects, as presented in the framework described in the report of the Toxicology Working Group of the Agency 10X Task Force entitled ''Toxicology Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health.'' (Toxicology Working Group, 1999).

The guidance document also considers the completeness of the toxicology data base and degree of concern in the selection and application of uncertainty factors when calculating the acute or chronic RfD and in the recommendations regarding the FQPA Safety Factor. The RfD derivation process takes into account deficiencies in the core toxicology data base and the potential for hazard to fetuses, infants and children (and, therefore, the degree of concern). The document articulates criteria for determining OPP's overall level of confidence in the hazard-related information and hazard assessment approaches employed. If, for some reason, an assessment does not meet this standard, then the assessment is said to contain ''residual uncertainties or concerns.'' Any residual concerns remaining after the hazard assessment is examined are dealt with when making the final FQPA Safety Factor decision(s). During the period after a determination is made to require new toxicology studies, but before they become part of the core toxicology data base, their absence is evaluated as part of ''residual uncertainties or concern'' in the FQPA Safety Factor assessment process. This document states OPP's intention to solicit broad public input regarding the appropriate consideration of the absence of these particular newly-required studies in the FQPA Safety Factor assessment process.

Just as for hazard potential, determination of the completeness of the exposure data base--in the context of aggregate exposure and risk assessment--is a primary consideration relative to the FQPA Safety Factor. As described in the report of the Exposure Working Group of the Agency 10X Task Force entitled ''Exposure Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health'' (Exposure Working Group, 1999), OPP estimates exposure using chemical-specific and other reliable empirical data as well as models and conservative assumptions, which also are based upon reliable data. The Office is confident that, in the great majority of cases, it is not underestimating exposure to infants and children or to the general population. The guidance document acknowledges the desirability of obtaining more extensive and specific exposure data and notes that OPP continues to pursue the acquisition of such data from the private sector and its own and other agencies' research efforts. If any residual concerns remain after the exposure assessment is examined, these are dealt with when making the final FQPA Safety Factor decision(s). The guidance states that the absence of detailed and specific exposure data would require the application of an additional safety factor unless OPP can determine that the available data and its assessment methodologies give a high degree of confidence that exposure to infants and children is not underestimated. However, because OPP's approach to estimating exposure in the absence of extensive, specific data is typically very conservative, OPP can

usually conclude, with a high degree of confidence, that its approach adequately protects infants and children, and the FQPA Safety Factor would not be needed to address uncertainties in the exposure data base.

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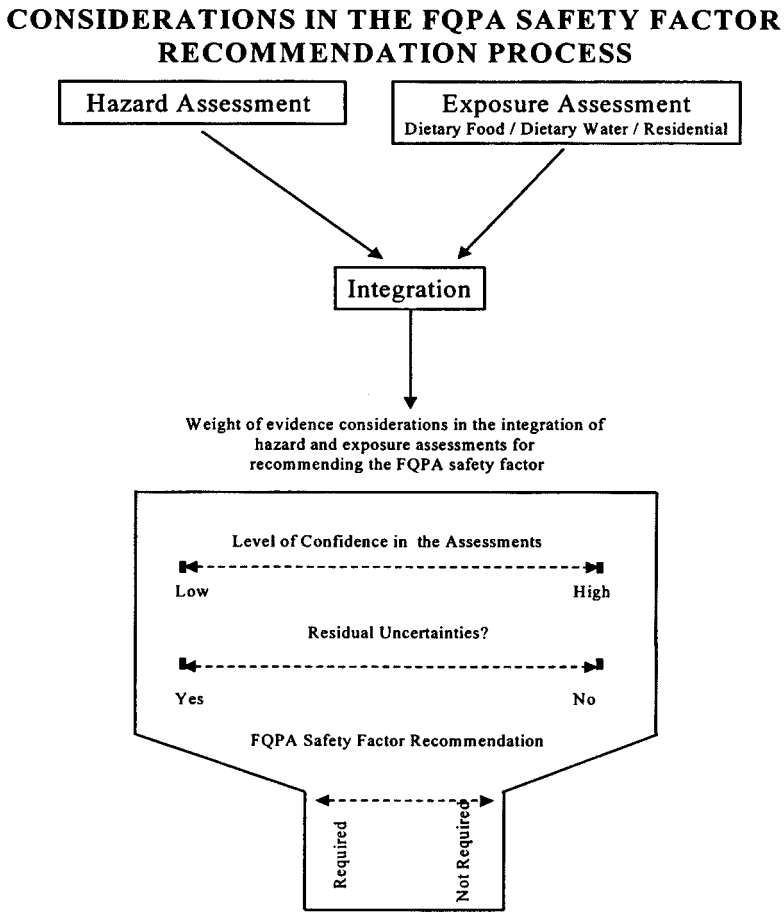

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The guidance document notes that the decision, either that the default FQPA Safety Factor is to be applied or that there are reliable data which support the application of a different factor, uses a ''weight-of-the-evidence'' approach. This approach simply means that all of the data with regard to both hazard and exposure are considered simultaneously as the total body of evidence with regard to the pesticide(s) being evaluated. The integration approach to evaluating the available hazard- and exposure-related information involves characterization of the overall confidence that infants and children will be protected. As illustrated in the figure above, the weight-of-the-evidence considerations include the level of confidence in the hazard and exposure assessments, and whether or not there are any residual uncertainties identified in the risk characterization. If there is a high level of confidence that the combination of the hazard and exposure assessments is adequately protective of infants and children, then the default FQPA factor would not be applied at this stage in the process. For example, the optimal case would be one in which there is a high level of confidence that the hazard and exposure assessments are sufficiently conservative and there are no residual uncertainties in the assessment; then it would not be necessary to apply an additional safety factor to protect infants and children. At the other extreme is the case where OPP may find that reliable data do not support a particular finding other than to retain the 10X default factor, given the low level of confidence that the hazard and exposure assessments are sufficiently conservative and there are residual uncertainties that have not been dealt with in the assessment. Alternatively, in other cases where there is also a low level of confidence in the hazard and exposure assessments and residual concerns remain, an additional safety factor other than the 10X default (perhaps even greater) would be applied. The size of the final factor would depend on the overall weight-of-the-evidence and the level of confidence in the assessment.

The recommendation concerning the FQPA factor is made based upon consideration of the nature and level of confidence in the hazard and exposure assessments, the degree of concern for potential hazard to the fetus, infants and children, and any residual uncertainties that are not accounted for in the hazard and exposure assessments. The final decision on the FQPA Factor is informed by the science presented in the risk characterization and the recommendation.

D. ''Standard Operating Procedures (SOP) for HED FQPA Safety Factor Committee''

The Standard Operating Procedures (SOP) is a working level document designed to obtain and organize information from disciplinary review

scientists regarding the following: (1) The contribution of the hazard and dose response evaluations in determining whether an additional FQPA safety factor is required; (2) the contribution of the exposure assessment(s) in evaluating the safety factor; and (3) the characterization of both the toxicology and exposure data bases. The Committee considers this information in making the safety factor recommendation for each pesticide on a case-by-case basis using a weight-of-the-evidence approach. On December 9, 1998, the OPP FQPA Safety Factor Committee presented to the FIFRA Scientific Advisory Panel (SAP) its SOP for recommending the safety factor for risk assessments prepared in support of tolerance decisions. The Committee has revised its draft Standard Operating Procedures (SOP) in accordance with the draft OPP Policy Document and the recommendations of the SAP; the committee is issuing this revised document for comment today.

V. Questions/Issues for Comment

Because the four science policy documents covered by this notice have many common issues, the Agency encourages the public to submit comments by issue or topic rather than for each separate document. To facilitate this approach to commenting, EPA has placed all four documents under the same docket number (see Unit I.C. of this document). In this way, commenters may efficiently address a science policy or other issues that are addressed in the different documents.

Although EPA is making four documents concerning the FQPA 10X Safety Factor available for review and public comment, the Agency encourages the public to focus particularly on the OPP Guidance Document, ''The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process.'' While OPP used the two papers produced by the Toxicology and Exposure Working Groups of the Agency's 10X Task Force in developing its guidance, at this time, the 10X Task Force is not planning to revise and reissue these documents following public comment. In addition, the OPP Standard Operating Procedure is largely derived from the OPP Guidance Document, and any changes in it following public comment should reflect changes in the Guidance Document. Therefore, of the four documents being made available, OPP considers its Guidance Document the most important for the public to review and comment on.

Following are several issues and associated questions for which EPA has particular interest in receiving comments:

General FQPA Safety Factor Issues

1. The OPP Guidance indicates that OPP will generally apply the FQPA Safety Factor only to food-use pesticides of ''conventional'' chemistry. Please comment on this approach. The Guidance also indicates that different decisions about the need for, and size of, an additional FQPA Safety Factor may be appropriate for different durations of exposure and different exposed populations. Please comment on this approach. Finally, the Guidance indicates that it would be appropriate to make only one FQPA Safety Factor decision for a single population/exposure period, even though such exposure might occur by different routes and pathways. Please comment on this approach.

2. Is a weight-of-the-evidence approach to making FQPA Safety Factor decisions appropriate, taking into consideration the toxicology and exposure data bases for a pesticide and the potential risks for the developing fetus, infant and child as well as other populations? If not, why not? Given the scope of the evidence which OPP intends to consider, are there any other types of information that OPP should consider in making its FQPA Safety Factor determinations?

3. Do you agree with the view that the models and assumptions used by OPP in the risk assessment process, together with reliable data available on specific pesticides and other reliable, empirical data, typically do not understate risk? If not, under what circumstances do you believe OPP's current approaches to assessing risks from aggregate exposure to a single pesticide produce risk assessments that understate the risks to infants and children?

4. Do you agree with OPP's view that the FQPA Safety Factor should be applied in addition to the interspecies and intraspecies uncertainty factors, but that the FQPA Safety Factor should not be applied in a manner that results in ''double-counting'' of uncertainties that are otherwise addressed in the toxicity and exposure assessments through, for example, the data base uncertainty factor or conservative exposure models? If you disagree, why?

Toxicology Issues

1. Please comment on OPP's proposed criteria for defining the core toxicology data base.

2. After having considered the recommendations from the FIFRA Scientific Advisory Panel and the Toxicology Working Group, OPP is beginning the process of calling in data for three studies (the acute and subchronic neurotoxicity studies in adult mammals and the developmental neurotoxicity study) for a subset of conventional chemistry food-use pesticides known neurotoxicants. In addition, OPP will be proposing to require the same set of studies for all conventional chemistry food-use pesticides in the revision of the part 158 regulations. Please comment on this two-stage approach.

3. The OPP Policy Guidance indicates that one of the critical issues is whether or not to apply an FQPA Safety Factor pending receipt of newly-required studies. There are a variety of possible approaches. One possible approach would be to apply the FQPA Safety Factor's data base uncertainty component to gaps related to new core data requirements only where there are specific concerns regarding the pesticide pertaining to the data requirement. Alternatively, OPP could apply the default 10X factor (or some other additional factor) whenever a new data requirement is added and/or whenever a testing guideline is changed. Please explain how you think the FQPA Safety Factor provision should be implemented when OPP makes such changes. In commenting, please address whether OPP should apply the default FQPA 10X factor, some different yet additional factor, or no factor at all in the following circumstances:

i. A minor change to testing guidelines.

ii. A major change to testing guidelines.

iii. An addition of a new required test.

iv. An addition of a new required test to core requirements.

4. In the absence of the results from any of the studies to be required through data call-in notices (i.e., the acute and subchronic neurotoxicity studies in adult mammals and the developmental neurotoxicity study), what information from existing studies on a specific chemical would increase or decrease the concerns about the potential for prenatal and postnatal hazard, in general, and for neurotoxicity and developmental neurotoxicity, in particular? Which, if any, of the seven criteria discussed in section V.A.1.a., footnote 4 and associated text of the OPP Guidance document is appropriate for judging whether there is increased concern about the potential for a pesticide to cause developmental neurotoxicity? Are there any other criteria which would be useful for informing this judgment?

5. Please comment on whether you would expect that developmental neurotoxicity studies would, for a

substantial number of chemicals, identify effects that are not detected in other studies and more fully characterize the potential risks of exposures during development. In addition, please comment on the sensitivity of these tests vis-a-vis other studies required and used for age-related comparisons for acute, intermediate, or chronic RfD derivation (e.g., prenatal developmental toxicity or multi-generation reproduction study, subchronic and chronic studies, etc.). Please explain the basis of your opinion.

6. OPP's Guidance states that currently five studies (a multi-generation reproduction study, prenatal developmental toxicity studies in two species, and chronic toxicity studies in a rodent and non-rodent species) comprise the toxicity data base necessary to produce a ''high confidence RfD,'' and that some additional data base uncertainty factor will be imposed if the data base on a pesticide lacks one or more of these studies. OPP proposes to expand this core data base to include the subchronic neurotoxicity study. Eventually, OPP also includes the acute neurotoxicity study in adult mammals and the developmental neurotoxicity study, once these studies have met the criteria for inclusion in the core toxicity data base. Please comment on OPP's proposed approach to imposing a data base uncertainty factor of 3x if one key study is missing from the data base and a factor of 10x if more than one is missing.

7. OPP is proposing to adopt the framework and its criteria/factors for assessing the degree of concern about the potential for prenatal and postnatal effects as recommended by the Toxicology Working Group. Please comment on the appropriateness of the proposed criteria/factors for use in this assessment process, and OPP's proposed approach for accommodating its concerns in the Reference Dose derivation and FQPA Safety Factor decision processes, in the near term, and in the longer term.

8. When the hazard to infants and children is well-characterized, and the data show that infants and/or children are more susceptible than adults, under what circumstances, if any, should this information lead OPP to employ an additional Safety Factor?

Exposure Issues

1. Subject to the qualifications expressed in the OPP Policy document and the report from the Exposure Working Group, OPP believes that each of the tiers for estimating exposure to a pesticide through food, in almost all instances, will not underestimate exposure to infants and children. Please comment on this conclusion, as it applies to each of the tiers.

2. OPP is developing a tiered approach to assessing the likelihood and magnitude of contamination of drinking water and its sources by a pesticide. As an interim approach, when direct assessment is not possible, is it reasonable and protective to regard the estimates generated by OPP's current screening methodology as upper bound pesticide concentrations for surface and ground water and to assume that this concentration generally will not be exceeded in drinking water?

3. OPP is developing approaches to assess the likelihood and magnitude of exposure to pesticides in residential and other non-occupational use scenarios. When direct assessment is not possible, is it reasonable and protective to regard the estimates of exposure for the major residential and other non-occupational exposure use scenarios developed by OPP as upper bound estimates of the exposure received by infants and children from such use?

4. In OPP's view, its aggregate exposure assessments generally do not underestimate the exposure to infants and children because the aggregate exposure is calculated by adding the high-end estimates of exposure to pesticides in food, to the high-end estimates of exposure to pesticides both in water and as a consequence of pesticide use in residential and similar settings. Please comment on this view.

VI. Policies Not Rules

The draft policy document discussed in this notice is intended to provide guidance to EPA personnel and decision-makers, and to the public. As a guidance document and not a rule, the policy in this guidance is not binding on either EPA or any outside parties. Although this guidance provides a starting point for EPA risk assessments, EPA will depart from its policy where the facts or circumstances warrant. In such cases, EPA will explain why a different course was taken. Similarly, outside parties remain free to assert that a policy is not appropriate for a specific pesticide or that the circumstances surrounding a specific risk assessment demonstrate that a policy should be abandoned.

EPA has stated in this notice that it will make available revised guidance after consideration of public comment. Public comment is not being solicited for the purpose of converting any policy document into a binding rule. EPA will not be codifying this policy in the Code of Federal Regulations. EPA is soliciting public comment so that it can make fully informed decisions regarding the content of each guidance document.

The ''revised'' guidance will not be unalterable. Once a ''revised'' guidance document is issued, EPA will continue to treat it as guidance, not a rule. Accordingly, on a case-by-case basis, EPA will decide whether it is appropriate to depart from the guidance or to modify the overall approach in the guidance. In the course of inviting comment on each guidance document, EPA would welcome comments that specifically address how a guidance document can be structured so that it provides meaningful guidance without imposing binding requirements.

VII. Contents of Docket

Documents that are referenced in this notice will be inserted in the docket under the docket control number ''OPP–00610.'' In addition, the documents referenced in the framework notice, which published in the **Federal Register** of October 29, 1998 (63 FR 58038) have also been inserted in the docket under docket control number OPP–00557.

List of Subjects

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests.

Dated: June 30, 1999.

Susan H. Wayland,

Acting Assistant Administrator for Prevention, Pesticides and Toxic Substances.

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