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Responses to Public Comments on the Office of Pesticide Program's Science Policy Document

Guidance for Performing Aggregate Exposure and Risk Assessment

OFFICE OF PESTICIDE PROGRAMS
ENVIRONMENTAL PROTECTION AGENCY
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I. Introduction

A. Background

On November 10, 1999 the availability of the draft *"Guidance for Performing Aggregate Exposure and Risk Assessment*" was published in the Federal Register (64 FR 61343) and public comments were requested on the overall content of the document and seven specific questions. This document summarizes those comments and provides OPP's response to 37 commenters who submitted critical appraisals during the public comment period. These comments have been organized into 12 topic areas, as depicted in the Table of Contents. The last three topic areas listed in the Table of Contents do not refer to specific questions posed by the Agency, but rather to overall comments about the merits of the policy and process. These topic areas emerged from the seven questions that OPP posed to the public in the draft Guidance document.

- The draft guidance document describes methodologies for assessing pesticide risks from single exposure pathways (food, residential and drinking water). Are these methodologies complete and satisfactorily described, or are changes/additions recommended? (See Part "G. Pathway Specific Issues" and "H. Current Practices in Risk Assessment)

- The draft guidance document describes a process for combining pesticide exposures and risk from multiple routes for a given pathway of exposure. Is the process, as described, logical, scientifically defensible, and complete? (See Part "B. Toxicological Endpoint Selection")

- A basic concept underlying the draft aggregate exposure and risk assessment methodology is that of the individual being exposed through calendar time with all model parameters referring back to that specific individual. Is use of this fundamental principle as the basis for the aggregate exposure and risk methodology appropriate and, if not, how should it be modified? (See Part "A. Selection of the Individual" and part "C. Time-frame of Exposure")

- The draft guidance document acknowledges the need to understand how exposures co-occur. OPP is developing standards to identify co-dependencies and interrelationships between events, and recognizes that product marketing data may be available to aid in this task. Are there any suggestions on how OPP can best evaluate and incorporate into its assessments co-occurrences of exposure events? (See Part "F. New Data Issues")

- During an aggregate exposure and risk assessment, some specific exposure scenarios may be identified as having a minimal contribution to the total aggregate risk. Is it appropriate to exclude specific exposure scenarios that contribute minimally to the total aggregate risk, and if so, at what risk level should an exposure scenario be dropped from further consideration? (See Part "I. Addition/Elimination of "Smaller Pathways")

- In certain cases and with certain pathways, it may not be necessary, advisable, or even possible to develop probabilistic exposure estimates and OPP may simply rely on deterministic (or point) estimates of a pathway-specific exposure instead. When aggregating, it will be necessary to combine the pathway-specific exposure estimates to develop an estimate of *aggregate* exposure. Is OPP's general approach to combining deterministic and probabilistic exposure estimates appropriate? If not, how should it be modified? (See Part "E. Statistical Issues")

- The draft guidance document describes three methods for combining risks from the three routes (oral, dermal, and inhalation). The Total MOE (MOE_T) and the Aggregate Risk Index (ARI) are currently being used by OPP. Should OPP continue to use these approaches or should OPP consider using the other described approach? (See Part "D. Risk Metrics")

The following is a summary of the public comments and provides OPP's responses. These are organized by major topic area, most of which overlap the questions presented by OPP in the draft Aggregate Guidance. A listing of public commenters as well as reference material used in the preparation of the following responses follows the Comment/Response section.

Please note that the revised document is called "General Principles For Performing Aggregate Exposure And Risk Assessments" and is referred to as the General Principles.

II. Comment Summaries and Responses

A. Selection of the Individual

1. "Most Sensitive Individual"

Comment: Many commenters expressed that the "*Guidance for Performing Aggregate Exposure and Risk Assessment*" (herein referred to as the Aggregate Guidance) should explicitly state that aggregate exposure assessments are to be based on the "most sensitive individual." They reiterate that the Food Quality Protection Act (FQPA) requires EPA to protect disproportionately and highly exposed persons in the population and must include all relevant exposure pathways. They remark that the current policy document fails to adequately protect these individuals by omitting the requirement that aggregate exposure assessments are to be based upon the most sensitive individual(s) in the population. They suggest that the revised document (i.e., the General Principles) should include specific mention of infants and children, those living on farms or in other areas where pesticide use is high, and those with pre-existing illness, socio-economic classes likely to be exposed, and chemically-hypersensitive individuals.

OPP Response: Commenters have identified two important areas of aggregate exposure and risk assessment: the identification and appropriate protection of sensitive individuals, particularly infants and children, within the population; and, the identification and appropriate protection of highly exposed individuals within the population. OPP believes both of the these issues are addressed in the aggregate exposure and risk assessment process laid out in the draft Aggregate Guidance. First, sensitivity among individuals in the population is addressed through the use of uncertainty factors, including the intraspecies factor that is specifically designed to protect against variable sensitivities in the human population. Additionally, FQPA directed EPA to use an additional tenfold margin of safety in assessing the risks to infants and children to take into account the potential for pre- and post-natal toxicity and the completeness of the toxicology and exposure databases. The statute authorized EPA to replace this default 10x "FQPA Safety Factor" with a different factor only if, based on reliable data, the resulting margin would be safe for infants and children. OPP makes FQPA Safety

Factor decisions when assessing risk to infant and children, women of child-bearing age and, on occasion, sexually mature males. This additional factor, through its consideration of pre- and post-natal toxicity, also serves to protect infants and children regarding potential greater susceptibility. Further, in making the determination of the adequacy of the exposure database in making FQPA Safety Factor decisions, OPP addresses all important sources, routes and pathways of exposure for the pesticide. (USEPA, 2000a and USEPA (draft), 1999).

To understand the most highly exposed individuals in the population-based aggregate assessment, OPP examines exposure data that show variability within the population. These data include a full range of food consumption patterns as, for example, identified in the Continuing Survey of Food Intake by Individuals (CSFII) often matched with distributions of residues on food commodities to more fully understand the variability in food exposure; residential pesticide use as collected in the National Home and Garden Pesticide Use Survey (NHGPUS); and, exposure to pesticide handlers through the Pesticide Handlers Exposure Database (PHED). These data, among others, reflect information about the variability in the population with respect to behavior, age, geography and other important exposure related characteristics.

Conceptually, OPP proposes to perform aggregate exposure and risk assessment for the total population comprised of potentially exposed "individuals." By potentially exposed "individuals," OPP is referring to a set of data or scientific judgements brought together based upon the characteristics of a hypothetical "individual" in the population. For example, an assessor may use currently available data sources such as the Continuing Survey of Food Intake of Individuals (CSFII) which provides characteristics of each survey respondent, e.g., gender, geographic location, time of interview (consumption). This "individual" information can be used to match other exposure related data back to the individual such as application of a pesticide in the home, consumption of certain food commodities, and likelihood of drinking water source (rural or urban). As this process of identification and combination of data sources proceeds and is refined, assessors will become better able to "link" data sets or other information and judgements together based upon individual characteristics of members of the population to create input assumptions that represent coordinated descriptions of potentially exposed hypothetical "individuals."

Other information such as pesticide use data on food/feed crops which are refined in their temporal and spatial resolution may also aid an assessor in developing coherent data sets that are based on a hypothetical "individual." OPP is investigating ways in which current food/feed pesticide use survey designs may be modified to collect temporal and spatial use information at a more refined level. For example, in one state, data are already collected in a sub-state locational basis. And as other states increase their pesticide use reporting requirements, data with increased spatial resolution may become more readily available.

Therefore, aggregate exposure assessment can be used to analyze the (representative) total population comprised of coherent "individuals" through the linking of data sources or use of professional judgement. The use of the FQPA safety factor and other uncertainty factors address the sensitivity among different individuals, especially infants and children, and assures that the aggregate exposure and risk assessment is adequately protective of public health. The use of exposure data which display variability among individuals in the population in terms of age, behavior, and other important characteristics supports the conclusion that the most highly exposed individuals are captured within aggregate exposure assessments. And the conceptual basis of the General Principles reflecting assessments based upon the collection of hypothetical individuals in the population includes those who are especially sensitive to chemical exposure, the "most highly exposed," as well as those whose exposure represents the central tendency, given the information is available. As always, OPP will utilize state-of-the-art risk assessment methodologies and all available data will be considered when making both hazard and exposure assessment determinations. OPP is confident that the use of these data in conjunction with the proposed policy will account for the most sensitive individuals and the most highly exposed individuals in the population.

2. Tolerances Should Be Set to Assure "Safety" of Infants and Children

Comment: Multiple commenters echoed the opinion that tolerance setting procedures should be performed to assure the "safety"of infants and children. Commenters stated that if the tolerance level does not assure the safety of infants and children, tolerances should be revoked. The commenters asked that OPP set tolerances at such a level that field trial data would result in exposures that would be safe to all individuals who consume that food.

OPP Response: OPP agrees that its decisions under FFDCA must assure that tolerances must include consideration of the safety of the food supply. In fact, the FFDCA (sec. 408(b)(2)(C)(i)(I)) requires EPA to make an explicit determination that "there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue." Thus, OPP's risk assessments continue to utilize the best practices to assure the safety of infants and children. However, the statute does not require EPA to evaluate the safety of the tolerance using the unrealistic assumption that all food will contain residues at the tolerance level. Although several bills were introduced that contained such an approach, Congress chose otherwise directing EPA in the FQPA to consider "available information concerning the aggregate exposure levels of consumers" and specifically mentioning use of residue monitoring data, percent crop treated data, and other data bearing on residue levels in assessing the safety of tolerances. See § 408(b)(2)(D), (E), and (F).

Whereas tolerance levels represent pesticide residues on foods which have been treated with the maximum application rate and the minimum pre-harvest interval, food commodities are often treated much differently and may undergo great changes in residues before consumption. The use of lower application rates, longer pre-harvest intervals, the treatment of less than 100% of the total acreage of a crop, as well as various food preparation practices all result in substantially lower residues than the tolerance level. OPP employs a number of study types to develop and further refine anticipated residue values in order to better determine the residues on foods as eaten. They include cooking and processing studies, bridging studies (to 'bridge' pesticide residue concentrations between maximum application rates used to determine tolerances and the range of more typical rates at which the pesticide is actually applied), residue decline studies, residue degradation studies, and certain use information such as the percent of total crop treated (USEPA, 2000b and USEPA, 2000d).

OPP believes that appropriately considering the full range and probabilities associated with real-world pesticide application practices (including the use of food monitoring data such as the Pesticide Data Program (PDP)) and, when available, incorporating this information into Agency risk assessments is consistent with the letter, spirit, and intent of the FQPA, as well as the intrinsic principles of risk assessment

The levels established in tolerances provide a maximum legal limit of pesticide chemical residues (a tolerance) above which agricultural commodities would be deemed unfit to enter into interstate commerce and assumed to be adulterated. Tolerance levels are initially selected taking into account the maximum residues that can be expected to occur from

the proposed use of the pesticide. Once a tolerance level is chosen, EPA then evaluates the safety of the pesticide tolerance using the process of risk assessment. That risk assessment incorporates all information available to EPA regarding human exposure to the pesticide including the tolerance level.

3. Do Not Refer to the "Average" Individual

Comment: Commenters stated that use of the term "average individual" in reference to the aggregate exposure population is incorrect because it implies that it is acceptable to expose some individuals to excessive levels of pesticides. Commenters further state that EPA must identify all populations at risk, profile them in aggregate exposure estimates while erring on the side of caution to protect the most sensitive individual.

Response: OPP believes there may be a misunderstanding as to what the term "average" applied in the policy document. OPP does not wish to imply that aggregate risk assessments will be performed based upon a set of average exposure events or by assessing only the central tendency of all possible exposure values. The draft Aggregate Guidance set out to assess all possible exposure scenarios and resulting exposure values to each "hypothetical" individual in the population. (See also the response to "Most Sensitive Individual" comment section.)

The term average was used in three main contexts within the draft Aggregate Guidance. The first instance was the use of the term as an arithmetic mean of a data set. For example, chronic food exposure is currently assessed through the use of the average of the two-day or three-day consumption records from the CSFII matched with the average residue value for each commodity in the assessment. The draft Aggregate Guidance also referred to the use of a weighted average percent of crop treated estimate when assessing chronic food exposures to pesticides. The third contextual reference to the term average in the draft Aggregate Guidance was a reference to the use of an average exposure value over a certain rolling-window time-frame. This, however, refers to an average exposure value over a specific time-frame *to each hypothetical individual in the population*. The goal of aggregate exposure and risk assessment is to seek to assess the range of total aggregate exposure and risks to all persons in the population, using uncertainty and safety factors to address special sensitivities with the population and using the exposure data which reflect variability in individual exposure characteristics such as age and behavior.

4. Explain the Use of Data Concerning the Temporal, Spatial, and Demographic Characteristics of Individuals Within the Population

Comment: Commenters expressed confusion about OPP's explanation of the use of temporal, spatial and demographic information in an aggregate exposure assessment. Specifically, one commenter asked how the information will be used in a regulatory decision making framework and speculated that OPP may engage in "time of year" and region-specific labeling procedures. Another commenter asked how OPP will identify representative temporal patterns of activity to be used in analyses as all possible temporal exposure patterns cannot possibly be identified. And another point of confusion relayed by commenters included whether OPP will utilize life-table analysis methods linked to time-line based exposure information. Commenters echoed a need for clarification within the expanded policy document as to how the temporal, spatial and demographic information will be used.

OPP Response: OPP agrees that the draft Aggregate Guidance document needs further clarification of the use of temporal, spatial, and demographic data. It is vital to understand that the emphasis of this General Principles document is on the use of temporal, spatial and demographic exposure information for risk assessment purposes when determining the inputs to the aggregate exposure and risk assessment to ensure that assessed hypothetical individuals are consistent e.g., exposure through a springtime concentration of a pesticide in drinking water is not combined with an exposure through a fall lawn application. The document is not intended to cover regulatory decision-making framework which is more appropriately considered under the topic of risk management.

It is clear that temporal patterns vary over time and OPP relies on surveys that are conducted over an entire year to capture the variability inherent in population-based aggregate exposure and risk assessment. OPP may consider "time of year" and region-specific labeling efforts. Additionally, life-table analysis was not among the proposals to consider when performing aggregate exposure and risk assessment. Life-table analyses, as the commenter implied, would apply current, cross-sectional exposure rates to groups of individuals in the population based upon some type of stratification scheme. Life-table analyses are similar to actuarial tables used by insurance adjustors. For example, males age 25-30 years would be assigned a probability of exposure based upon current exposure rates. In the same example, probabilities of exposure for each age cohort (calculated from the exposure rates) would be applied throughout a life, resulting in the total exposure for the population.

OPP is confident that data based on a potentially exposed hypothetical "individual," can be preliminarily developed using available data sources which adequately and accurately assess the temporal, spatial and demographic characteristics of a representative population. (See example in "Most Sensitive Individual" response.) OPP anticipates future data sources will be developed as assessors move toward a more realistic analysis of aggregate exposure and risk as depicted in the General Principles. For example, OPP is aware of the Residential Exposure Joint Venture (REJV) data on co-occurrence of residential pesticide use that is currently in development. Other publicly available data sources include the Continuing Survey of Food Intake by Individuals (CSFII) and the U.S. Census data and National Health and Nutrition Evaluation Survey (NHANES) data, among others. These surveys detect differences between individuals and can be used to assess temporal, spacial and demographic variability across individuals. OPP does not propose creating a few representative data sets, but proposes to utilize any and all data sets that are available to assess aggregate exposure and risk using the concept of the hypothetical "individual." OPP acknowledges that these data sources will likely need to be formatted or otherwise joined within some type of software modeling system.

5. How the Individual is "Selected"

Comment: Commenters expressed interest in understanding more fully how OPP will select the individuals upon which the aggregate exposure and risk assessments will be based. They state that the assessment should be for the individuals who are "most highly exposed" to be the most protective of the public's health. Commenters ask whether OPP anticipates performing worst case only or realistic distributions of exposure. They inquire, also, how representative the exposure scenarios will be and how exposure data values will be assigned to the individual. Additionally, commenters ask how a reasonable certainty principle will be applied not only to the average individual, but also to the more sensitive in the population. Will there be a designated population at risk in each aggregate exposure analysis, they ask. Another important point mentioned is how many individuals will be selected and how OPP will select exposure characteristics for individuals.

OPP Response: The consistent application of temporal, spatial and demographic characteristics to each hypothetical "individual" in the representative sample population is key to the expanded General Principles. For example, an aggregate exposure estimate should not reflect the diet (record) of an infant in an urban setting (known from a CSFII record, for example), the residential exposure pattern/estimate of an

applicator, and the drinking water estimate using a rural estimate because it is not reasonable that an infant would apply a pesticide or a person in an urban setting would receive similar drinking water exposure as person in a rural community, among other things. Further, if the type of individual being evaluated for a day's exposure is a female on one day, she cannot assume exposure patterns, e.g., consumption record, represented by a male on another day. By "individual" OPP is referring to a coherent set of data, judgements or other measures (representing the food, residential, and drinking water pathways) which reflect potential aggregate exposure for each type of person, for each day in that person's life, over time. In other words, characteristics used to assess an individual's aggregate exposure over time are consistent in temporal, spatial and demographic characteristics.

The hypothetical individuals included in the aggregate exposure population will include the "most highly exposed," those at the high-end of the exposure distribution, as well as those who represent points across the entire range of the exposure distribution. OPP examines exposure data that show variability within the population. These data include, for example, a full range of food consumption patterns as identified in the Continuing Survey of Food Intake by Individuals (CSFII) often matched with distributions of residues on food commodities to more fully understand the variability and uncertainty in food exposure; residential pesticide use as collected in the National Home and Garden Pesticide Use Survey (NHGPUS); and, exposure to pesticide handlers through the Pesticide Handlers Exposure Database (PHED). These data, among others, include specific information about the variability in the population with respect to behavior, age, geography and other important exposure related characteristics.

Using this approach, OPP intends to not only include exposure scenarios of the "most highly exposed" individual, but all potential exposures in the population, based upon available data and justifiable assumptions. Therefore, OPP does not support the creation of only worst-case, bounding estimates, although these are valuable for the purpose of comparison, but the entire range of realistic exposure values. The hypothetical individuals included in the aggregate exposure population must be representative of the full population from which they are drawn. The size of the analysis, or the type and number of representative "individuals" examined, should include consideration of model stability at the tails of the aggregate exposure distribution and the representativeness of the data for the particular chemical of concern. For this reason, sample size would need to be sufficiently large to detect variability among individuals in the population with respect to key exposure characteristics such as age, gender, region of the country. OPP is familiar with aggregate software modeling tools which utilize the population of CSFII respondents, or the U.S. Census birth records, and OPP believes there are other possible data sources available. In this way, exposure characteristics are not arbitrarily assigned to each individual, but merely drawn from the collected data set, i.e., U.S. Census and the CSFII provide key demographic information which could be applied in an aggregate assessment. OPP does not advocate one over the other, but encourages multiple attempts to develop software that estimates aggregate exposure and risk.

OPP does not intend to select only certain sub-sets of individuals, either the potentially most highly exposed or the average individual. Instead, OPP intends to utilize all available data to assess aggregate exposure to the total population. The type, number and exposure characteristics of the individual are not predefined, but rather are extracted (or randomly assigned) from available data sources. This process, it is hoped, will utilize data representing the entire distribution of possibly exposed hypothetical "individuals." In this way, it is not only the "average"or the "high-end" exposure value ("individual" as a point in time and space), but the entire distribution.

B. Toxicological Endpoint Selection in Aggregate Exposure and Risk Assessment

1. Use of Non-Cancer/Cancer Endpoint and its Selection

Comment: Commenters requested additional information in the General Principles document concerning the assessment of both threshold and non-threshold cancer risk within an aggregate scenario. Specifically, commenters indicated that the document did not provide sufficient guidance concerning the assessment of non-threshold cancer endpoints. Another commenter cited an apparent inconsistency between the aggregate policy document and the recently expanded Cancer Assessment Guidance which suggested the use of an MOE when the dose-response function based on an animal model is non-linear. An additional point mentioned by the commenters is whether OPP will use a probabilistic approach to dose-response curve estimates within the aggregate exposure and risk assessment framework.

OPP Response: OPP believes that implementation of the General Principles for cancer endpoints is not dependent upon the method of quantification. The methods described are sufficiently flexible to accommodate a variety of approaches. In general, the selection of endpoints for cancer and non-cancer effects is made by peer review committees based upon the available toxicology data. These data are used to obtain to the extent possible an understanding of the mechanism by which pesticides exert adverse effects of concern and also to determine the appropriate basis for regulating pesticidal exposures. Selection of appropriate endpoints includes interpretation of route specific data when available, or extrapolation among routes when necessary. In all cases, the goal of endpoint selection is to establish a public health protective basis for regulating pesticide use.

OPP has adopted the Agency stance that carcinogens should be regulated using the full understanding of the mode of action of the carcinogen and its dose response characteristics. Where available data indicate that the mode of action of a pesticide results in a non-linear dose response, an MOE approach is used to estimate carcinogenic risk. The regulatory endpoint upon which the MOE is based may be early signs of tumor response or the occurrence of precursor events. Where data indicate that the mode of action is non-linear in its dose response characteristics and sufficient data are not available to understand the mode of action, a linear approach to estimating cancer risk will be assumed. Where a non-linear approach to estimating cancer risk is adopted, the application of the General Principles will approximate that

described for other non-linear, non-cancer effects evaluated using an MOE approach for exposures above the identified toxicological threshold.

OPP does not intend to move toward the use of a probabilistic dose-response function at this time.

2. Description and Definition of Toxicological Endpoints/Effects

Comment: Commenters relayed suggestions for clarifying toxicological endpoint selection. One commenter stated that the selection (and non-selection or elimination) of certain toxicological endpoints and accompanying exposure scenarios should be done judiciously. For example, including only the oral route of administration because no effects are seen by the inhalation or dermal routes may not be appropriate since there are many effects for which dermal and inhalation studies may not be predictive, e.g., dermal neurotoxicity study. In other words, there could be significant toxicological effects via the two routes of exposure, but they were not evaluated for nor detected in the studies. Another commenter requested that benchmark doses should be included in the document as a replacement for No Observed Adverse Effect Levels (NOAELs) and Lowest Observed Adverse Effect Levels (LOAELs). Also, one commenter specifically mentioned that genetic variation in the detoxification ability of individuals should be considered when defining toxicological endpoints.

One commenter believes that the toxicological effect must not only affect the same target organ via different routes of administration, but also have the same mode of action. They referred to OPP's statement that aggregate risk assessment is based on the evaluation of the same toxic effect that is produced by exposure through different routes, and, therefore, the toxicological effects must be the same if the dose and risks are to be aggregated.

OPP Response: To perform aggregate risk analysis, exposure scenarios must be matched with appropriate toxicological endpoints. OPP attempts to accommodate the complexities of multi-route toxicity in its hazard evaluation process. During the endpoint selection process, OPP attempts to ensure that the potential for cross-route toxicity is included in its deliberations. The occurrence of effects measured in route-specific studies are carefully evaluated. OPP also considers the likelihood that effects observed by the oral route but not measured in dermal or inhalation studies might have occurred had they been measured. The intent of OPP is to develop reasonable, public health protective endpoints that can be applied to the full range of potential pesticidal exposures included in an aggregate assessment. OPP agrees that logical exposure

scenarios for a particular chemical review without toxicological endpoints can be included in an aggregate assessment through use of extrapolation methods which have been reviewed and approved by the Agency (i.e., route-to-route extrapolation).

OPP agrees in concept that the estimation of points of departure using approaches such as bench mark dose may be more descriptive of the actual toxic potential of a pesticide. However, these approaches require an adequate description of the dose-response characteristics of the pesticidal effect of concern. Use of NOAELs and LOAELs to estimate hazard will continue to be used where data do not support the use of bench mark dose estimates.

OPP requires the submission of a battery of toxicology data to support the registration and reregistration of pesticides. This battery of studies is designed to measure a broad range of toxic effects and to estimate the likely metabolism and elimination of the pesticide from the body. Because of dosing requirements and the subsequent application of uncertainty factors to account for inter- and intraspecies variability, OPP is confident that the endpoints selected are protective of public health, including the differences in individuals' ability to detoxify chemicals in the body. OPP will continue to employ the default 100-fold uncertainty factor to its toxicological endpoints reflecting both interspecies variability (10x) and intraspecies variability (10x). In fact, analysis of the proportion of the population covered by the 10-fold default factor for intraspecies variability suggested that more than 99.9% of the population of healthy adults was covered (Renwick, 1999 (p.5)).

OPP does not agree that the mode of action of the toxicological effect must be the same. A toxicological effect may be the same via different routes of administration but the mode of action may differ. Although the specific mechanism of toxicity for each route of exposure to the pesticide may not specifically be known, a determination that the effects by each route are qualitatively similar (i.e., same target organ and essentially type of adverse effect) must be made in order to determine that exposures in an aggregate assessment should be combined. OPP anticipates that multiple aggregate exposure and risk assessments may be performed per chemical under review based upon different toxicological endpoints evaluated.

3. Developmental and Reproductive Toxicants

Comment: A number of commenters stated that they believe separate hazard and exposure assessments should be performed for developmental and reproductive toxicants. They state that short-lived

exposures during critical time periods can be very important for certain chemicals and that OPP, therefore, should do short-term aggregate exposure assessments for developmental and reproductive toxicants. They provided an example that a peak exposure to a testicular toxicant can be a major problem if an individual is trying to father a child or that a short-term exposure to a teratogen during a critical period of gestation can result in an adverse health outcome. Therefore, the commenters stated that they would like to see explicit guidance to perform short-term risk assessment for these toxicants.

OPP Response: OPP agrees that developmental and reproductive toxicants should be considered in an aggregate exposure and risk assessment. OPP considers reproductive and development effects to be an endpoint associated with short-term exposure. OPP is moving toward short-term exposure assessments for developmental and reproductive effects which are separate from one-day assessments. When reproductive and developmental toxicity appears to be the choice for a short-term RfD, OPP will do a short-term exposure assessment. In the absence of good exposure data, OPP uses one-day calculations but as exposure data become more available, especially for residential and drinking water assessments, OPP will do more refined short-term exposure estimates. It is only with the advent of the expanded aggregate exposure and risk assessment methods that a series of short-term exposures (e.g., three-day rolling window) could be matched with a developmental or reproductive effect which may occur only during critical periods because aggregate exposure and risk assessment includes use of a rolling time window of exposure.

C. Time-frame of Exposure

1. Rolling Window Time-frame of Exposure

Comment: Commenters requested clarification as to how the rolling window time-frame of exposure is to be used in an aggregate exposure and risk assessment. Particularly, commenters asked how the time period of exposure is to be identified and how the appropriate "averaging time" would be determined, including how a "time-weighted average" may be obtained. Also, commenters requested further explanation of how the rolling window of exposure relates to the time to onset of effect. Ultimately, commenters asked how the use of the rolling window of exposure would be used in regulatory decision making.

OPP Response: OPP has modified the guidance document to present a clearer discussion of this topic. The rolling time-frame of exposure refers to a technique for calculating a series of sequential calendar-based averages for each individual in the population. For example, the initial value for a seven-day rolling average would include an average exposure over the period from January 1 through January 7, and the 2nd average would include exposure values for January 2nd through January 8th, etc. A calendar-based rolling average provides OPP with a much more realistic representation of exposure over time. It also presents greater flexibility in matching human exposure duration with the exposure duration in an animal study which produced a toxicological effect. The appropriate "averaging time" or rolling window is ideally determined through the toxicological study of interest. The matching of exposure time-frames with toxicological time-frames is a new and exciting element of the expanded General Principles. The rolling-window concept is used to better link the exposure duration required to elicit an effect in an animal study with the exposure duration in which a potential effect may occur in humans exposed to chemicals in an aggregate scenario. The use of the rolling window helps to better define the exposure distribution over the time period of interest. The use of the rolling window time-frame is a tool to better relate the duration of the toxicity study upon which the endpoint is based and the exposure period assessed. The average length of the toxicity study and the duration of exposure are the likely factors to define the rolling window. The use of the rolling window does not indicate the creation of a new distribution of exposures. Time to onset of effect is a slightly different concept which relates the time of exposure to the time to the occurrence of the adverse effect.

D. Selection and Use of a Risk Metric in Aggregate Exposure

and Risk Analysis

1. Risk Metric

Comment: Many commenters, in response to OPP's question (#7), presented opinion and ideas concerning the use of an appropriate aggregate risk metric. Three risk metrics were proposed in the draft Aggregate Guidance, the Hazard Index (HI), the Total MOE approach, and the Aggregate Risk Index (ARI). The following specific comments were given regarding these three choices:

- the HI and ARI are reciprocals of each other and they should be considered one approach;
- the total MOE may be appropriate for a screening tool, but not for any assessment beyond screening;
- the total MOE approach using a single, common uncertainty factor is preferable and should be considered the basis of aggregate exposure assessment;
- the total MOE approach loses too much information and is therefore not appropriate to use;
- the "inverse" ARI (the ARI<1 is preferable) is "odd" and OPP should incorporate a more common-sensical approach;
- all three approaches tend to compound conservatism due to the nature of uncertainty factors that appear in the RfD/RfC and in the interpretation of the acceptable risk metric; and,
- none of the risk metrics proposed were adequate–OPP should develop a completely new aggregate risk metric.

Another commenter advocated the use of *non-parametric data visualization* techniques. They stated:

> "Large n-dimensional data sets and the complex probability distributions attendant to such analyses should never, however, be aggregated by conversion to deterministic risk values (e.g., MOEs, Ufs, RIs, RfDs, and ARIs) and simple mathematical summation. All the richness inherent in the data is lost! By their nature, such data sets already portray the aggregate if only observed in the right manner. The use of non-parametric data visualization techniques of analysis should be considered as a much more powerful means of examining aggregate exposures and risk and identifying specific situations where mitigation measures should be taken to protect public health."

OPP Response: OPP appreciates the diversity of comments received in response to the specific question posed. OPP agrees that the HI and ARI are substantially the same. The Hazard Index (HI) is merely the addition of the Hazard Quotient (HQ) for each route.

HQ=(Exposure)/RfD and RfD=NOAEL/UF.
Therefore, the HQ is also the exposure/(NOAEL/UF).
And, This function can be algebraically manipulated to equal the UF/(NOAEL/exposure)/1.

ARI=1/(1/RI $_{o}$ + 1/RI $_{inhl}$ + 1/RI $_{der}$) and RI(risk index)=MOE/UF.
Therefore, the MOE=NOAEL/UF.
And, ARI=1/(NOAEL/exposure)/UF.

Alternatively, the ARI is therefore the reciprocal of the hazard index. The ARI is preferred over the HI because of its ability to accommodate dissimilar uncertainty factors. OPP has eliminated the Hazard Index in the expanded General Principles.

OPP disagrees with commenters who state both that the use of risk metric is only for screening level assessment, and, that none of the risk metrics presented are appropriate for use. OPP believes this policy document goes substantially beyond the screening level assessments and these risk metrics can be used in a higher level assessments. OPP intends the policy paper to provide a picture of how detailed aggregate assessments would be performed including the use of one of these risk metrics.

OPP will continue to employ either the total MOE or the ARI in its aggregate exposure and risk assessments. The flexibility that the two options provide, especially in addressing dissimilar uncertainty factors, is desirable to the Office. OPP does not believe that the total MOE approach using a single, common uncertainty factor is the only suitable option. Nor does OPP believe that the total MOE approach should not be used because it loses too much information. The risk metrics included in the expanded General Principles document intend to distill large amounts of data; inevitably some information will less visible. OPP believes that the increased accuracy and reality of the expanded General Principles, however, will compensate for this. The use of the ARI will be retained for use when there are dissimilar UF's for each pathway. These tools are adequate to make aggregate exposure calculations. OPP agrees that the interpretation of the ARI (represented by values which fall below 1) must be made clearly and explicitly in the risk characterization section of any aggregate assessment. OPP believes the use of uncertainty factors which is inherent in either the total MOE or the ARI approach is appropriate and

necessary, unless empirical data are available to support removal. OPP understands that the use of uncertainty factors may lead to conservative assessments, but believes this is the preferred approach to adequately protect the public's health, especially infants and children. And, OPP will use either the total MOE or the ARI and will not embark upon developing a new aggregate risk metric at this time. OPP will also consider the suggestion to employ certain non-parametric data analysis methods in the absence of a sufficient data set.

2. Application of Uncertainty Factors

Comment: Commenters discussed five main points relating to the use of uncertainty factors in aggregate exposure and risk assessment. First, the application of uncertainty factors must be kept separate from the hazard assessment process and the risk calculation process. The inclusion of the uncertainty factor within these two risk assessment steps represents an inappropriate mixing of science and policy. Second, uncertainty factors should not be assigned for the lack of route-specific (toxicological) information because it is generally recognized that most toxicity is expressed as a result of the systemic concentration of the chemical at a target organ. Next, another commenter suggested that OPP apply a probabilistic determination of the uncertainty factor in a manner similar to other EPA offices. In this way, the commenter stated, an assessor can determine how these uncertainty factors need to be modified so the degree of confidence and conservatism inherent in the aggregate assessment matches that deemed necessary when single pathways are originally considered. Another commenter stated that the quantitative impact of any uncertainty factors should be explicitly identified. And, fifth, the FQPA safety factor need not be applied on a route-specific basis in aggregate exposure analysis.

OPP Response: OPP disagrees that the current applications of uncertainty factors during the risk assessment process is an inappropriate mix of science and science policy. The selection of an uncertainty factor rightly takes place during the review of the hazard database and, further, OPP may include an additional uncertainty factor for lack of a route-specific toxicological data set. The "*Policy on the Determination of the Appropriate FQPA Safety Factors for use in the Tolerance Setting Process*" indicates that in addition to the 100X typically applied to toxicological data set to account for differences between species (when extrapolating from animal studies) and the differences between humans, the FQPA Safety factor would include other uncertainty or modifying factors used in the calculation of the hazard values, for example, the database uncertainty factor that is applied when one or more critical core studies are missing (USEPA(draft), 1999). An uncertainty factor may be assigned for lack of critical core studies, including route-specific studies.

The probabilistic identification of uncertainty factors is a topic considered in the past, at which time the need for specific physiologically based pharmocokinetic (PBPK) modeling data was also identified. Related to this topic is the acknowledgment that others have investigated the ability to separate the traditional 100 fold safety factor into 10-fold factors representing kinetic and dynamic defaults to better define uncertainty factors and identify the degree of confidence and conservatism in the assessment (Renwick, 1999). However, this investigation has also concluded that the usual default of 100 remains appropriate for most cases. And, it has been shown that mechanistic and toxicokinetic data rarely contribute to the selection of the uncertainty factor. OPP does not plan to pursue the probabilistic determination of uncertainty factors at this time.

OPP is working toward determining the quantitative impact uncertainty factors have on the aggregate risk assessment. However, these methods and processes are not fully defined at this time. Further the FQPA safety factor is not applied on a route-specific basis, but on a population-specific basis, depending upon the toxicological data presented for each chemical analysis and the possible exposure scenarios defined. See the "*Policy on the Determination of the Appropriate FQPA Safety Factors for use in the Tolerance Setting Process*" (USEPA (draft), 1999) for more information about the determination and application of the FQPA safety factor.

E. Statistical Issues

1. Cross-Sectional vs. Longitudinal Data in Aggregate Assessments

Comment: One commenter noted that most data for aggregate exposure are from cross-sectional databases and are not longitudinal in nature. Cross-sectional databases are those which collect information across a population, at a specific point in time, e.g., the CSFII. Longitudinal databases follow the same individuals over time, assessing changes in exposure to the specific individual over time, e.g., the Framingham Study of Cardiovascular disease. The commenter suggested that additional guidance be included within the policy document concerning how to extrapolate cross-sectional data to the type of longitudinal data needed for aggregate risk assessments.

OPP Response: OPP agrees that many data sources which could be used for aggregate exposure and risk assessment are cross-sectional in nature, but disagrees that longitudinal data cannot be modeled with available data sources. For example, the Residential Exposure Joint Venture (REJV) pilot is now collecting field data for the residential pathway, including information on home pesticide use for 1000 people over one year. There are National Agricultural Statistics Service (NASS) data which assessors could use in identifying co-occurrence of pesticide use on agricultural commodities. There are also data sources for activities of an individual (NHAPS) and insights into use of products can be gained from labels and marketing data. These cross-sectional data sources can be linked with individuals based upon unique exposure characteristics such as age, gender, and region of the country defined in large data sets from which an aggregate population may be identified. Examples include the population of CSFII respondents and the U.S. Census records. In this way, the personal exposure characteristics can be the link between individuals in the aggregate population and exposure factors identified in empirical exposure data sets cited above. These types of empirical data can be used repeatedly within an assessment to simulate many individuals or they can be used to inform judgements about pesticide use and exposure over time. Alternatively, more chemical specific information can be used for each assessment. Assessments can be performed individual-by-individual, day-by-day, until an entire population is developed over some period of calender time. OPP agrees that it will likely never have one omnibus longitudinal, population-based survey. However, OPP is confident we can use the information available and combine the data in ways which reflect exposures to a potentially exposed hypothetical "individual" to investigate these questions.

2. Use of Probabilistic and Deterministic Types of Data Within an

Assessment

Comment: Several commenters expressed thoughts about the simultaneous inclusion of both probabilistic and deterministic types of data within an aggregate assessment. Most commenters supported a move toward total probabilistic analysis. A number of commenters were not in favor of combining exposure estimates for different pathways using deterministic and probabilistic analyses together within an aggregate assessment. One commenter suggested that the appropriateness of combining point estimates used in deterministic analyses with distributional data used in probabilistic assessments will require validation, which could possibly be as simple as combining different data sets using both types of data and comparing the results (sensitivity analysis). In addition to the need to validate this method of combining these different types of data, a commenter also stated the following problems with combining deterministic and probabilistic assessments:

> "the resulting assessment will be neither deterministic nor truly probabilistic. It will not be possible to state the percentile of the population associated with any particular risk estimate, and so the power of probabilistic methods to inform decision-making will be lost; and, the pathways that are not treated probabilistically will have a greater chance of being identified in the sensitivity analysis as the most significant contributors to aggregate risk, when they would not be so identified in a fully probabilistic assessment. This will be a natural consequence of applying default conservative assumptions to these pathways while using more realistic values for the pathways that are treated probabilistically."

The commenter continued to say that if pathways using different types of data are combined, one must ensure that central tendency values are included in the deterministic pathways. Otherwise, the commenter stated, the resulting variability distributions for aggregate exposure will not be an accurate description of actual exposures. The upper-tail of the distribution of actual exposures will be over-represented and it will not be possible to specify the degree to which this over-representation is present. Also, the combination will lead to a false depiction of the sensitivity of risk to specific pathways. Therefore, the commenter stated, assessments must use central tendency values when identifying deterministic values.

Another major comment in this area concerned how to develop and describe data distributions. One commenter stated that although the methodology for developing the necessary distributions from existing data sets is described in the document, there is no description in the document of how, or even whether the Agency will consider uncertainty in generating a full probabilistic assessment for any pathway. The danger, said the commenter, in failing to address uncertainty formally is that it may be combined inappropriately with variability analysis resulting in probability density functions that are descriptors of neither variability nor uncertainty. Quantitative variability and uncertainty analyses within the aggregate assessment were also suggested by commenters.

One commenter concluded by saying that there is little reason to combine deterministic and probabilistic approaches. Methods exist for performing probabilistic assessments of all pathways, including uncertainty analysis. According to the commenter, combining probabilistic and deterministic approaches would represent a step backwards scientifically. The hybrid between probabilistic and deterministic would be impossible to interpret.

OPP Response: OPP has designed the General Principles document to accommodate the use of probabilistic analysis for all three pathways of exposure. However, OPP understands that in many cases the methodologies nor the data are available to fully support this approach at this time. OPP agrees with the commenter that moving toward a more fully probabilistic type of aggregate assessment is vital. Until this goal is fully realized, however, OPP believes it is appropriate to combine deterministic point estimates and probabilistic distributions within one aggregate exposure assessment. OPP believes that *qualitative* assessment of the uncertainty/variability in the assessment can be performed using sensitivity analysis, but the separation of the two influences requires more sophisticated techniques. The National Academy of Science has recommended that the distinction between variability and uncertainty should be maintained rigorously at the level of individual components of the assessment as well as in the overall assessment. OPP concurs with the stated need for two-dimensional analyses in aggregate risk assessments and will move toward this goal over time.

However, OPP believes it is reasonable to estimate and describe the distribution of exposure using a mixture of deterministic and probabilistic analyses if probabilistic data are available for only certain exposure routes or pathways. OPP recognizes that the use of high-end deterministic values may overestimate exposures in the tails if exposure estimates are sensitive to these specific inputs, but this would indicate that it was important for valid probabilistic data to be gathered for these deterministic inputs while OPP sees that the routine use of deterministic central tendency data in probabilistic assessment would more likely underestimate exposures at the tail of the distribution. OPP also recognizes that use of high-end deterministic estimates where probabilistic data are not available might tend to overestimate exposure in the tails. For this reason, OPP retains the option to perform sensitivity analysis on those situations where a deterministic estimate appears to contribute significantly to high-end exposures. The ILSI panel (ILSI, 1998) and the SAP (Kendall, 1999) have stated that it is acceptable to combine probabilistic and deterministic types of data in the food pathway. The "*Guiding Principles for Monte Carlo Analysis*" (USEPA, 1997a) states that from a computational standpoint, a Monte Carlo analysis can include a mix of point estimates and distributions for the input parameters to the exposure model. However, the *Guiding Principles* document goes on to say the risk assessor and risk manager should continually review the basis for "fixing" certain parameters as point values to avoid the perception that these are indeed constants that are not subject to change. OPP intends to continue to move forward. In the draft Aggregate Guidance, OPP stated that there are situations for which the use of probabilistic data may or may not be appropriate. OPP believes that a full understanding of the uncertainty and a careful characterization of the results, including sensitivity analysis, is vital when combining these types of data.

3. Biomonitoring

Comment: Commenters agreed with OPP that biomonitoring could provide a crucial tool to validate aggregate assessment. However, one commenter also states that the lack of correlation between biomonitoring results and estimated exposure levels, to the extent that it is known, could have to do with the use of high-end exposure estimates, or the lack of highly exposed individuals being monitored. Data quality of both the modeling estimates and the biomonitoring data makes it difficult to use biomonitoring data as a tool to validate exposure estimates. Another commenter suggested additional studies are needed for this purpose and that the Agency should conduct such studies.

OPP Response: OPP appreciates the support for the use of

biomonitoring. OPP also acknowledges the difficulty of resolving discrepancies between modeled estimates and biomonitoring data. However, these studies, to the extent they are available, are still a good source of data for validation. The National Health and Nutrition Examination Survey (NHANES) is perhaps the largest collection of biomonitoring data, and in a recent survey design biological samples have been analyzed for a subset of pesticides. These data, among others, may be used to aid in the model and assessment validation process.

4. Selection of the Percentile of Exposure

Comment: Several commenters expressed the need for a specific percentile of exposure to be identified by OPP within the policy document. One commenter stated that without at least rudimentary decision criteria, the decision maker could use the distribution to justify almost any policy. The danger, according to the commenter, is that the "target" percentile of risk will be chosen to produce the desired policy outcome, rather than concerns for consistency and transparency. Other commenters echoed this same concern adding that "case-by-case" decision-making creates erratic and not necessarily desirable public policy.

Another commenter suggested that, depending on the percentile of exposure selected, the inter-subject variability and the influence of a certain pathway would be significantly impacted. For example, it may be possible to obtain reasonably accurate estimates of the central tendency value, the 75th percentile, and perhaps as high as the 95th percentile. But, values beyond the 95th percentile are unlikely to be accurate without significant new research. The amount of evidence needed will depend upon the target percentile selected. Also, the percentile of exposure selected (for decision-making) will affect the influence of certain pathways. A given pathway might influence the 70th percentile, but would be of lesser importance in defining the 99th percentile. Without specifying the percentile to be considered in decisions, it will not be clear to the assessor how to perform the sensitivity analysis.

OPP Response: OPP disagrees that an explicit "bright line" definition an acceptable percentile of exposure should be made for all aggregate exposure and risk assessments, and supports use of a case-by-case assessment of the appropriateness of the exposure level used in decision-making. Data sets defining and describing aggregate exposure and risk can differ significantly among different chemicals in their quality, completeness, representativeness and other factors. As stated in the "*Response to Public Comments in the Office of Pesticide Program's Draft Science Policy Document: Choosing a Percentile of Acute Dietary*

Exposure As a Threshold of Regulatory Concern," which addresses the use of a percentile of acute dietary exposure but not aggregate exposure (USEPA, 2000c). OPP would potentially be concerned about the level of exposures to the general population or specific subgroup of concern, for any exceedence beyond some threshold of regulatory concern, but these potential concerns could be appropriately addressed by a full characterization of the issues including the inherent uncertainties and biases in the assessment. In some situations involving estimates of food exposure, the document states, a threshold based on a lower population percentile may be appropriate and would be determined on a case-specific basis. The commenters should refer to the OPP Science Policy document "*Choosing a Percentile of Acute Dietary Exposure as a Threshold of Regulatory Concern*" which describes the criteria OPP would use in defining a percentile of exposure for a well defined approach to estimating exposure (USEPA, 2000a). OPP agrees that the "case-by-case" evaluation should be used in an open and transparent manner. OPP believes a full, independent review of the percentile of exposure through public commenting and other means should be used in decision-making for each chemical case.

5. Population Weighting Factor

Comment: Some commenters expressed confusion over the use of population weighting factors as described in the document. They requested clarification in the final document as to the reason OPP is proposing to use population-weighted data, how the population-weighting would be done, and how the population to be weighted would be defined. Specifically, one commenter stated that the Agency fails to explicitly indicate why population-weighted exposure estimates are desirable, according to the commenter, the implication is that overexposure to pesticides if they occur to relatively small populations are acceptable. Another asks whether, in Step 2 of the description in the draft policy document, a population weighted exposure value should be calculated. Another commenter states that differences in data quality, completeness, and defensibilty can be incorporated as weighting factors in distributional analyses and the effects of using weighting factors can be accounted for in a sensitivity analysis.

OPP Response: OPP acknowledges that the term "population-weighted" has been used in different contexts within the draft Aggregate Guidance. The purpose of a population-weighting factor is to ensure sample results can be applied accurately and appropriately to the total population. At times, surveys are conducted in such a way as to over sample certain sub-population which represent a small portion of the total population but are of interest to the research question being investigated. For example, the CSFII data were collected in such a way as to over sample certain low income populations. OPP emphasizes that the purpose of population weighting information is not to justify overexposure to a small population but rather to assure that sub-populations of interest, such as children, are sufficiently sampled to allow for robust statistical analysis of the sub-population while at the same time allowing for the appropriate incorporation of survey results to permit statistical statements to be made concerning the total population. Population-weighting is usually performed by assuring that any over- or under-representation in sampling among one sub-population is "normalized" by applying a weighting factor to that population. Population weighting, if employed, would be different between different data sets. In this context, the population to be weighted would be defined in the sample design of the study from which the data set were collected. Concerning the commenters' question related to the second question to consider when performing aggregate assessments, identifying the potential exposures scenarios, a population-weighting factor could be used in this step in the process. However, this is part of the assessor's task in identifying available data, including data which may need to be weighted in order to be applied to the entire population.

The last comment refers to another use of the term population weighting. In this case, population weighting would be applied to different data sets within an aggregate assessment to account for differences in data quality, completeness, and defensibility. This approach would have to be fully defined and explained within any aggregate assessment.

F. New Data Issues with the Advent of Aggregate Exposure Estimates

1. General

Comment: One commenter expressed concern that the aggregate exposure and risk assessment requirements of FQPA would require new data call-in letters, resulting in a significant outlay of resources and a decrease in efficiency of approval of various pesticides and uses including inerts and antimicrobials. These concerns, to the commenter, illustrate the incompatibility between the draft Aggregate Guidance and current conceptual framework upon which the Guidance is built.

OPP Response: OPP disagrees with the commenter that the implementation of the aggregate exposure and risk assessment guidance will lead to inefficiencies in pesticide approval, including inerts and antimicrobials, and it may not lead to substantially new or different data call-in letters. OPP is confident that aggregate exposure and risk analysis can be performed with the types of data currently required as part of the risk assessment process. Pesticide companies, however, are always welcome to provide additional data to allow a better understanding and more refined estimates of aggregate exposure and risk.

2. Aggregate Exposure and Risk Assessment Poses Significant Data Limitations

Comment: Several commenters identified data limitations inherent in performing an aggregate exposure and risk assessment at this time. Commenters suggested that directed research into specific exposure pathways and support of data collection efforts such as the National Contaminant Occurrence Database (NCOD) are key areas of research. Commenters suggested that the limitations of the input data set and potential bias of default assumptions which are generally conservative should be recognized and considered during the interpretation of results, and that these limitations affect the ability to discriminate between hypothetical risk drivers and real ones.

OPP Response: OPP agrees that the results of an aggregate exposure and risk assessment may be sensitive to the values used for particular parameters estimates in the assessment (e.g., percent of crop treated, residues concentrations which have less than the Limit of Detection, values or parameters are assigned by the Residential SOPs) but believes that as long as: (1) values used for particular parameters are

well-explained, reasonable, and transparent; (2) sensitivity analyses are performed to determine if any values used for particular parameters are "driving" the risk or control the resulting risk estimate; and, (3) the resulting risk estimate is properly characterized and incorporates the results of the sensitivity analyses, then the risk estimates are an adequate basis for regulatory decision.

Furthermore, the "*Guiding Principles for Monte Carlo Analysis*" suggests that when data for an important pathway/parameter are limited, it may be useful to define plausible alternative scenarios to incorporate some information on the impact of that variable in the overall assessment (USEPA, 1997a). In doing this, the *Guiding Principles* suggest, the risk assessor should select the widest distributional family (allows greatest degree of exploration of the impact of that of that variable in the overall risk assessment) consistent with the state of knowledge and should, for important parameters, test the sensitivity of the findings and conclusions to changes in the distributional shape. OPP agrees that limitations of data ought to be considered during the interpretation of results and in risk characterization.

The National Drinking Water Contaminant Occurrence Database (NCOD) was developed to satisfy the statutory requirements set by Congress in the 1996 Safe Drinking Water Act (SDWA) amendments. The purpose of the database is to support the U.S. Environmental Protection Agency's (EPA) decisions related to identifying contaminants for regulation and subsequent regulation development. The NCOD contains occurrence data from both Public Water Systems (PWSs) and other sources (like the U.S. Geological Survey National Water Information System) on physical, chemical, microbial and radiological contaminants for both detections and non-detects.

G. Pathway Specific Aggregate Methods

1. How, When, and, Why Aggregate Assessments Should Be Performed

Comment: Commenters requested additional information as to how, when and why aggregate assessments should be performed and requested that the revised document include an expanded description of the methodologies (pathway specific and total) of aggregate assessment. Another commenter plainly stated that the draft policy as written is too confusing and cumbersome and suggested that the limited resources of the Agency be placed in identifying high-end exposure estimates, which would assure protection of public health. Still other commenters relayed

specific ideas regarding the description of aggregate methodologies in the draft Aggregate Guidance including the idea that the food and drinking water pathways and not the residential pathway would be aggregated for the acute (one-day) duration of exposure. These commenters pointed out the potential for confusion over the different terms used to describe the food pathway of exposure (short-term, acute, long-term, and chronic) given that short term and acute were defined differently in the document.

Another commenter requested that before OPP seeks to include drinking water exposure or non-dietary, non-occupational exposure in aggregate exposure calculations, it should explain in detail how it proposes to do this, and should obtain public comments on its proposal. The commenter felt that the draft Aggregate Guidance does not set forth enough detail about how the pathways will be analyzed and brought together in aggregate assessment.

Another commenter is concerned that the draft Aggregate Guidance implies that the OPP will select a mini-population of "individuals" each of whom will be presumed to have, for each route, the highest aggregate exposure such that those "individuals" conceivably could have. The commenter expressed further concern that these highest exposed individuals would be used to make tolerance revocations and other adverse actions.

A third major comment in this area concerns the use of the "risk cup" concept. The commenter stated:

> "[...] the risk cup establishes a total, or aggregate risk that may be created by the use of a chemical pesticide. This total comes primarily from food ingestion, water ingestion and residential applications. If any two of these pathways are considered by the Agency to constitute 'baseline' or 'background' exposures for the third, the Agency will be forced to control exposures through the third route at levels that prevent filling the risk cup. The problem, therefore, is not with the idea of a risk cup itself, but with the way in which the idea is used in conjunction with aggregate assessment to focus regulatory attention onto specific pathways of exposure. The danger is that ingestion of water will be treated routinely as the third pathway, with the majority of the risk reduction efforts being focused on that pathway not because it is truly the most significant pathway, but simply because the other two pathways are placed first into the 'risk cup' and treated as baseline exposures. Relative risk reduction should not be based on the pathway that is first or last in the risk cup but rather risk should be evaluated equally."

The same commenter proposed a five-step process for performing aggregate exposure and risk assessment which follows the above comment. It includes:

(1) an assessment of the exposures from each pathway would

be performed

(2) the total or aggregate exposure would be calculated

(3) the total or aggregate risk would be calculated

(4) the relative contribution to this aggregate risk from each pathway would be assessed

(5) risk mitigation strategies would focus on some combination of policies that reflect the relative sensitivity of the risk estimate to each exposure pathways and an equitable distribution of the burden of mitigation across individuals or institutions that play some role in the pathway from source to exposure.

The commenter also identified many questions they felt went unanswered within the draft Aggregate Guidance including: are decisions to be based on the estimate of the fraction of the total U.S. population whose risk is above some value, the fraction of the population in some maximally exposed geographic region, the fraction of some sensitive sub-population, or the fraction which has at least one effect (pesticide induced) appearing during a normal lifespan (in contrast to the mean probability of effect)?

OPP Response: Aggregate exposure and risk assessments should be performed by assessing pathway specific exposure, bringing those exposures together (food, drinking water and residential) based upon the individual (exposure related) characteristics for each member of the population, and assessing risks based upon a common toxicological endpoint among the three routes of exposure (oral, dermal, and inhalation). More than one aggregate assessment may be performed for each chemical based upon known differences in toxicological effect via different routes of exposure. FQPA mandates that EPA assess aggregate exposure to assure there is a reasonable certainty of no harm to infants and children, and the total population, when making tolerance decisions and performing risk assessment (FFDCA 408 (b)(2)(C)). OPP believes that the pathway-specific aggregate exposure issues are defined in sufficient detail within the draft Aggregate Guidance. The purpose of this draft policy document is not to define in detail any one way to perform aggregate exposure and risk assessment, but to describe general concepts to be considered in any aggregate exposure and risk assessment method. OPP disagrees with the commenter that stated the aggregate methods as described are too complex and confusing, and OPP should instead perform high-end estimates of aggregate exposure.

Inherent within any aggregate exposure and risk assessment is the inclusion of reasonable high-end exposure estimates, in addition to the total distribution of aggregate exposures. OPP believes that the draft Aggregate Guidance as written represents a significant step forward in risk assessment and will not limit its assessment exclusively to those individuals who are at the extremes of the exposure distribution.

Detailed comments on pathway specific assessment methods are appreciated. Aggregate assessments will include estimates for all pathways (when appropriate) for the short and long term as well as acute and chronic exposure durations. OPP understands that these terms have been defined differently and will clarify them. Using the rolling-window time-frame in aggregate exposure assessment, it is possible to more easily and more accurately assess multiple exposure durations within an assessment. The duration of exposure leading to the manifestation of the toxicological effect seen in animal studies can be used to determine the rolling window time-frame in the exposure model. In this way, assessors are not limited to pre-defined judgements about what constitutes short-term or chronic exposure, but may use the exact time-frame in which the effect is seen in the animal model. OPP disagrees that the acute exposure scenario should only include food and drinking water pathway and believes that all pathways may be assessed accurately using the rolling window time-frame of exposure and other aspects of aggregate assessment.

A commenter asked that OPP establish additional guidance on how and why non-dietary pathways are to be included in aggregate assessments. OPP disagrees that this is necessary as aggregate assessment which include non-dietary pathways have been performed and have received substantial public comments. The Interim Aggregate Guidance (USEPA, 1998) put forth OPP's methods for assessing aggregate exposure and risk for all pathways. Also, the Guiding Principles document is an extension of the Interim Aggregate Guidance.

OPP does not anticipate creating a mini-population of individuals each of whom will be presumed to have, for each route, the highest aggregate exposure such that those individuals conceivable could have. Additionally, OPP does not intend to select only certain sub-sets of individuals, either the potentially most highly exposed or the average individual. Instead, OPP intends to utilize all available data to assess aggregate exposure to the total population. The type, number or exposure characteristics of the individual are not predefined, but rather can be extracted (or randomly assigned) from available data sources. This process, it is hoped, will utilize data representing the entire distribution of possibly exposed hypothetical "individuals." It is not only the "average"or the "high-end" exposure value ("individual" as a point in time and space), but the entire distribution.

Concerning the use of the "risk cup" concept in aggregate exposure and risk assessment, OPP envisions this policy document as a significant step away from the idea of the 'risk-cup' and toward a more holistic view of aggregate assessment which considers all exposure pathways. The 'risk-cup' concept refers to the relative contribution of each pathway to the total aggregate risk. The current process outlined for incorporation of drinking water exposures into aggregate exposure assessments is described in detail in OPP (USEPA (draft), 2000e). This process provides screening-level estimates at pesticides concentrations in surface water and ground waters and consequently is not factored quantitatively and directly into the aggregate exposure assessment. These estimated concentration values are compared to theoretical upper limit in drinking water that is based on an estimate of exposure through food and residential uses. Comparisons are performed to determine whether the addition of potential exposures from the drinking water risks will exceed the level of concern for the chemical, based on available toxicological information. However, if the conclusion of the comparison is that the addition of exposure by the drinking water pathway will exceed the Agency's level of concern for the aggregate risk of the chemical, more information is then analyzed. Available data sources are reviewed to learn whether there are monitoring data available and the validity of certain assumptions are more carefully reviewed. However, even at this stage, where information is lacking, OPP will err on the side of a high-end assumption, to ensure a measure which is protective of public health. Order of consideration of the pathways will not skew the impact of any risk mitigation measures. OPP does not disagree in principle with the steps provided by the commenter, but will continue to use the steps presented in the General Principles document to outline the possible ways in which aggregate exposure and risk assessment can be performed. OPP continues to move forward in refining estimates of exposure for the drinking water pathway.

The following questions are in the realm of risk management and will not be addressed in this document: whether decisions are to be based on the estimate of the fraction of the total U.S. population whose risk is above some value or whether assessments are to be based upon the fraction of the population in some maximally exposed geographic region or the fraction of some sensitive sub-population, and, how the fraction who have at least one effect (pesticide induced) appearing during a normal lifespan (in contrast to the mean probability of effect).

OPP plans to apply the following principles when making this judgement: assessments must be performed to protect the public health which means high end of a reasonable exposure estimate will be evaluated and not a theoretical worst-case; OPP intends to pay attention to potentially more highly exposed sub-populations as long as they are identifiable; and, the percentile of exposure selected for regulatory decision-making will depend upon how the aggregate exposure estimate was calculated and will be informed by sensitivity analyses. The way in which populations of individuals are determined is discussed above in the section "Selection of Individuals." OPP considers the draft Aggregate Guidance to be a description of aggregate risk assessment methods and not the appropriate place to consider risk management or how and where these methods will be used.

2. Drinking Water Pathway

Comment: There were many commenters who supplied information concerning the assessment of the drinking water pathway and the inclusion of the pathway within the total aggregate assessment. Comments fell into four areas: assumption of treatment of water; distribution of risk mitigation measures across all pathways; need for more monitoring data; and, the need to expand the definition of the drinking water pathway.

A commenter stated that the draft policy document says treatment will be incorporated into the effects of drinking water in the aggregate assessment, but the commenter asks to what level of treatment does OPP refer. Another commenter believed that drinking water sources are rarely treated and OPP, therefore, should not assume that treatment of drinking water occurs in the assessment of aggregate risk.

Also, commenters suggested that the use of the DWLOC may be inappropriate in aggregate exposure and risk assessment because this tool merely measures the portion of the "cup" left over after the other pathways are considered and is not a true measure of the contribution of drinking water to aggregate exposure and risk. As proffered by one

commenter:

> "EPA predetermines that the only 'significant' levels of drinking water contamination are those which force total aggregate exposure to the pesticide over EPA's levels of safety, exceedence of the DWLOC. A much better approach would be for the EPA to estimate drinking water exposures, including dermal and inhalation exposures, to tap water and assume that any addition to aggregate exposure that is non-negligible should be incorporated into the aggregate exposure assessment. This latter approach would be more transparent since it would reflect all available information while under EPA's current approach the aggregate assessment would likely only discuss drinking water exposures estimated to lie above the DWLOC. It is better science since it would not permit sub-DWLOC exposures through drinking water to simply disappear from the aggregate assessment. Finally, it would be more health protective since drinking water makes up a much larger portion of a child's diet."

Additionally, commenters raised the issues that drinking water estimates based on conservative models such as PRZM/EXAMS and SCIGROW may create an unfair burden of risk mitigation to the drinking water pathway since other pathways do not include this level of conservatism. Both the use of conservative model estimates and the assumption of treatment of water, commenters feared, may lead to an unequal and unfair burden of aggregate risk mitigation on the drinking water pathway.

Another major area of comment raised the issues of the need for more monitoring data, both national and regional. One commenter states that "there is a need for sampling to establish distribution of exposure for the water pathway, but there is no mention, however, whether they will be required before an aggregate assessment will be attempted." The commenter asked if monitoring will be conducted through a revision to the Unregulated Contaminant Monitoring Rule or whether it will be a separate research program by the registrants. Another commenter added that the draft document implies the availability of regionalized data. It is unlikely, according to the commenter, that regionalized data will be available for most chemicals, except for specific "hot spots" and certain chemicals of interest. Furthermore, the commenter added, for a useful exposure assessment to be carried out, regional water data should span all seasons thereby allowing a realistic weekly, monthly, yearly exposure picture to be developed.

The last major area of comments included the need for an expanded definition of the drinking water pathway. One commenter stated that the discussion of exposure through water does not mention potential dermal or inhalation routes of exposure. The commenter continued saying that the Agency must make clear that the oral route is not the only pathway of concern for pesticides in water, especially since children's skin

is more permeable than that of adults. Children may absorb a pesticide through their skin while bathing at home or while swimming in a lake or river. Additionally, the commenter stated, some pesticides in water can be inhaled while bathing or washing. These exposures, the commenter believed, must be included in aggregate risk assessments or the assessment will potentially underestimate exposure. A second commenter echoed these same thoughts saying the dermal and inhalation routes of exposure associated with the drinking water pathway were not addressed in detail in the document. Still another commenter on this topic added other ways in which the determination of the drinking water pathway can be expanded to include consumption of locally caught fish/shellfish.

OPP Response: OPP disagrees that drinking water assessments should necessarily be restricted to including only untreated (unfinished) water. There are sub-populations in the country who have treated water and, therefore, both types of water sources should be considered. It is a fundamental misconception that all the risk mitigation burden will be placed on one exposure pathway using the General Principles document. Residues that are present in either surface water or groundwater are present as a result of specific agricultural pesticidal uses. If aggregate risk is unacceptable, OPP will investigate all mitigation options, not just those associated directly with the drinking water pathway. OPP is working to move beyond the screening-level approach for incorporating drinking water exposures into aggregate risk assessments, which utilize the DWLOC and the concept of the 'risk-cup' while incorporating more holistic aggregate exposure and risk methodologies. The OPP is also working to develop in conjunction with the USGS linear regression models to estimate pesticide concentrations at drinking water intakes for surface water. Monitoring data could be used to build linear regression models for estimating pesticide concentrations at drinking water intakes sourced by surface water. Alternatively, the models developed for benchmark compounds for which extensive monitoring data are available could necessarily be modified for other compounds based on each compound's specific usage, and physical and chemical properties. OPP agrees that regional monitoring data are not yet readily available, but are being collected for a handful of chemicals and believes it will continue to be collected for other chemicals. OPP also agrees with the expansion of the drinking water pathway to include shower/bathing, swimming, for the dermal and inhalation routes of exposure and these things are reflected in the residential SOPs.

The commenters' statement that conservative assumptions found in the drinking water pathway are not found in other pathway assessments is incorrect. For resource efficiency reasons, OPP employs a tiered process

for all the exposure pathways. For example, the food exposure pathway usually begins by using tolerance level residue estimates and the assumption that 100% of the crop is treated in all cases. If these assumptions result in an exposure level which exceeds OPP's level of concern, further effort is placed into refining the assumptions. This is true for the current method for assessing drinking water exposure as well, in all cases in which the conservative assumptions lead to exposure estimates that exceed OPP's level of concern, refinements of the conservative assumptions are made. In fact, as part of the current process OPP always refines the food analysis, if possible, prior to working toward more refined drinking water estimates.

OPP believes that there is likely significant variation in exposure from pesticides in surface water and groundwater. Therefore, it is likely that OPP aggregate risk assessment will combine regional water exposures with either national or regional estimates of exposure to pesticides in foods. In order to do this with the highest level of accuracy, OPP may acquire regional drinking water data. OPP has engaged in discussions through the International Life Sciences Institute (ILSI) concerning this issue, which was described in "*A Framework for Estimating Pesticide Concentrations in Drinking Water for Aggregate Exposure Assessments*" (ILSI, 1999). Those discussions concluded that care must be taken in combining residue distributions of pesticide concentrations in drinking water to form a national distribution. The definition of "region" must be made consistently and held the same throughout the assessment of drinking water based on regional water data. The ILSI document states:

> "Depending on the scope and purpose of the risk assessment, it is conceivable that complete probability distributions of pesticide concentrations in drinking water might be needed for one or more of the following assessment scales: Local; Regional; or National. A local scale implies some type of site-specific assessment of an individual supply. A regional-scale assessment might include a number of water supplies within the use region of an assessment area whereas the national-scale assessment incorporates some aggregation of water supplies from several assessment areas. [...] local sampling would most likely be targeted at a most vulnerable supply, if such a supply could reliably be identified *a priori*. However, defining the one most vulnerable supply in an assessment area based on site characteristics and pesticide loading and fate and transport properties is conceptually and practically very problematic, and the designation of "most vulnerable" could change as weather, pesticide use, and other dominant factors change over the years in the assessment area. Therefore, although it is conceivable that a full pesticide concentration distribution from a single water supply might need to be characterized, it is the least likely scenario to be assessed. More often for risk assessments that need to define the upper tail exclusively or particularly accurately, sampling of a class of vulnerable supplies is a more defensible choice. In a modeling exercise, however, a single site can be parameterized based on prior knowledge to simulate a known level of

vulnerability based on site characteristics and climate, and simulation of a class of sires may be unnecessary."

OPP agrees with the commenter who stated that OPP should quantify the exposure from the drinking water pathway into the aggregate exposure assessment. This is a preferable approach which OPP does incorporate when data are available to quantify the drinking water exposure. Unfortunately, data are often lacking for this assessment. In these instances, OPP must determine if aggregate risk is potentially a problem. Calculation of a DWLOC allows this determination. However, OPP does not believe that current use of model estimates produced by GENEEC, SCI-GROW, and PRZM-EXAMS models are reliable enough to include *quantitatively* in an exposure assessment for drinking water. These models are considered useful for screening-level assessments, only. It is important to recognize that model results from PRAM/EXAM and SCIGROW are not used to determine where mitigation is necessary but only where refinement of the risk/exposure estimate is needed. OPP does not want to ignore potential contributions to exposure via the drinking water pathway for lack of water data and has therefore, developed a screening-level assessment for this pathway.

OPP will continue to move forward in refining the screening-level approach. OPP plans to move beyond the screening level assessment by using distributional data for the drinking water pathways. As stated earlier, OPP is currently investigating the use of linear regression techniques as applied across occurrence data for pesticides in surface water. Once validated for benchmark compounds and modified for other pesticides, this technique could be used to quantitatively estimate concentrations of the benchmark compounds as well as other pesticides downstream at drinking water intakes sourced by surface water. The technique is intended to provide a distribution of pesticide concentrations at drinking water intakes prior to treatment that may be used in a probabilistic analysis for drinking water exposure. In this and other ways, OPP is moving toward an aggregate assessment method which goes beyond the screening level approach.

3. Residential Pathway of Exposure

Comment: Commenters offered many perspectives concerning the evaluation of the residential pathway and whether this evaluation should be done independently within the evaluation of aggregate exposure and risk assessment. The comments can be defined in three broad areas: expansion of the pathways definition, need for and availability of additional data for this pathway, and, appropriateness of use of data.

Many commenters stated that additional exposure scenarios ought to be considered in the residential exposure pathway. Areas of expansion included:

> "Skin absorption or inhalation of pesticide contaminated tap water in the shower or bath; pesticide drift from nearby agricultural fields, golf courses, or other sprayed land; track in of chemicals used on lawns or agricultural fields into homes and carpets; eating contaminated local fish, shellfish or crayfish that contain pesticide residues, dermal and ingestion exposures from swimming in contaminated lakes, creeks and rivers; pesticides residues on skin, hair and clothing of anyone who handles pesticides or produce for a living, especially farmers or farm workers resulting in exposures to their children; children who accompany their parents to the fields; exposures to the fetus of pregnant women who work in agricultural levels on food are increased by spraying of railroad cars and trucks to transport produce and the spraying in canneries, warehouses, supermarkets and restaurants."

In addition, non-occupational exposures from agricultural workers should be considered including food fresh from the field; take home exposures on clothing; indoor air contamination (off-gassing of clothes); contaminated soil in children's play areas; children in fields including unborn children; and pesticides in breast milk.

Another commenter suggested that in the residential post-application boxes of Figure 1 of the Aggregate Guidance, an important pathway which is absent is the exposure and risk from dermal route (toddlers). Also, they said, it appears that the handler/ post-application scenarios for residential lawns is significantly different from that of the other 12 scenarios. They said that it may be useful to demonstrate that the other handler/post-application scenarios are not significantly different from the residential lawn. Other commenters echoed these concerns, saying that children's micro-environments in the home must be taken into consideration–crawling on the floor for which there is potential for higher pesticide concentrations.

Commenters also discussed the need for and availability of additional data sources for the residential exposure pathway. One commenter presented data sources concerning dislodgeable residues of 2,4-D tracked indoors and accumulated in carpet dust as well as pesticide drift for chemicals dichloropropene, methyl bromide and other organophosphorous pesticides. Another commenter outlined the limitations of a major data source for the residential/non-occupational pathway PHED. They noted that although PHED may be used to estimate residential handler exposure, however, for homeowner application scenarios, PHED data is limited in quality and quantity.

The final area of comment is the use or interpretation of the available residential data. One commenter suggested that studies of the distribution pattern of some pesticides have shown that exposures can actually increase over time, especially for some populations (such as children). They say these exposures can occur for weeks, not days, after use. The Agency, the commenter believed, should not be instructing risk assessors to assume that subsequent exposures will decline over time. Another commenter believed that reliable information does not exist to perform a residential exposure analysis. They said that the Agency should only use the Residential SOPs as a first tier screen to determine whether more data and/or high-tier exposure assessment are needed. The SOPs should not be used in aggregate risk assessments or to show that a pesticide use causes a certain actual amount of exposure or poses a certain level of risk that warrants action against a registration, reregistration application or tolerance. The same commenter also identified certain specific types of data that are not available. They say product use across time and its association with typical residential activities have not been adequately characterized to allow for more realistic use of existing exposure monitoring data in the construction of plausible aggregate scenarios. The guidance document, they say, needs to include temporal information necessary for development and parameterization of realistic aggregate exposure scenarios (.e.g., the likelihood of co-occurrence of product use events and thus potential exposures during time frames relevant to the toxicological endpoints of interest).

OPP Response: OPP considers all non-occupational, non-dietary (including non-dietary water exposures) exposures as residential exposures, whether the exposures occur in the home or in public areas. OPP welcomes the data sources mentioned by the commenter above including data on dislodgeable residues and pesticide drift. OPP is familiar with these potential avenues of exposure and strives to conduct the most complete residential exposure assessment possible. Data sources considered by EPA include the Agricultural Health Study (AHS), the National Health and Nutrition Examination Survey (NHANES) and the Hispanic Health and Nutrition Examination Survey (HHANES), the EPA/ORD Border Study, the National Human Exposure Assessment Survey (NHEXAS), and other studies. The residue decline example in the draft policy document was an example, not a definitive statement of how residues would always be considered. OPP always tries to use the most appropriate data to assess exposure.

Regarding the specific residential exposure pathways which commenters believe should be added to any aggregate assessment, the OPP has added a number of residential exposure scenarios to be evaluated in each assessment. Residential exposure to pesticides through showering/bathing is based largely on the current swimmer model currently used in the SOPs. And the track-in of pesticides from the outdoors to the indoors will also be included in the SOPs and is based on the work performed by Nishiola et al., 1996 and 1999. The first reference provides a basis for estimating the transfer of lawn chemicals by shoes onto carpets and the second deals with the migration of those residues throughout the household base on the activity patterns (traffic patterns) of the household members. Exposure to those residues will be assessed via existing SOPs (e.g., hand-to-mouth). Finally, OPP will use AgDrift (a model developed by OPP/USDA/and industry) to predict deposition onto residential surfaces from agricultural applications (groundboom, airblast and aerial). Exposure to those residues will be assessed with current SOPs (e.g., hand-to-mouth and others). Track-in of those residues will be addressed via methods presented in Nishioka and SOPs as discussed above. Other residential exposure scenarios mentioned by the commenters, including fresh fish consumption, swimming, parent to child pesticide transfer, and others can be considered when data become available.

There are very few data addressing pesticides in breast milk. Available data have evaluated lipophilic compounds such as DDT, dieldrin, hexachlorobenzene (HCB) and hexachlorocyclohexane that are very persistent in the environment. The Agency believes most pesticides currently marketed in the United States are less persistent and more rapidly metabolized than the aforementioned cyclodiene pesticides. However, animal metabolism data (e.g., rats, dairy goats, or dairy cattle) may trigger the need to characterize this pathway. To substantiate the existence of widely used modern pesticides in breast milk, the Agency is funding research being conducted by the University of California's, Berkeley Child Health Center. The center will evaluate nursing mothers and their babies in the migrant field worker community. The mother's breast milk will be measured for pesticides. OPP will review these data when available and incorporate them as appropriate.

The Pesticide handlers Exposure Database (PHED) was designed by a task force consisting of representatives from the US EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association (APCA). PHED is a generic database containing voluntarily submitted exposure data for workers involved in the handling or application of pesticides in the field (i.e., PHED currently contains over 2000 monitored exposure events). The basic assumption underlying the system is that exposure to pesticide handlers can be calculated generically, based on the available empirical data for chemicals, as exposure is primarily a function of the formulation type and the handling activities (e.g., packaging type, mixing/loading/application method, and clothing scenario), rather than chemical-specific properties. OPP disagrees with commenters who state the PHED is only appropriate for lower tier assessments and contends that some PHED studies match well with those encountered in residential settings for example, aerosol cans. OPP utilizes all data available and uses surrogate data when necessary in order to provide the most accurate and comprehensive picture of aggregate exposure possible. Again, the General Principles document is meant to be a description of general principles and not a comprehensive definition of how an aggregate assessment is to be performed.

The final set of comments on this topic stated that (residential) pesticide use across time that are associated with typical residential activities have not been adequately characterized. This hinders more realistic use of existing exposure monitoring data in the construction of plausible aggregate scenarios. OPP is familiar with efforts to collect similarly described data. The Residential Exposure Joint Venture is implementing a longitudinal, pesticide use and usage survey with input from OPP's Office of Research and Development (ORD) and Office of

Pesticide Programs (OPP). In addition, representatives of Health Canada's PMRA and California's Department of Pesticide Program have also participated in the development of the survey questionnaire.

H. Current Practice of Risk Assessment

1. General Comments

Comment: Many commenters reported opposition to risk assessment practices currently employed by the OPP such as the use of percent of crop treated data and food monitoring data such as the Pesticide Data Program (PDP) in the food pathway exposure analysis. Additionally, commenters expressed opinions concerning Agency action on certain organophosphorous pesticides including malathion and chlorpyrifos. Concerning, the use of percent of crop treated data, commenters said:

> "Using figures on the percent of crop treated is problematic for similar reasons. First, percent of crop treated with any given chemicals can change markedly over time due to cost, pest pressures, availability of alternatives, and other factors. Utilizing historic data on the percent of crop treated in no way guarantees that a similar percent of crop will be treated in the future. Second, if the crop treated with a given chemical is concentrated in a particular geographic region, individuals living in that region may encounter residues on 100% of the crop available to them for purchase, even if nationally a far smaller percentage of the crop is treated. Therefore, (commenter) strenuously objects to using percent of crop treated and to using FDA and USDA pesticide residue data to represent the risk, since neither of these assumptions are sufficiently protective of some segments of the population."

Furthermore, the commenter stated the following about the use of government food monitoring data, such as the FDA and USDA PDP data:

> " ...Use of food residue data obtained later in the chain of commerce certainly underestimates exposures to other consumers. Many individuals bring food home directly from the fields, pick their own food, or purchase food from roadside stands, small stores, or farmers markets. Residues on these foods are likely to be higher than food stored for longer periods of time. Use of residue data collected by the USDA or the FDA is not sufficiently protective of these people. Therefore, USDA and FDA residue data should not be considered the 'gold standard' of a refined dietary assessment."

Others commenters expressed disagreement with current and past Agency policy and actions concerning the regulation and use of both the chemicals malathion and chlorpyrifos.

OPP Response: OPP disagrees with the commenter on these points. It is important to remember that the function of a risk assessment is the use of all reasonably available information to provide a best estimate of a risk or range of risks for use by the risk manager. To summarily reject better representations of reality, as provided through both the use of percent of crop treated data and food monitoring programs, in an attempt to produce "appropriate conservatism" is to blur the classic distinctions between our risk assessment and risk management activities. The use of both percent of crop treated data and FDA- and USDA-collected pesticide residue on food (monitoring) data enable OPP to gain a more realistic picture of residue on foods as consumed. OPP is highly aware of the need to ensure risk assessment methods are sufficiently protective of all individuals in the population, especially infants and children, and OPP believes that utilization of these state-of-the-art pesticide risk assessment tools helps ensure all are protected from potential pesticide exposure.

When examining the food exposure pathway, OPP is interested in both the acute and chronic time frames of exposure. In chronic exposure assessment, the risk assessor is attempting to estimate a person's average food exposure over the long term (e.g., several years to a lifetime). Consequently, the use of average (or mean) residue values for each food commodity, average (or mean) consumption of food commodities, and average percent of crop treated is appropriate. In an acute exposure assessment, the risk assessor is trying to estimate the range of exposures that individuals could encounter on a single day and determine the exposure to which "high-end" persons could be subjected (where "high-end" is defined as a plausible estimate of exposure for those individuals at the upper-end of the exposure distribution). Consequently, the use of high-end residue values, high-end consumption, and high-end percent of crop treated is appropriate. (USEPA, 2000d)

Regarding the use of percent of crop treated data, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and FQPA are silent on the issue of whether OPP can use PCT adjustments for acute dietary (food) risk assessments. In fact, the statutory language is constructed to place certain restrictions on the use of PCT information in chronic risk assessments which suggests that Congress was merely setting out rules for the use of PCT information in these situations, not making a broader statement about use of this information generally. Furthermore, and perhaps more importantly, the use of PCT information in probabilistic acute assessments not only allows the Agency to take into account the

"hot potato," but also the probability that a high level of exposure will occur. In other words, if some percentage of a crop is not treated this would lower the probability that a consumer would eat a treated commodity, but not alter the range of estimates of the residue levels on that treated commodity. By generally using the 99.9th percentile of the population in estimating reasonable high end exposure, OPP continues to account for the higher end exposures.

OPP has chosen to incorporate percent crop treated into acute probabilistic exposure estimates as well as chronic assessments for the food pathway, since use of these data provide a better estimate of real exposure probabilities. It is true, however, that the assumption of a uniform distribution may be less true, however, in situations where fresh commodities may be locally available on a seasonal basis and/or remain in the local agricultural shed. These types of commodities may be less inclined to undergo national distribution. Therefore, individuals in these areas may be more regularly exposed to certain treated commodities than would be expected on a purely statistical basis. For this reason, certain conservative protections are incorporated into risk assessments processes. Information is available regarding the places where the majority of uses of a particular chemical on a specific crop are located. If this does not correlate well with the locations in which the majority of the crop is grown, further elucidation of exposure pattens and peculiarities may be necessary.

If there were actual concerns about certain sub-populations in isolated geographic areas being overexposed by dint of their consumption habits and/or local agricultural practices, there are a number of actions the Office could take to further investigate the potential problem. Probabilistic analyses permit the risk assessor to perform separate analyses by geographic region and/or season and account for different residue levels by region and season. If there was a specific concern, for example, for Washington State apple eaters during the fall apple harvest, a separate analysis could be done for that region in the country in that season. In this case, estimates could be provided for that region of the U.S. and an analysis could be performed for that region of the country selecting pesticide residue concentrations expected to result from agricultural practices specific to Washington state.

EPA recognizes that the percent of a crop treated can change from year to year. This fact is taken into account in how percent crop treated estimates are made so that these estimates are unlikely to understate percent crop treated. Finally, OPP is working to implement a system involving regular verification of percent crop treated estimates over time.

OPP acknowledges its preference for using PDP and FDA data in most instances for assessing dietary risk from residues in food, when such data are available. OPP has developed methods to use PDP data to the greatest extent possible in its assessments. PDP data are collected at the food distribution warehouses, not at the end-point of the distribution cycle, the grocery stores. PDP data are analyzed as composite samples and OPP now incorporates statistical methods to “decomposite” samples. This allows estimation of the range of possible residue values in single food items within a composite sample. This method and others allow better estimation of food residues as consumed. PDP and FDA data are not available for all food commodities, nor are they available for all pesticides. EPA works closely with the PDP and FDA programs to determine which pesticides, metabolites, and food commodities are most critical to monitor, and what modifications can be made to the program each year. For those commodities for which OPP does not have monitoring data, field trial data or anticipated residues are utilized. There are a range of residue types used in food pathway assessments, not all of which represent the endpoint of the food distribution cycle, the grocery store.

Regarding the potential exposures to those who consume foods earlier in the chain of commerce, OPP does not assess potential exposures from food that might be obtained from roadside stands or "pick-your-own" operations *per se* due to lack of data on how many people consume foods from these sources and what proportion of their individual diets is from such sources. However, OPP anticipates that a very small percentage of the U.S. population derives more than a negligible portion of their food in this manner. Moreover, some harvested crops are distributed so quickly to wholesale and retail outlets that the residues in them would be very similar to the levels in crops sold near where they are grown.

I. Add/Eliminate Certain Pathways from the Aggregate Assessment

1. General

Comment: Many commenters responded to the OPP question as to whether it is appropriate to eliminate certain pathways/routes of exposure from an aggregate assessment if it is clear that the pathway/route presents a negligible risk to health and the environment. Some commenters agreed, but others disagreed with this approach, and others presented guidance they recommended for making a decision whether to exclude a pathway/route from an aggregate assessment. Some commenters expressed that OPP must err on the side of protecting public health and make an exposure estimate where no data are available. It is inappropriate, the commenter stated, to assume that the contribution from a route of exposure is zero unless it is perfectly clear that the assumption is valid. Another commenter, expressing a similar opinion, said that in cases where data do not exist, the Agency cannot assume that the contribution from a route of exposure is zero. For example, the Agency cannot assume that there would be no household exposure to a pesticide only permitted for exterior use, unless it has data indicating that there would be no track-in, take home or drift exposures to that pesticide. Also, the commenter stated, the Agency cannot assume that pesticides registered only on minor crops can only result in minor exposures. Overall, these commenters agreed that the Agency must make conservative, protective assumption in the absence of adequate data.

Another perspective on this topic is given by a third commenter who said that careful consideration is recommended prior to the exclusion of routes or uses. For example, the exclusion of uses with limited contributions could have an additive effect if the product has many small uses (e.g., some products may be used on more than 100 crops).

Other commenters supported eliminating certain pathways/routes and suggested methods which could be used to make the determination that a pathway/route is limited. One commenter said “We agree that OPP should include only major exposure scenarios, excluding those that are unlikely to contribute significantly to overall risk.” However, the commenter said, “we discourage the Agency from setting bright line criteria for excluding exposure pathways and believe that the Agency should consider a range of potential minor exposures (for example, pathways that contribute less than 10%).” The commenter further stated that the decision to include or exclude any pathway must be assessed and determined on a case-by-case basis. Another commenter suggested that

pathway/route elimination should only take place if the screening level assessment for that pathway/route yields results that suggest that risk at the 95th percentile for that pathway is less than 10% of the risk cup. This, the commenter thought, will ensure that the risk estimate in the upper tail of the final, aggregate assessment (which now excludes that pathway) will be sufficiently accurate.

Furthermore, the commenter stated that there may not be any computational advantage for eliminating pathways because once the framework (for the risk assessment) is in place with the supporting exposure factors loaded into the database there is little to be gained by eliminating the pathway. The commenter suggested that OPP should consider developing such a modeling framework, since such effort at the beginning (which would require some significant initial investment of resources) would pay off in the long run by removing the need to guess which pathways will be significant at all percentiles of the distribution.

OPP Response: OPP appreciates the diversity of responses to this topic and will consider all comments in its deliberations. OPP would like to point commenters to the document "*Guiding Principles for Monte Carlo Analysis*" (USEPA, 1997a) which states that resources might be saved by excluding unimportant exposure pathways (e.g., those that do not contribute appreciably to the total exposure) from full probabilistic analyses or from further analyses altogether. This concept is not meant to be used to minimize potential exposures but to conserve resources to investigate those that are potentially most significant. This guidance document suggests that unimportant parameters may be excluded from full probabilistic treatment and for important parameters, empirical distributions or parametric distributions may be used, which are more resource intensive. In all cases, however, OPP believes that numerical experiments should be conducted to determine the sensitivity of the output to different assumptions. OPP will continue to consider the exclusion of certain "minimal" exposure pathway scenarios as a resource saving measure, but will do so with the utmost care on a case-by-case basis.

2. Inclusion of Non-pesticidal Uses/Antimicrobials in Aggregate Assessment under FQPA

Comment: One commenter disagreed that OPP can include non-pesticidal and antimicrobial pesticide uses in an aggregate assessment. The commenter states:

> "(We) strongly disagree that FQPA authorizes EPA to include non-pesticidal uses of antimicrobial chemicals in aggregate exposure and risk assessments performed under FIFRA. (We) are very concerned with respect to EPA's apparent intent to include non-pesticidal products and uses in aggregate exposure and risk assessments for household pesticide products. For this reason, (we) and the REJV jointly submitted a letter to EPA on August 4, 1999 outlining our concerns on Aggregate Exposure and Risk Assessment for Antimicrobial Pesticides."

And,

> "The jurisdictional reach of FIFRA depends on the pesticidal claims, if any, which are contained on the label. Products whose labels do not include pesticidal claims are not within the purview of FIFRA or under the authority of EPA and, as such, cannot be considered in any plausible aggregate exposure scenario for a particular active ingredient. Non-FIFRA regulated products must be left out of any such calculations."

OPP Response: OPP believes that both non-pesticidal uses of pesticide chemicals and antimicrobial uses of pesticide chemicals can be considered in the aggregate exposure and risk assessment process. See § 408(b)(2)(D)(vi) (directing EPA to consider "available information on aggregate exposure . . . to the pesticide chemical and to other related substances").

J. Examples/Illustrations

1. See Other OPP Models

Comment: One commenter suggested that OPP seek the experience of other areas of the Agency in making aggregate exposure and risk assessment methods development. Specifically, the commenters states:

> "The sensitivity of the risk to a particular pathway may depend on the percentile of the risk distribution (PDF) under consideration. A pathway may be insignificant in the central tendency estimate, but significant in the upper tail of a distribution (or the inverse). Rather than trying to make such decisions, the OPP might want to draw on the lessons from modeling programs such as TRIM or Models 3 within the Agency, where a common framework of assessment is being developed."

OPP Response: The commenter has made an excellent point with respect to the sensitivity of the risk estimate to a particular pathway being dependent upon the percentile of the risk PDF under consideration. This demonstrates the importance of the risk assessor's understanding the entire distribution of exposures through a particular pathway and how this distribution relates to other exposure pathways (qualitatively and quantitatively). With respect to the comments urging that OPP draw lessons from other modeling efforts within OPP, we note that OPP is aware of these efforts and will keep abreast of them. With the OAQPSs TRIM model, for example, OPP personnel served as Agency technical reviewers of the draft document prior to release to the public.

2. Case Study Needed

Comment: Many commenters agreed that the draft policy document needs to include a case study to better illustrate the aggregate exposure and risk assessment process as envisioned by OPP in the document. They state that a case study would not only help to illustrate the process but also the identify problems or gaps in the current thinking of aggregate exposure and risk assessment.

OPP Response: OPP appreciates the need for a case study to illustrate the concepts presented in the draft Aggregate Guidance, however a case study is not presented in the finalized document. As OPP moves toward full incorporation of these new approaches, OPP will make examples available to the public.

K. The Process

1. General

Comment: Many commenters made statements about the process by which OPP has engaged the public in the aggregate exposure and risk assessment policy-making process and suggestions for improvements. Specifically, commenters asked the OPP to make clear what types of activities (for aggregate) can be done now and what must come later. Also, they asked for more specific ideas as to where, when and how aggregate assessment will be performed by OPP; one commenter suggested a different approach altogether for addressing aggregate exposure and risk assessment to pesticides. That commenter suggested the following process:

(1) Begin each aggregate exposure assessment with a clear designation of the high-risk groups selected for evaluation, and why such groups were selected;

(2) Select a reasonable number of individuals from each high-risk group for aggregate exposure assessment;

(3) Perform aggregate exposure assessment without engaging in excessively complex and ultimately academic discussion about such issues as patterns of home weed control by lawn care operators versus homeowners;

(4) Assure that the aggregate risk assessment include all non-negligible routes of exposure, including (as relevant on a case-by-case basis) those discussed above but not in the current Agency's draft Aggregate Guidance;

(5) Use appropriately health-protective assumptions as needed to streamline the process or where data are unavailable;

(6) Take immediate risk reduction measures if a preliminary exposure assessment indicates a potential risk to children, even if additional 'refined' data are pending; and

(7) Assure that proposed tolerances are safe for infants and children, and revoke tolerance that are not.

Commenters also encouraged OPP to continue an open process for policy making.

OPP Response: OPP agrees that the policy making process should and will continue to be an open process. As to clarifying what the Agency can do now and later, OPP has made it clear in the Aggregate policy document that as the Agency and other interested parties move toward a more realistic, probabilistic assessment of aggregate exposure and risk according to the principles laid out in the draft Aggregate Guidance document, OPP will be utilizing the *Interim* aggregate guidance. As the Agency and the risk assessment community moves forward toward use of the principles laid out in the General Principles document, specific policies and procedures will be fully vetted.

Concerning the seven step process for aggregate assessment outlined by one commenter, OPP believes this commenter may have misunderstood the way in which OPP proposes to perform aggregate exposure and risk assessment in the *Expanded* aggregate policy section and refers the commenter to the section of this Response to Comment document entitled "How the Individual is Selected." Essentially, as is stated in the aforementioned section, there is no set of criteria for selection, but ideally available data would be utilized to devise exposure histories for "hypothetical individuals" in the population upon which the aggregate assessment would be based. It is these types of individually based data sets, that are temporally, spatially and demographically consistent, that comprise the aggregate "hypothetical population."

L. "Reliable Data and Information"

The IWG and others in industry commented extensively on the term "reliable information" in section 408(b)(2)(A)(ii). Similar comments were also filed by the IWG in response to EPA's draft policy paper on the Children's Safety Factor. These comments also discussed the term "reliable data" appearing in section 408(b)(2)(C). The NRDC's comments on the draft policy concerning the Children's Safety Factor addressed both of these terms and took a sharply different position than the IWG's comments. Due to the overlapping issues involving these terms as they relate to both of these policies, EPA has drafted a joint response which appears below as well as in the response to comment document for the Children's Safety Factor Policy.

1. Introduction and Statutory Background

Several commenters raised the issue of how the terms "reliable data" and "reliable information" in the FQPA should be interpreted. These comments pertain to many FQPA implementation issues including aggregate exposure assessment and the application of the children's safety factor. Because this interpretational issue should not be viewed in isolation, OPP has attempted to address below all of the comments provided on this issue.

The two primary statutory provisions cited by commenters are the general definition of safety in section 408(b)(2)(A)(ii) and the language in section 408(b)(2)(C) addressing when it is appropriate for OPP to select an FQPA safety factor "different" from the additional tenfold factor to protect infants and children. Section 408(b)(2)(A)(ii) states:

> [T]he term "safe" . . . means that [OPP] has determined 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 exposure for which there is reliable information.

Section 408(b)(2)(C) provides that:

> Notwithstanding such requirement for an additional margin of safety, [OPP] 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.

2. Public Comments

i. Industry Comments

Essentially, industry's view is that the "reliable information" language in section 408(b)(2)(A)(ii) is a screen for both what exposures can be considered in making the safety determination and what exposures can be considered in judging the completeness of the exposure database for children's safety factor purposes. According to IWG, Congress' intent in including the "reliable information" language in section 408(b)(2)(A)(ii) was to ensure that data on pesticide exposure, other than exposure through residues in food, would only be taken into account in assessing aggregate exposure if there exist data providing "a reasonable estimate of the actual, real-world level of exposure to the pesticide . . . includ[ing] information on the distribution of the

exposure, so that probabilistic estimates of aggregate exposure can be made."[1] Moreover, IWG argues that the reliable information language in section 408(b)(2)(A)(ii) not only serves as a screen for what information is considered in calculating aggregate exposure but also as a screen for what exposure scenarios should be considered in determining, for children's safety factor purposes, the completeness of the exposure database. As stated by IWG, "[w]e do not think that Congress meant that when OPP is assessing the acceptability of the risk from a well-defined exposure, it should have to add a 10X factor to account for some other possible exposure for which there are no reliable data" (IWG Roadmap at VIII-7). Thus, IWG asserts that if OPP does not have reliable information on a non-food exposure scenario, that exposure scenario should be completely excluded from the frame of reference in making safety factor decisions. In other words, IWG does not believe that the "reliable data" test for assigning a different FQPA safety factor even comes into play as to non-food exposure scenarios lacking reliable information *precisely because OPP does not have reliable data on this exposure scenario*.

Given this legal interpretation, IWG criticizes OPP's approach to dealing with drinking water and residential exposure issues raised in regard to the children's safety factor by using models to insure that exposure is not underestimated. IWG claims that this approach is unnecessary because "[m]odels designed to produce conservative overestimates, and the overestimates that they generate, cannot be considered 'reliable information' for purposes of the "aggregate exposure" computation . . . ." (IWG Comments at 39).

There are several building blocks to the IWG's legal

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[1]The FQPA Implementation Working Group, Comments on the "Office of Pesticide Programs' Policy Titled 'The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-setting Process" 39 (October 7, 1999) [hereinafter cited as "IWG Comments"]. Similar comments were filed by the IWG on OPP's draft policy on aggregate risk assessment, Implementation Working Group, Comments of the FQPA Implementation Working Group on the Office of Pesticide Programs Science Policy Document, *Guidance for Performing Aggregate Exposure and Risk Assessments*, *OPP Docket No. OPP-00625*, (February 9, 2000), and in an earlier submission to OPP, The Implementation Working Group, A Science-based, Workable Framework for Implementing the Food Quality Protection Act: Implementation Working Group's "Road Map" Report (June 1998) [hereinafter cited as "IWG Road Map"]

interpretation. First, IWG asserts that the phrase in subsection (b)(2)(A)(ii) "for which there is reliable information" applies not to the requirement to consider "all anticipated dietary exposures" but only to consideration of "all other exposures . . . . ." Thus, according to IWG, subsection (b)(2)(A)(ii) imposes a reliability test on non-dietary exposures but no such test on dietary exposures. IWG claims that Congress chose not to impose a "reliability criterion" on dietary exposure information because Congress was aware of the quality of the data on such exposure already in OPP files and the reliability of government residue monitoring programs. Second, IWG contends that the term "dietary exposure" only extends to pesticide residues in food and not residues in drinking water. Thus, IWG argues that the reliability criterion attaches to exposure to pesticide residues in drinking water. Although IWG admits that "water is often thought of as a component of the diet," IWG asserts that the language of the statute and a pre-FQPA action by OPP and FDA suggest that drinking water is not included in the term dietary exposure. The statutory language IWG cites is section 408(b)(2)(D)(vi) that describes aggregate exposure as "including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources." The OPP/FDA action noted is the joint agency interpretation following passage of the Safe Drinking Water Act that the term "food" in the FFDCA does not include drinking water.

IWG does not contend that this legal interpretation is compelled by the statute; however, it does assert that its interpretation is a permissible one. It claims that "[i]t would be extremely arbitrary for OPP to proceed to use worst-case model estimates without stating publicly whether it has the legal authority to do so, and whether it would be good policy" (IWG Comment at 40).

ii. NRDC Comments

NRDC takes a dramatically different approach to the terms "reliable data" and "reliable information" as they are used in subsections 408(b)(2)(C) and 408(b)(2)(A)(ii), respectively. NRDC argues that OPP has inappropriately merged the concepts of reliable data and reliable information. Although NRDC does not explain how it would define either of these terms, it does make clear that it believes "reliable information" sweeps more broadly than "reliable data." Importantly, as to the children's safety factor, NRDC asserts that exposure estimates based on models are not

data. According to NRDC such model estimates are information–information that must be considered in calculating aggregate exposure–but not data sufficient to address concerns about the completeness of the exposure database and not reliable data sufficient to justify choosing a different safety factor than the additional tenfold children's safety factor.

In support of this argument NRDC points out that in two places, section 408(b) refers to both data and information in a single provision. See § 408(b)(2)(E)(i) and (b)(2)(F).

3. OPP's Response

The IWG's and NRDC's approaches to the terms "reliable data" and "reliable information," exposure estimates from models, and the children's safety factor could not be more polar . IWG claims model estimates may not be considered as reliable information and, therefore, IWG would not include model estimates of exposure in aggregate exposure. Further, IWG believes that exposures excluded from consideration under aggregate exposure are irrelevant to the children's safety factor decision and, thus, in their view, the inability of a model to yield reliable information for an exposure scenario would not necessitate retention of an additional tenfold safety factor due to incompleteness of the exposure database. In contrast, NRDC argues that model estimates are reliable information but not reliable data. Thus, NRDC would include model estimates in calculations of aggregate exposure and would conclude that, if OPP is using a model to estimate exposure, reliable data do not exist to permit removal of the additional tenfold children's safety factor.

OPP views both of these positions as extreme and cannot agree with either one. Each of the points raised by the commenters is discussed fully below.

i. The Reliable Information Requirement in Subsection (b)(2)(A)(ii) and Aggregate Exposure

OPP believes that IWG misreads the statutory requirements pertaining to reliable information on aggregate exposure. The IWG argues that Congress, by inserting the reliable information requirement in that provision, was erecting a special standard of reliability applicable to non-dietary exposures whereas no reliability requirement was applied to dietary exposures. (See IWG Comment at 38 ("Regarding dietary exposure, the statute does not impose a 'reliable information' requirement.")). Not only does this special standard have a limited applicability, but, according to IWG, it has a broad scope, not just addressing whether there is reliable information that exposure occurs through a particular route but whether there is reliable information concerning the magnitude of exposure. Finally, in regard to the magnitude of exposure, IWG argues that reliability requirement as it applies to the magnitude of exposure has a substantive content: data must demonstrate a specific type of information ("actual, real-world exposure levels") through a particular type of data ("information on the distribution of exposure"). IWG Comment at 39.

In isolation, IWG's limited applicability argument is not necessarily problematic. However, when this limited applicability argument is coupled with IWG's interpretation of the scope of the reliability requirement (i.e., the reliability requirement has a broad substantive scope addressing the magnitude of exposure), IWG's approach becomes implausible. Taken to its logical conclusion, IWG's argument would suggest that although Congress required reliable information on the magnitude of non-dietary exposures it was willing to allow OPP to rely on *unreliable* information in estimating the magnitude of dietary exposure. This contradicts not only common sense but the statute itself. Subsection (b)(2)(D)(i) directs OPP to consider the "reliability" of data. IWG's attempt to go further and infuse the reliability requirement with a definite substantive content is also not supported by the statutory language itself. IWG takes a term relating to evidentiary process–reliable information–and attempts to give it substantive content. Yet, IWG offers no reasonable justification as to why such an unorthodox interpretational approach should be taken. These issues are discussed in more detail below.

Scope of the Reliable Information Requirement

OPP believes that there exist two more reasonable interpretations regarding the scope of the reliability requirement in subsection (b)(2)(A)(ii). Both of these interpretations are more consistent with the general principles of administrative law and practice and with the other language of the statute. They take into account both the "reliable information" requirement in subsection (b)(2)(A)(ii) and the requirement in subsection (b)(2)(D)(i) that OPP consider "the validity, completeness, and *reliability* of the available data from studies of the pesticide chemical and pesticide chemical residue."

The first, and OPP's preferred interpretation, is that the reliable information requirement in subsection (b)(2)(A)(ii) is directed primarily at identifying *whether exposure occurs* by a certain pathway or route (i.e., non-dietary) and that the reliability consideration in subsection (b)(2)(D)(i) more broadly insures that exposure estimates (addressing the magnitude and distribution of exposure) are reliable, whether that exposure is dietary or non-dietary. Two reasons support this interpretation. First, the "reliable information" requirement in subsection (b)(2)(A)(ii) is in a clause specifically discussing routes/pathways of exposure ("dietary exposure and all other exposures"). Second, as discussed above, reading the reliable information requirement more broadly contradicts the direct command of subsection (b)(2)(D)(i) (consider the reliability of data) by implying that reliability is not a pertinent consideration as to dietary exposure data, and does so in a manner that appears to condone arbitrary agency decision-making . On the other hand, the more narrow (route-specific) construction of the reliability requirement in subsection (b)(2)(A)(ii) can logically be squared with subsection (b)(2)(D)(i). It makes sense for Congress not to have imposed a reliability requirement on the question of whether exposure *occurs* by the dietary route/pathway. After all, this statutory section addresses setting maximum levels for pesticide residues in food, an important part of the diet. Setting a tolerance level for a pesticide residue in food presupposes that there will be some exposure to the pesticide through the dietary route/pathway. For these exposure issues under section 408, reliability considerations apply principally, if not entirely, to the question of amount of exposure.

The second interpretation is that the phrase in subsection (b)(2)(A)(ii) referencing "reliable information" applies to both dietary and non-dietary exposure and thus reinforces the reliability

consideration in subsection (b)(2)(D)(i). The basis for this interpretation is that the statute is ambiguous as to whether the phrase "for which there is reliable information" modifies only "other exposures" or both "other exposures" and "all anticipated dietary exposures."

Either of these two interpretations is more reasonable than IWG's interpretation because they do not impute to Congress an intent to authorize arbitrary action by an administrative agency (i.e., the agency may rely on unreliable data). In the absence of a clearer statutory pronouncement, or at least some support in the legislative history, OPP is unwilling to endorse an approach that presumes such congressional intent. OPP prefers the first interpretation to the second because it appears to be the more natural construction of the language in subsection (b)(2)(A)(ii) and because it gives some separate purpose for the inclusion of the reliability language in subsection (b)(2)(A)(ii). That purpose is to direct OPP to examine whether some trustworthy information is available to show that exposure would occur (or is occurring) by the non-dietary pathway.

Under OPP's preferred interpretation, OPP can agree with IWG that the subsection (b)(2)(A)(ii) does not explicitly impose a reliable information requirement as to whether pesticide exposure occurs by the dietary route/pathway. Further, in theory, OPP can agree with the gatekeeper argument advanced by IWG regarding the "reliable information" language in subsection (b)(2)(A)(ii)–namely, if OPP does not have reliable information that pesticide exposure is occurring by a non-dietary pathway, OPP should not assume that such exposure will occur in its estimation of aggregate exposure. However, as discussed below, because OPP disagrees with IWG concerning the "substance" of the reliable information test.

The Substance of the Reliable Information Requirement

The common meaning of "reliable information" is information that is trustworthy, or in the scientific sense, information that is reproducible. Accordingly, OPP believes that the reliable information requirement in subsection (b)(2)(A)(ii) simply is designed to ensure that information considered by OPP is trustworthy and reproducible. (OPP sees a similar role for the reliability consideration in subsection (b)(2)(D)(i).) IWG's argument that OPP should depart from this plain meaning of the term "reliable information" and impute a more substantive role for the reliability requirement is unpersuasive.

IWG argues that the general language in the subsection (b)(2)(A)(ii) establishing a reliability criterion for non-dietary exposure imposes more than some type of reproducibility test. According to IWG, the reliable information requirement substantively defines what the information must show and the specificity of the information itself. IWG states that "[f]or information to be considered reliable . . ., it must provide a reasonable estimate of the actual, real-world level of exposure to the pesticide . . . [including] information on the distribution of the exposure, so that probabilistic estimates of aggregate exposure can be made." IWG Comment at 39. IWG's logic is as follows: (1) Congress has imposed no reliability requirement on dietary exposure data; (2) IWG claims this was because OPP often has data on the actual, real-world levels of pesticide residues on food including data on the distributions of those residue levels; and, thus, (3) there is a "strong implication" that for information on the non-dietary route/pathway to be reliable it must be comparable to the information OPP has on dietary exposure.

Each of the three steps in this argument, however, is faulty. The first premise–that there is no reliability requirement pertaining to dietary exposure data–has already been shown to be untenable if asserted broadly (i.e., not just applying to whether there is exposure by a given route), as the IWG comment does. As noted, it is illogical to suggest that Congress removed any constraint regarding the need for reliable information on dietary exposure data pertaining to the magnitude and distribution of exposure. Second, IWG's claim that the lack of a reliability requirement as to dietary exposure data is due to the nature of the data that OPP collects on dietary exposure is nothing more than speculation. IWG cites no authority to support this proposition. Moreover, as noted above, there is an alternative and logical reason appearing on the face of

the statute as to why Congress might not have imposed a reliability criterion on exposure through the dietary route– this statutory section addresses setting maximum levels for pesticide residues in food. Given this explanation based on the statutory structure there is no need to speculate concerning other motivations. Finally, even if the first two steps of IWG's argument are correct (that there is no reliability requirement pertaining to the magnitude and distribution of dietary exposure and that dropping that requirement is due to the quality of OPP's exposure data on food), it does not follow that data on non-dietary exposure must be comparable to food exposure data collected by OPP. At most, there would be an implication that one type of data–data on actual real-world levels of pesticides including information on the distribution of residue levels–would be considered reliable. It would not preclude other data from meeting the reliability requirement.[2]

Application of the Reliable Information Requirement

As indicated, OPP's preferred interpretation of the reliability requirement in subsection (b)(2)(A)(ii) is that it directs OPP to consider whether there is trustworthy and reproducible information on whether there is exposure occurring by the non-dietary pathway in assessing the aggregate risk imposed by a pesticide. If OPP concludes there is no reliable information showing exposure by a non-dietary pathway, OPP will not assume that there is non-dietary exposure to the pesticide. If OPP finds that reliable information does show exposure by a non-dietary route/pathway, OPP must take such exposure into account in assessing the aggregate risk posed by the pesticide whether or not OPP is able to quantify the level of such non-dietary exposure.

As to reliable data bearing on whether exposure occurs by a given route/pathway, OPP believes that information can reliably demonstrate exposure by a given route/ pathway even if OPP does not have data documenting the magnitude of exposure levels to humans. For example, OPP has a large body of data showing that

[2]IWG does not address the difficult interpretation raised by such an approach concerning how OPP is to decide what non-dietary data is comparable to dietary exposure data. Despite IWG's claims to the contrary, OPP has several gradations of data on actual, real-world pesticide residue levels in food. For some pesticides, OPP has full-blown studies from retail markets; in other cases, it may have varying amounts of monitoring data; and, in many cases, it may have only data from the crop field trials. The amount of distributional data OPP has on pesticide residues in food is also variable.

pesticide exposure can occur when there is residential use–e.g., insecticides are applied as a crack or crevice spray in a dwelling or other occupied structure, applied the lawn, etc. Further, OPP has compiled extensive data detailing the physical properties and characteristics of those pesticides that potentially may result in human exposure under this use scenario. Thus, where the physical properties and characteristics of a specific pesticide, when considered in light of the generic data OPP has on pesticide exposure in non-occupational settings, show that it is likely that the presence of that pesticide will result in human exposure if used in under a given scenario, OPP would have reliable information showing such non-dietary exposure. (See also the additional discussion on models and the reliability requirements below.)

ii. The Reliable Information Requirement in Subsection (b)(2)(A)(ii) and the Children's Safety Factor

Once the limited nature of the reliability requirement in subsection (b)(2)(A)(ii) is recognized, OPP can agree with IWG on the legal point that if OPP does not have reliable information showing that exposure is occurring by a non-dietary route/pathway, OPP generally should not take the position that the children's safety factor should be retained because of an absence of reliable data on exposure pertaining to that route of exposure. OPP appears to differ with IWG, however, on what constitutes "reliable information" showing that exposure is occurring by a non-dietary route/pathway. IWG asserts that such a showing cannot be made absent a full database addressing the magnitude and distribution of exposure. As explained above, OPP believes that the reliable information threshold is crossed once it can be shown that exposure is more likely to occur than not by the route/pathway in question, whether or not the information can precisely define the level or distribution of exposure.

IWG's approach is unsound because it essentially reads the completeness of the exposure database factor out of the statute as concerns non-dietary exposure. IWG argues that the exposure considerations relative to the children's safety factor only relate to food exposure. See IWG Comments at 40. Under the IWG's approach, no possible scenario would justify retaining an additional safety factor due to concerns regarding the database on non-dietary exposure. If the database contains full information on the magnitude and distribution on non-dietary exposures, IWG would argue that the exposure database is complete and therefore no additional safety factor is warranted. If the database does not fully

address the magnitude or duration of exposure, then IWG would conclude that there is no reliable information on non-dietary exposure and, therefore, it would be inappropriate to consider the completeness of the non-dietary exposure database in making a decision on the children's safety factor. Instead, IWG would insist that "reliable data" support removing the additional safety factor.

Ultimately, IWG's error flows from its strained reading of the "reliable information" requirement in subsection (b)(2)(A)(ii). Perhaps nothing better illustrates the vacuity of IWG's legal interpretation than a concise summary of IWG's explanation of the interaction of the "reliable information" requirement in subsection (b)(2)(A)(ii) and the "reliable data" requirement in the children's safety provision. According to IWG, the absence of "reliable information" on the magnitude or distribution of non-dietary exposure necessarily means that there is "reliable data" on non-dietary exposure such that the additional safety factor for the protection of children can be removed.

iii. Models and Reliable Information/Data

OPP objects to the IWG's conclusory suggestion that models can never produce "reliable information" and NRDC's similar conclusion regarding models and "reliable data." After all, any exposure estimate is a model of some sort. It is a false dichotomy to suggest that models and data (or information) are opposite extremes. Rather, models, as "users" of both empirical data and assumptions based upon empirical data and informed by scientific judgment, allow scientists to generalize from a less than perfect data set (and data sets are never perfect). For example, short of measuring the pesticide residues in every sip of water and every bite of food as it is being consumed, OPP must model or estimate exposure values for residues in drinking water and food. The need for models exists whether the exposure estimate is based on monitoring values in drinking water and food, residue values from field studies, or data on a pesticide's properties and characteristics which are used to predict anticipated residue levels in water and food. Monitoring data may produce a more realistic and reliable estimate of exposure, but the reliability of any method of estimating exposure will have to be evaluated based on what data the method relies upon.

In any event, the IWG seems more concerned with a particular drinking water model (the farm pond model) and the residential exposure SOPs than models generally. OPP is aware of

the criticisms that have been leveled at these screening level models and continues to take steps to improve the drinking water modeling techniques used in FQPA risk assessments. (USEPA, 1997d; USEPA, 2000e) Similarly, NRDC has expressed concern with the accuracy of OPP models, particularly with regard to non-dietary exposure. As with IWG's criticisms, OPP has taken steps to address the inadequacies identified by NRDC. (USEPA, 1997d)

iv. The Diet Does Not Include Drinking Water Argument

Given the common, everyday meaning of the term diet as including both food and water, IWG would have to find some fairly explicit statutory language to support its claim that "dietary exposure" does not include exposure from drinking water. This IWG cannot do. The IWG cites to subsection (b)(2)(D)(vi) describing aggregate exposure as "including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources" as supporting its position. Presumably, the IWG is assuming that the only exposure "under the tolerance" would be from residues in food, and therefore, since exposure in drinking water is captured by the phrase "exposure from other non-occupational sources," it must be non-dietary exposure. Even assuming the IWG's interpretation of "under this tolerance" is correct, this language does not advance its position. The flaw in the IWG's argument is that the statute has grouped drinking water exposure not under a category labeled non-dietary exposure but simply under the description of "exposure from other non-occupational sources." It is not inconsistent to state that dietary exposure includes drinking water and also group it with non-dietary exposures under a category labeled exposure from other non-occupational sources.

Also unpersuasive is the IWG's argument that because OPP and FDA have treated drinking water as not a "food" under the FFDCA, drinking water is not part of the diet. This argument fails to recognize that the question is not whether water is food, but whether water is part of the diet. Furthermore, OPP and FDA decided to interpret the term "food" as not encompassing drinking water based on their conclusion that Congress' passage of the Safe Drinking Water Act was an implied repeal of OPP and FDA's tolerance setting authority over pesticides in drinking water under the FFDCA. See 44 FR 42775 (July 20,1979). However, here, there has been no action by Congress that would suggest that the

term “dietary” should be read in other than its dictionary sense.

v. The Difference Between Information and Data

Although NRDC claims the statute draws a clear distinction between “data” and “information,” NRDC does not explain or elaborate on that distinction other than to state that, in the context of drinking water exposure, data means “monitoring data” and not exposure estimates from models. NRDC does not address the fact that OPP’s drinking water models are based both on generic environmental and pesticide data and empirical data on a pesticide’s specific properties and characteristics.

OPP would note that the dictionary defines data and information by cross-referencing between these terms and thus information is defined as data and data is defined as information. See, e.g., Webster’s New World Dictionary (2d College Ed. 1976). Given this overlap, it seems unlikely Congress intended OPP to make critical regulatory decisions by dissecting the fine distinctions between the terms “data” and “information.” In any event, even if the term “data” is regarded somehow as only capturing some type of information derived from a scientific study, OPP believes its models are based on information meeting this description.

vi. Conclusion

In sum, OPP disagrees with the major policy implications that both the IWG and NRDC ascribe to the terms "reliable data" and "reliable information" based on either a rather hyper-technical reading of the statute or little more than mere speculation. OPP has been unable to find any legislative history, and the commenters have cited none, that supports the notion that the use of the term "reliable information" or "reliable data," or the use of the term "data" instead of "information" and vice-versa, were intended to have far reaching policy significance.[3] OPP believes Congress' inclusion of the terms "reliable data" and "reliable information" had a much more prosaic purpose–Congress merely wanted to reconfirm that reliability is a necessary criterion for any data or information, or model based on data or information, used in risk assessment under the FFDCA.

M. Petition for Rulemaking

1. Overview

OPP requested comments on how this policy could be structured so as to provide meaningful guidance without at the same time imposing binding requirements on either the government or outside parties. OPP received a few, if any, comments on this issue. OPP will, however, take this opportunity to respond to a petition from pesticide manufacturer and grower groups requesting, among other things, promulgation of a regulation "specifying the routes of exposure that may need to be considered in establishing tolerances and describing how exposure from the specified routes will be assessed." Petition for Rulemaking to Develop Policies and Procedures for Implementing the Food Quality Protection Act of 1996 27 (May 22, 1998).

2. Petition

[3]If anything, the statutory structure suggests that the "reliable information" requirement did not carry great importance. For example, Congress repeated the "reasonable certainty" safety standard in the provision addressing risks to infants and children, section 408(b)(2)(C), but even though it adopted the safety standard word-for-word from subsection (b)(2)(A)(ii), it neglected to include the phrase "including all anticipated dietary exposures and all other exposure for which there is reliable information" after the reference to aggregate exposure.

The pesticide manufacturer/grower petition requested that the Agency undertake rulemaking on a number of topics including implementation of the requirement to take aggregate exposure into account in evaluating the safety of tolerances. Rulemaking on aggregate exposure was deemed needed for three reasons. First, the petitioners asserted that OPP was using "screening" assumptions rather than "actual, reliable data" in calculating aggregate exposure and that, "[b]ecause [these] assumptions embody policy choices on the part of the Agency, it is imperative that such choices be identified and debated by all affected parties prior to being implemented." Petition at 26. Second, the petitioners claim there is a "lack of predictability as to what information may be needed to 'rebut' the assumptions that form the basis of EPA's current aggregate assessment policies. Id. Third, the petitioners argue that rulemaking is necessary because EPA's assumptions are inconsistent with the statutory requirement that aggregate exposure may only be conducted where reliable information is available. Id. at 27.

The petition also lists various generic policy and legal reasons for issuing rules regarding FQPA implementation. The policy reasons include: (1) a rule provides greater transparency because the notice-and-comment process will provide formal notification of EPA's views; (2) rulemaking will give all parties a chance to participate in the development of policy not just those invited to Agency advisory committees; (3) in a rulemaking EPA must respond to public comments on the public record and must provide a concise statement of the basis and purpose for the rule; (4) a rule provides certainty and stability because rules are subject to judicial review and legal issues can be resolved once and for all; (5) the advisory committee process and SAP review of policies has not adequately provided for public participation; and (6) rulemaking on individual tolerances has not been an adequate substitute for generic rulemakings. The legal reasons listed in the petition include: (1) that FQPA policies 'impose obligations' and have 'significant effects on private interests' and thus are, in fact, legislative rules requiring notice-and-comment procedures; (2) the FQPA "requires EPA to use notice-and-comment rulemaking to establish general requirements or procedures for implementing the key provisions of the FQPA." Pet. at 15

3. EPA Response

After considering the petition, OPP does not believe that any of the specific reasons relating to aggregate exposure assessments warrant issuing the aggregate exposure policy as a rule. First, the fact that the policy addresses policy choices does not suggest use of rulemaking procedures is necessary. The APA specifically excludes policies from rulemaking requirements. 5 U.S.C. § 553(b). Further, by seeking public comment on the policy OPP has ensured that the issues in the policy are "identified and debated" by the public.

Second, to the extent petitioners seek revision and expansion of OPP's current data requirements for pesticides, OPP is undertaking such a revision. However, to the extent petitioners are hoping that, through promulgation of a rule pertaining to aggregate exposure assessments, OPP can reduce the aggregate exposure assessments to a routine process, petitioners underestimate the complexity of such assessments. The difficult science issues raised by aggregate exposure assessment require consideration of numerous factors including rapidly developing scientific concepts, techniques, and methodologies. Such decisions cannot be translated into prescriptive black letter rules without removing the scientific judgment that is critical to producing a sound scientific conclusion.

This position is consistent with the manner in which the Agency generally approaches complex risk assessment issues and has resolved questions regarding other science policies under the FQPA. Thus, EPA's views on major risk assessment topics have been issued as policy guidances not binding rules. See e.g., Guidelines for Carcinogen Risk Assessment, 51 FR 33992 (September 24, 1986); Guidelines for Reproductive Toxicity Risk Assessment, 61 FR 56274 (October 31, 1996); Guidelines for Exposure Assessment, 57 FR 22888 (May 29, 1992); Proposed Guidelines for Carcinogen Risk Assessment, 61 FR 17960 (April 23, 1996). Similarly, EPA's FQPA policy addressing the selection of the population percentile used in calculating the threshold of regulatory concern in acute risk assessments was issued as a policy not a rule. See XX. In their petition, the pesticide manufacturers and growers cited to one EPA proposed rule that included "models and assumptions for estimating public exposure" concerning certain air emission standards. See 59 Fed. Reg. 15504 (April 1, 1994). However, OPP would note that when that rule was finalized, the portions addressing risk assessment were omitted. 61 Fed. Reg. 68384 (December 27, 1998).

Finally, petitioners' disagreement with the type of information relied by OPP in certain specific pesticide does not convince OPP that it should

break with its past practice regarding science policies. OPP cannot hope to resolve through a rule the reliability of the myriad forms of information bearing on pesticide exposure. If petitioners question whether specific OPP tolerance actions are supported by reliable information, the statute provides avenues to seek both administrative and judicial review. OPP has attempted through the policy document to provide general information regarding its approach to consideration of several different types of exposure data. Finally, in responding to comments, OPP has provided its interpretation of the terms "reliable information" and "reliable data" as they appear in the section 408.

EPA found none of the generic arguments set forth in the rulemaking petition to be persuasive. Each of those arguments are addressed in turn below.

Transparency. The petition argued that a rule would provide greater transparency because there would be formal notification of all parties concerning the rulemaking. However, this formal notification concern was met by the procedure EPA followed in developing this policy. EPA published notice of the draft policy in the Federal Register. That notice provided a concise summary of the policy and requested public comment on the policy. Further, EPA put a full copy of the policy on its Internet Web site and generally made copies available to the public.

Public Participation. The petition argued that a rulemaking would allow all affected parties to participate not just advisory committee members. That concern, however, has also been met by EPA's public comment process.

Response to Comments. The petition expressed a concern that without a requirement to respond to comments and to provide a statement of the basis and purpose for the policy, OPP would not in fact produce such documents. OPP, however, believes that its policy document clearly articulates the basis and purpose of the policy and that this Response to Comments document has adequately addressed all significant comments.

Judicial Review. The petition argued that a rule provides certainty and stability because unlike a policy document it would be subject to judicial review. Generally, policy statements are not reviewed as ripe for review until they have been applied to a concrete regulatory action. Similarly, generic rules are often found unripe on the same grounds. On occasion, courts will review a generic rule in the absence of a concrete application of the rule where a challenge to the rule presents purely legal questions and there would be hardship to the challenger in delaying review. This policy is primarily devoted to policy and science issues. Although this Response to Comments document does address OPP's interpretation of the terms "reliable information" and "reliable data," OPP believes that these interpretations are of the variety that judicial review of the interpretation would benefit from application of the interpretation in a concrete context. Thus, whether these interpretations are included in this document as interpretive rules or promulgated as binding legislative rules, is likely to have little effect on their reviewability. Codifying the interpretations does not necessarily affect their ripeness. Accordingly, this consideration does not appear to strongly support issuance of the policy as a rule.

Advisory Committee Process and SAP Review. The petition claimed that Agency attempts to get outside input into its policies through various advisory committees and the FIFRA SAP have been inadequate. OPP believes the advisory committee process and SAP review have provided important input. However, to the extent these processes have provided only a limited forum for public participation, the notice-and-comment process for the policy has addressed any such concern.

Individual Tolerance Rulemakings. The petition argued that OPP has not opened its policies up for comment in rulemakings addressing individual tolerances. The petition also implies that application of OPP policies in the context of such tolerance actions is not subject to judicial review. Pet. at 24. Although EPA has not specifically requested comments on its policies in tolerance actions, such comments would certainly be appropriate to the extent the policy formed part of the basis for OPP's decision. Moreover, the petition is clearly incorrect if it is suggesting that the lack of an explicit request for comment on policies underlying a specific tolerance decision somehow insulates the policy's application from administrative and judicial review.

FQPA Requirement for Rulemaking. The petition claimed that section 408(e)(1)(C) requires that general procedures for

implementing section 408 must be promulgated as rules. The language of section 408(e)(1)(C), however, is clearly permissive–"EPA *may* issue a regulation . . . " (emphasis added). This language authorizes EPA to establish rules for "general procedures and requirements to implement this section;" it does not mandate such rules.

Accordingly, OPP denies the petition to the extent it sought promulgation of a regulations on aggregate exposure assessments.

III. List of Commenters

Private Citizens (25)

Governmental:	Health Canada; City Health Departments of L.A. County
Trade Associations:	American Water Works Association; Michigan Farm Bureau
Industry:	CSMA; CMA; Novartis; IWG
Consultants:	Keller and Heckman, LLP; Margory Exton
Advocacy Groups:	Children's Environmental Health Network; NRDC; MCS: Health and Environment; Citizens for a Responsible Alternatives to Malathion

IV. Definitions

Absorbed dose: The amount of a substance penetrating across the absorption barriers (or the exchange barriers) of an organism, via either physical or biological processes. Synonymous with internal dose. (US EPA, 1992).

Active ingredient (ai): The chemical component of a pesticide formulation or end-use product that is intended to act as a pest deterrent. The biologically active chemical agent in a pesticide product (US EPA, 1997a).

Aggregate dose: The amount of a single substance available for interaction with metabolic processes or biologically significant receptors from multiple routes of exposure.

Aggregate exposure: The amount of a chemical available at the biological exchange boundaries (e.g., respiratory tract, gastrointestinal tract, skin) for all routes of exposure.

Aggregate exposure assessment: A process for developing an estimate of the extent of a defined population to a given chemical by all relevant routes and from all relevant sources (ILSI, 1998 p. A-2).

Aggregate risk: The likelihood of the occurrence of an adverse health effect resulting from all routes of exposure to a single substance.

Biomonitoring: Measurement of a pesticide or its metabolites in body fluids of exposed persons, and conversion to an equivalent absorbed dose of the pesticide based on a knowledge of its human metabolism and pharmacokinetics (Woollen, 1993).

Cumulative risk: The likelihood of the occurrence of an adverse health effect resulting from all routes of exposure to a group of substance sharing a common mechanism of toxicity.

Dislodgeable residue: The portion of a pesticide (which may or may not include its metabolites) that is available for transfer from a pesticide treated surface (US EPA, 1997a).

Dose: The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism (US EPA, 1992).

Dose rate: Dose per unit time (e.g., mg/day). Also called dosage. Dose rates are often expressed on a per-unit-body-weight basis (mg/kg/day). Dose rates may also be expressed as an average over a time period (i.e., lifetime) (US EPA, 1992).

Exposure: Contact of a chemical, physical, or biological agent with the outer boundary of an organism. Exposure is quantified as the concentration of the agent in the medium in contact integrated over the time duration of that contact (US EPA, 1992).

Exposure assessment: The qualitative or quantitative determination or estimation of the magnitude, frequency, duration, and rate of exposure of an individual or population to a chemical.

Exposure scenario: A combination of facts, assumptions, and inferences that define a discrete situation or activity where potential exposures may occur (US EPA, 1997a).

Intake: The process by which a substance crosses the outer boundary of an organism without passing an absorption barrier, e.g., through ingestion or inhalation. (See also potential dose) (US EPA, 1992).

Level of Comparison: A drinking water level of comparison is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses.

Lowest Observed Adverse Effect Level (LOAEL): The lowest dose at which an adverse effect is seen.

No Observed Adverse Effect Level (NOAEL): The dose at which no adverse toxic effect is seen.

Pathway: The physical course a chemical or pollutant takes from the source to the organism exposed. Also called **exposure pathway** (US EPA, 1992).

Population Adjusted Dose (PAD): The RfD adjusted for the FQPA safety factor.

Potential Dose: The amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin (US EPA, 1992).

Reference Concentration (RfC): NOAEL (inhalation)/UF.

Reference Dose (RfD): NOAEL/UF.

Route: The way a chemical or pollutant enters an organism after contact, e.g., by ingestion, inhalation, or dermal absorption. Also called **exposure route** (US EPA, 1992).

Surrogate data: Substitute data or measurements on one substance (or population) used to estimate analogous or corresponding values for another substance (or population).

Transfer coefficient: Residue transfer rate to humans during the completion of specific activities (e.g., cm^2 per hour), calculated using concurrently collected environmental residue data (US EPA, 1998).

Uncertainty: Lack of knowledge about specific factors, parameters, or models.

Uncertainty factor: Uncertainty factors applied to account for inter- and intraspecies differences in relation to toxic effects, and uncertainties associated with the data.

Unit exposure: The amount of a pesticide residues to which individuals are exposed, normalized by the amount of active ingredient used.

Uptake: The process by which a substance crosses and absorption barrier and is absorbed into the body (US EPA, 1992).

Variability: Differences attributed to true heterogeneity or diversity in a population or exposure parameter.

V. References

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