ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2005–0050; FRL–8079–8]

Alachlor, Chlorothalonil, Methomyl, Metribuzin, Thiodicarb; Order Denying Petition To Revoke Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Order.

SUMMARY: In this Order, EPA denies, in part, a petition requesting the modification or revocation of the pesticide tolerances for alachlor, chlorothalonil, methomyl, metribuzin, and thiodicarb established under section 408 of the Federal Food, Drug, and Cosmetic Act (''FFDCA''). The petition was filed on December 17, 2004, by the States of New York, California, and Connecticut, and the Commonwealth of Massachusetts (''the States''). In their petition, the States contend that the risks posed by these pesticide tolerances must be assessed utilizing the additional tenfold (10X) safety factor for the protection of infants and children and that once this additional factor is included the challenged tolerances no longer meet the safety standard under FFDCA section 408. EPA is denying the petition to modify or revoke as to the tolerances for the pesticides alachlor, chlorothalonil, and metribuzin. EPA is deferring action on the petition as regards the tolerances for methomyl and thiodicarb given the ongoing Agency proceedings to address the safety of these pesticides.

DATES: This Order is effective August 2, 2006. Objections and requests for hearings must be received on or before October 2, 2006, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: EPA has established a docket for this action under Docket identification (ID) number EPA–HQ–OPP–2005–0050. All documents in the docket are listed in the index for the docket. Although listed in the index, some information is not publicly available, i.e., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available in the electronic docket at *http://www.regulations.gov*, or, if only available in hard copy, at the OPP Public Docket, in Rm. S–4400, One Potomac Yard (South Building), 2777 S. Crystal Drive, Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: Terria Northern, Special Review and Reregistration Division, (7508P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001; telephone number: 703–305–7093; fax number: 703–308–7070; e-mail address: *northern.terria@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS code 111)
- Animal production (NAICS code 112)
- Food manufacturing (NAICS code 311)
- Pesticide manufacturing (NAICS code 32532)

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. To determine whether you or your business may be affected by this action, you should carefully examine the applicability provisions in [insert appropriate cite to either another unit in the preamble or a section in a rule]. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under.

B. How Can I Access Electronic Copies of this Document?

In addition to accessing an electronic copy of this **Federal Register** document through the electronic docket at *http://www.regulations.gov*, you may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at *http://www.epa.gov/fedrgstr*. You may also access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's pilot e-CFR site at *http://www.gpoaccess.gov/ecfr*.

C. Can I File an Objection or Hearing Request?

Under section 408(g) of the FFDCA, as amended by the FQPA, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. The EPA procedural regulations which govern the submission of objections and requests for hearings appear in 40 CFR part 178. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2006-0050 in the subject line on the first page of your submission. All requests must be in writing, and must be mailed or delivered to the Hearing Clerk on or before October 2, 2006.

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing that does not contain any CBI for inclusion in the public docket that is described in **ADDRESSES**. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit your copies, identified by docket ID number EPA-HQ-OPP-2006-0050, by one of the following methods:

- *Federal eRulemaking Portal. http://www.regulations.gov*. Follow the on-line instructions for submitting comments.
- *Mail*. Office of Pesticide Programs (OPP) Regulatory Public Docket (7502P), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.
- *Delivery*. OPP Regulatory Public Docket (7502P), Environmental Protection Agency, Rm. S-4400, One Potomac Yard (South Building), 2777 S. Crystal Drive, Arlington, VA. Deliveries are only accepted during the Docket's normal hours of operation (8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays). Special arrangements should be made for deliveries of boxed information. The Docket telephone number is (703) 305–5805.

II. Introduction

A. What Action Is the Agency Taking?

In this Order, EPA denies, in part, a petition requesting the modification or revocation of the pesticide tolerances for alachlor, chlorothalonil, methomyl, metribuzin, and thiodicarb established under section 408 of the FFDCA. The petition was filed on December 17,

2004, by the States of New York, California, and Connecticut, and the Commonwealth of Massachusetts (''the States'') (Ref. 1). In their petition, the States contend that EPA is lacking data for each of the five pesticides on developmental neurotoxicity, endocrine effects, and/or cumulative effects of exposure to pesticides with a common mechanism of toxicity. The States argue that this lack of these data mandates that EPA retain the additional tenfold (10X) safety factor for the protection of infants and children. The States further allege that once the 10X safety factor is retained, the challenged tolerances no longer meet the safety standard under FFDCA section 408 and must be modified or revoked.

In today's Order, EPA is denying the petition to modify or revoke as to the tolerances for the pesticides alachlor, chlorothalonil, and metribuzin. As to alachlor and metribuzin, EPA is denying the petition because the tolerances for these pesticides would continue to meet the safety standard even if the additional 10X safety factor sought by the States is applied. For chlorothalonil, EPA has determined, after reviewing the legal and factual contentions of the States, that there is reliable data showing that the additional 10X safety factor is not needed to protect the safety of infants and children. EPA is deferring action on the petition as regards the tolerances for methomyl and thiodicarb given the ongoing Agency proceedings to address the safety of these pesticides.

B. What Is the Agency's Authority for Taking This Action?

Under section 408(d)(4) of the FFDCA, EPA is authorized to respond to a section 408(d) petition to revoke tolerances either by issuing a final rule revoking the tolerances, issuing a proposed rule, or issuing an order denying the petition.

III. Statutory and Regulatory Background

A. Statutory Background

1. *In general.* EPA establishes maximum residue limits, or ''tolerances,'' for pesticide residues in food under section 408 of the FFDCA. (21 U.S.C. 346a). Without such a tolerance or an exemption from the requirement of a tolerance, a food containing a pesticide residue is ''adulterated'' under section 402 of the FFDCA and may not be legally moved in interstate commerce. (21 U.S.C. 331, 342). Monitoring and enforcement of pesticide tolerances are carried out by the U.S. Food and Drug Administration and the U. S. Department of Agriculture. Section 408 was substantially rewritten by the Food Quality Protection Act of 1996 (''FQPA''), which added the provisions discussed below establishing a detailed safety standard for pesticides, additional protections for infants and children, and the estrogenic substances screening program.

EPA also regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (''FIFRA''), (7 U.S.C. 136 et seq). While the FFDCA authorizes the establishment of legal limits for pesticide residues in food, FIFRA requires the approval of pesticides prior to their sale and distribution, (7 U.S.C. 136a(a)), and establishes a registration regime for regulating the use of pesticides. FIFRA regulates pesticide use in conjunction with its registration scheme by requiring EPA review and approval of pesticide labels and specifying that use of a pesticide inconsistent with its label is a violation of Federal law. (7 U.S.C. 136j(a)(2)(G)). In the FQPA, Congress integrated action under the two statutes by requiring that the safety standard under the FFDCA be used as a criterion in FIFRA registration actions as to pesticide uses which result in dietary risk from residues in or on food, (7 U.S.C. 136(bb)), and directing that EPA coordinate, to the extent practicable, revocations of tolerances with pesticide cancellations under FIFRA. (21 U.S.C. 346a(l)(1)).

2. *Safety standard for pesticide tolerances.* A pesticide tolerance may only be promulgated by EPA if the tolerance is ''safe.'' (21 U.S.C. 346a(b)(2)(A)(i)). ''Safe'' is defined by the statute to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.'' (21 U.S.C. 346a(b)(2)(A)(ii)). Section 408(b)(2)(D) directs EPA, in making a safety determination, to:

> consider, among other relevant factors- . . .
>
> (v) available information concerning the cumulative effects of such residues and other substances that have a common mechanism of toxicity; . . .
>
> (vi) available information concerning the aggregate exposure levels of consumers (and major identifiable subgroups of consumers) to the pesticide chemical residue and to other related substances, including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources.
>
> (viii) such information as the Administrator may require on whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects. . . .

(21 U.S.C. 346a(b)(2)(D)(v), (vi) and (viii)).

Section 408(b)(2)(C) requires EPA to give special consideration to risks posed to infants and children. Specifically, this provision states that EPA:

> shall assess the risk of the pesticide chemical based on-- . . .
>
> (II) available information concerning the special susceptibility of infants and children to the pesticide chemical residues, including neurological differences between infants and children and adults, and effects of *in utero* exposure to pesticide chemicals; and
>
> (III) available information concerning the cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity. . . .

(21 U.S.C. 346a(b)(2)(C)(i)(II) and (III)). This provision further directs that ''[i]n the case of threshold effects, . . . an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children.'' (21 U.S.C. 346a(b)(2)(C)). EPA is permitted to ''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.'' (Id.). [The additional safety margin for infants and children is referred to throughout this Order as the ''children's safety factor.'']

3. *Procedures for establishing, amending, or revoking tolerances.* Tolerances are established, amended, or revoked by rulemaking under the unique procedural framework set forth in the FFDCA. Generally, the rulemaking is initiated by the party seeking to establish, amend, or revoke a tolerance by means of filing a petition with EPA. (See 21 U.S.C. 346a(d)(1)). EPA publishes in the **Federal Register** a notice of the petition filing and requests public comment. (21 U.S.C. 346a(d)(3)). After reviewing the petition, and any comments received on it, EPA may issue a final rule establishing, amending, or revoking the tolerance, issue a proposed rule to do the same, or deny the petition. (21 U.S.C. 346a(d)(4)). Once EPA takes final action on the petition by either establishing, amending, or revoking the tolerance or denying the petition, any affected party has 60 days to file objections with EPA and seek an evidentiary hearing on those objections. (21 U.S.C. 346a(g)(2)). EPA's final order on the objections is subject to judicial review. (21 U.S.C. 346a(h)(1)).

4. *Estrogenic Substances Screening Program.* Section 408(p) of the FFDCA

creates the estrogenic substances screening program. This provision gives EPA 2 years from enactment of the FQPA to ''develop a screening program . . . to determine whether certain substances may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect as the Administrator may designate.'' This screening program must use ''appropriate validated test systems and scientifically relevant information.'' (21 U.S.C. 346a(p)(1)). Once the program is developed, EPA is required to take public comment and seek independent scientific review of it. Following the period for public comment and scientific review, and not later than 3 years following enactment of the FQPA, EPA is directed to ''implement the program.'' (21 U.S.C. 346a(p)(2)).

The scope of the estrogenic screening program was expanded by an amendment to the Safe Drinking Water Act (SDWA) passed contemporaneously with FQPA. That amendment gave EPA the authority to provide for the testing, under the FQPA estrogenic screening program, ''of any other substance that may be found in sources of drinking water if the Administrator determines that a substantial population may be exposed to such substance.'' (42 U.S.C. 300j–17).

B. Setting and Reassessing Pesticide Tolerances Under the FFDCA

1. *In general*. The process EPA follows in setting and reassessing tolerances under the FFDCA includes two steps. First, EPA determines an appropriate residue level value for the tolerance taking into account data on levels that can be expected in food. Second, EPA evaluates the safety of the tolerance relying on toxicity and exposure data and guided by the statutory definition of ''safety'' and requirements concerning risk assessment. Only on completion of the second step can a tolerance be established or reassessed. This bifurcation between selection of a tolerance level and evaluation of the safety of a tolerance has ramifications on how EPA responds when a tolerance is found to no longer meet section 408's safety standard. Generally, if an existing tolerance is shown to raise safety concerns, EPA would not address these concerns by modifying the tolerance through decreasing the tolerance level unless there were pesticide residue data showing how such a lower level could be achieved. Rather, where safety concerns are demonstrated and there is no available data demonstrating that a different application pattern would produce lower residue levels in food, the only appropriate action would be to revoke the tolerance. Below, EPA explains in detail, the reasons for this approach.

2. *Choosing a tolerance value*. In the first step of the tolerance setting or reassessment process (choosing a tolerance value), EPA evaluates data from experimental crop field trials in which the pesticide has been used in a manner, consistent with the draft FIFRA label, that is likely to produce the highest residue in the crop in question (e.g., maximum application rate, maximum number of applications, minimum pre-harvest interval between last pesticide application and harvest). (Refs. 2 and 3). These crop field trials are generally conducted in several fields at several geographical locations. (Ref. Id. at 5, 7 and Tables 1 and 5). Several samples are then gathered from each field and analyzed. (Id. at 53). Generally, the results from such field trials show that the residue levels for a given pesticide use will vary from as low as non-detectable to measurable values in the parts per million (ppm) range with the majority of the values falling at the lower part of the range. EPA then chooses a value to be used in the tolerance by identifying the highest residue value found and rounding that value up or adding a small increment to it. (See 70 FR 46706, 46731, August 10, 2005). (As discussed below, the safety of the tolerance value chosen is separately evaluated.).

There are three main reasons for closely linking tolerance values to the maximum value that could be present from maximum label usage of the pesticide. First, EPA believes it is important to coordinate its actions under the two statutory frameworks governing pesticides. (See The Pesticide Coordination Policy; Response to Petitions, (61 FR 2378, 2379; January 25, 1996)). It would be illogical for EPA to set a pesticide tolerance under the FFDCA without considering what action is being taken under FIFRA with regard to registration of that pesticide use. (Cf. 40 CFR 152.112(g) (requiring all necessary tolerances to be in place before a FIFRA registration may be granted)). In coordinating its actions, one basic tenet that EPA follows is that a grower who applies a pesticide consistent with the FIFRA label directions should not run the risk that his or her crops will be adulterated under the FFDCA because the residues from that legal application exceed the tolerance associated with that use. Crop field trials require application of the pesticide in the manner most likely to produce maximum residues to further this goal. Second, choosing tolerance values based on FIFRA label rates helps to ensure that tolerance levels are established no higher than necessary. If tolerance values were selected solely in consideration of health risks, in some circumstances, tolerance values might be set so as to allow much greater application rates than necessary for effective use of the pesticide. This could encourage misuse of the pesticide. Finally, closely linking tolerance values to FIFRA labels helps EPA to police compliance with label directions by growers because detection of an overtolerance residue is indicative of use of a pesticide at levels, or in a manner, not permitted on the label.

3. *The safety determination - risk assessment*. Once a tolerance value is chosen, EPA then evaluates the safety of the pesticide tolerance using the process of risk assessment. To assess risk of a pesticide, EPA combines information on pesticide toxicity with information regarding the route, magnitude, and duration of exposure to the pesticide.

In evaluating toxicity or hazard, EPA examines both short-term (e.g., ''acute'') and longer-term (e.g., ''chronic'') adverse effects from pesticide exposure. (Ref. 2 at 8–10). EPA also considers whether the ''effect'' has a threshold - a level below which exposure has no appreciable chance of causing the adverse effect. For non-threshold effects, EPA assumes that any exposure to the substance increases the risk that the adverse effect may occur. At present, EPA only considers one adverse effect, the chronic effect of cancer, to potentially be a non-threshold effect. (Ref. 2 at 8–9). Not all carcinogens, however, pose a risk at any exposure level (i.e., ''a non-threshold effect or risk''). Advances in the understanding of carcinogenesis have increasingly led EPA to conclude that some pesticides that cause carcinogenic effects only cause such effects above a certain threshold of exposure. EPA has traditionally considered adverse effects on the endocrine system to be a threshold effect; that determination is being reexamined in conjunction with the endocrine disruptor screening program.

Once the hazard for a durational scenario is identified, EPA must determine the toxicological level of concern and then compare estimated human exposure to this level of concern. This comparison is done through either calculating a safe dose in humans (incorporating all appropriate safety factors) and expressing exposure as a percentage of this safe dose (the reference dose (''RfD'') approach) or dividing estimated human exposure into

an appropriate dose from the relevant studies at which no adverse effects from the pesticide are seen (the margin of exposure (''MOE'') approach). How EPA determines the level of concern and assesses risk under these two approaches is explained in more detail below. EPA's general approach to estimating exposure is also briefly discussed.

a. *Levels of concern and risk assessment*—(i) *threshold effects*. In assessing the risk from a pesticide's threshold effects, EPA evaluates an array of toxicological studies on the pesticide. In each of these studies, EPA attempts to identify the lowest observed adverse effect level (''LOAEL'') and the next lower dose at which there are no observed adverse affect levels (''NOAEL''). Generally, EPA will use the lowest NOAEL from the available studies as a starting point in estimating the level of concern for humans. In estimating and describing the level of concern, however, the chosen NOAEL is at times manipulated differently depending on whether the risk assessment addresses dietary or non-dietary exposures.

For dietary risks, EPA uses the chosen NOAEL to calculate a safe dose or RfD. The RfD is calculated by dividing the chosen NOAEL by all applicable safety or uncertainty factors. Typically, a combination of safety or uncertainty factors providing a hundredfold (100X) margin of safety is used: 10X to account for uncertainties inherent in the extrapolation from laboratory animal data to humans and 10X for variations in sensitivity among members of the human population as well as other unknowns. Further, under the FQPA, an additional safety factor of 10X is presumptively applied to protect infants and children, unless reliable data support selection of a different factor.

To quantitatively describe risk using the RfD approach, estimated exposure is expressed as a percentage of the RfD. Dietary exposures lower than 100 percent of the RfD are generally not of concern. Further complicating matters, EPA's Office of Pesticide Programs, in implementing FFDCA section 408, also calculates a variant of the RfD referred to as a Population Adjusted Dose (''PAD''). A PAD is the RfD divided by any portion of the FQPA safety factor that does not correspond to one of the traditional additional safety factors used in general Agency risk assessment. (Ref. 4 at 13–16). The reason for calculating PADs is so that other parts of the Agency, which are not governed by FFDCA section 408, can, when evaluating the same or similar substances, easily identify which aspects of a pesticide risk assessment are a function of the particular statutory commands in FFDCA section 408. For simplicity, this document refers to all safe dose calculations as RfDs. Today, RfDs are generally calculated for both acute and chronic dietary risks although traditionally a RfD was only calculated for chronic dietary risks.

For non-dietary, and often for combined dietary and non-dietary, risk assessments of threshold effects, the toxicological level of concern is not expressed as a safe dose or RfD but rather as the margin of exposure (MOE) that is necessary to be sure that exposure to a pesticide is safe. A safe MOE is generally considered to be a margin at least as high as the product of all applicable safety factors for a pesticide. For example, if a pesticide needs a 10X factor to account for interspecies differences, 10X factor for intraspecies differences, and 10X factor for FQPA, the safe or target MOE would be a MOE of at least 1,000. To calculate the MOE for a pesticide, human exposure to the pesticide is divided into the lowest NOAEL from the available studies. In contrast to the RfD approach, the higher the MOE, the safer the pesticide. Accordingly, if the level of concern for a pesticide is 1,000, MOE's exceeding 1,000 would generally not be of concern. Like RfDs, specific MOEs are calculated for exposures of different durations. For non-dietary exposures, EPA typically examines short-term, intermediate-term, and long-term exposures. Additionally, non-dietary exposure often involves exposures by various routes including dermal, inhalation, and oral.

The RfD and MOE approaches are fundamentally equivalent. For a given risk and given exposure of a pesticide, if the pesticide were found to be safe under a RfD analysis it would also pass under the MOE approach, and vice-versa.

(ii) *Non-threshold effects*. For risk assessments for non-threshold effects, EPA does not use the RfD or MOE approach. Rather, EPA calculates the slope of the dose-response curve for the non-threshold effects from relevant studies using a model that assumes that any amount of exposure will lead to some degree of risk. The slope of the dose-response curve can then be used to estimate the probability of occurrence of additional adverse effects as a result of exposure to the pesticide. For non-threshold cancer risks, EPA generally is concerned if the probability of increased cancer cases exceed the range of 1 in 1 million. Because the States' petition concerns the children's safety factor and the children's safety factor is only applicable to threshold risks, no further discussion of non-threshold risk assessment is included here.

b. *Estimating human exposure*. Equally important to the risk assessment process as determining the toxicological level of concern is estimating human exposure. Under FFDCA section 408, EPA is concerned not only with exposure to pesticide residues in food but also exposure resulting from pesticide contamination of drinking water supplies and from use of pesticides in the home or other non-occupational settings. (See 21 U.S.C. 346a(b)(2)(D)(vi)). The focus of the States' petition, however, appears to be on pesticide exposure from food. There are two critical variables in estimating exposure in food: (1) The types and amount of food that is consumed; and (2) the residue level in that food. Consumption is estimated by EPA based on scientific surveys of individuals' food consumption in the United States conducted by the U.S. Department of Agriculture. (Ref. 2 at 12). Information on residue values comes from a range of sources including crop field trials, data on pesticide reduction due to processing and other practices, information on the extent of usage of the pesticide, and monitoring of the food supply. (Id. at 17).

In assessing exposure from pesticide residues in food, EPA, for efficiency's sake, follows a tiered approach in which it, in the first instance, conducts its exposure assessment using the worst case assumptions that 100 percent of the crop in question is treated with the pesticide and 100 percent of the food from that crop contains pesticide residues at the tolerance level. (Id. at 11). When such an assessment shows no risks of concern, EPA's resources are conserved because a more complex risk assessment is avoided and regulated parties are spared the cost of any additional studies that may be needed. If, however, a first tier assessment suggests there could be a risk of concern, EPA then attempts to refine its exposure assumptions to yield a more realistic picture of residue values through use of data on the percent of the crop actually treated with the pesticide and data on the level of residues that may be present on the treated crop. These latter data are used to estimate what has been traditionally referred to by EPA as ''anticipated residues.''

Use of percent crop treated data and anticipated residue information is appropriate because EPA's worst case assumptions of 100 percent treatment and residues at tolerance value significantly overstate residue values. There are several reasons this is true.

First, all growers of a particular crop would rarely choose to apply the same pesticide to that crop; generally, the proportion of the crop treated with a particular pesticide is significantly below 100 percent. Second, as discussed above, the tolerance value is set above the highest value observed in crop field trials using maximum use rates. There may be some commodities from a treated crop that approach the tolerance value where the maximum label rates are followed, but most generally fall significantly below. If less than the maximum legal rate is applied, residues will be even lower. Third, residue values in the field do not take into account the lowering of residue values that frequently occurs as a result of degradation over time and through food processing and cooking.

EPA uses several techniques to refine residue value estimates. (Id. at 17–28). First, where appropriate, EPA will take into account all the residue values reported in the crop field trials, either through use of an average or individually. Second, EPA will consider data showing what portion of the crop is not treated with the pesticide. Third, data can be produced showing pesticide degradation and decline over time, and the effect of commercial and consumer food handling and processing practices. Finally, EPA can consult monitoring data gathered by the Food and Drug Administration, the U.S. Department of Agriculture, or pesticide registrants, on pesticide levels in food at points in the food distribution chain distant from the farm, including retail food establishments.

Another critical component of the exposure assessment is how data on consumption patterns are combined with data on pesticide residue levels in food. Traditionally, EPA has calculated exposure by simply multiplying high-end consumption by average residue values for estimating chronic risks and high-end consumption by maximum residue values for estimating acute risks. Although using average residues is a realistic approach for chronic risk assessment due to the fact that variations in residue levels and consumption amounts average out over time, using maximum residue values for acute risk assessment tends to greatly overstate exposure in narrow increments of time where it matters how much of each treated food a given consumer eats and what the residue levels are in the particular foods consumed. To take into account the variations in short-term consumption patterns and food residue values for acute risk assessments, EPA has more recently begun using probabilistic modeling techniques for estimating exposure when more simplistic models appear to show risks of concerns.

All of these refinements to the exposure assessment process, from use of food monitoring data through probabilistic modeling, can have dramatic effects on the level of exposure predicted, reducing worst case estimates by 1 or 2 orders of magnitude or more.

C. EPA Policy on the Children's Safety Factor

As the above brief summary of EPA's risk assessment practice indicates, the use of safety factors plays a critical role in the process. This is true for traditional 10X safety factors to account for differences between animals and humans when relying on studies in animals (inter-species safety factor) and differences among humans (intra-species safety factor) as well as the additional 10X children's safety factor added by the FQPA.

In applying the children's safety factor provision, EPA has interpreted it as imposing a presumption in favor of applying an additional 10X safety factor. (Ref. 4 at 4, 11). Thus, EPA generally refers to the additional 10X factor as a presumptive or default 10X factor. EPA has also made clear, however, that this presumption or default in favor of the additional 10X is only a presumption. The presumption can be overcome if reliable data demonstrate that a different factor is safe for children. (Id.). In determining whether a different factor is safe for children, EPA focuses on the three factors mentioned in section 408(b)(2)(C) - the completeness of the toxicity database, the completeness of the exposure database, and potential pre- and post-natal toxicity. In examining these factors, EPA strives to make sure that its choice of a safety factor, based on a weight-of-the-evidence evaluation, does not understate the risk to children. (Id. at 24–25, 35). EPA's implementation of the safety factor provision is explained in greater detail in Unit VII.D.1.c.

D. Endocrine Disruptor Screening Program

To aid in the design of the endocrine screening program called for in the FQPA and SDWA amendments, EPA created the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), which was comprised of members representing the commercial chemical and pesticides industries, Federal and State agencies, worker protection and labor organizations, environmental and public health groups, and research scientists. (63 FR 71542, 71544, Dec. 28, 1998). The EDSTAC presented a comprehensive report in August 1998 addressing both the scope and elements of the endocrine screening program. (Ref. 5). The EDSTAC's recommendations were largely adopted by EPA.

As recommended by EDSTAC, EPA expanded the scope of the program from focusing only on estrogenic effects to include androgenic and thyroid effects as well. (63 FR at 71545). Further, EPA, again on the EDSTAC's recommendation, chose to include both human and ecological effects in the program. (Id.). Finally, based on EDSTAC's recommendation, EPA established the universe of chemicals to be screened to include not just pesticides but some 87,000 chemical substances and common mixtures. (Id.). As to the program elements, EPA adopted EDSTAC's recommended two-tier approach with the first tier involving screening ''to identify substances that have the potential to interact with the endocrine system'' and the second tier involving testing ''to determine whether the substance causes adverse effects, identify the adverse effects caused by the substance, and establish a quantitative relationship between the dose and the adverse effect.'' (Id.). Tier 1 screening is limited to evaluating whether a substance is ''capable of interacting with'' the endocrine system, and is ''not sufficient to determine whether a chemical substance may have an effect in humans that is similar to an effect produced by naturally occurring hormones.'' (Id. at 71550). Based on the results of Tier 1 screening, EPA will decide whether Tier 2 testing is needed. Importantly, ''[t]he outcome of Tier 2 is designed to be conclusive in relation to the outcome of Tier 1 and any other prior information. Thus, a negative outcome in Tier 2 will supersede a positive outcome in Tier 1.'' (Id. at 71554–71555).

The EDSTAC provided detailed recommendations for Tier 1 screening and Tier 2 testing. The panel of the EDSTAC that devised these recommendations was comprised of distinguished scientists from academia, government, industry, and the environmental community. (Ref. 5, Appendix B). As suggested by the EDSTAC, EPA has proposed a battery of short-term *in vitro* and *in vivo* assays for the Tier 1 screening exercise. (63 FR at 71550–71551). Validation of these assays, however, has proved difficult and, more than 7 years after proposing the assays, validation of all of the assays in the battery is not yet complete. As to Tier 2 testing, EPA, on the recommendation of the EDSTAC, has

proposed using five longer-term reproduction studies that, with one exception, ''are routinely performed for pesticides with widespread outdoor exposures that are expected to affect reproduction.'' (Id. at 71555). EPA is examining, pursuant to the suggestion of the EDSTAC, modifications to these studies to enhance their ability to detect endocrine effects.

E. Lawsuit Seeking the Revocation of Tolerances

In 2003, the States of New York, New Jersey, Connecticut, and Massachusetts, filed suit against EPA seeking the revocation of the same pesticide tolerances challenged in this petition. The lawsuit, containing allegations nearly identical to those in this petition, argued that EPA's tolerance reassessment decisions as to alachlor, chlorothalonil, methomyl, metribuzin, and thiodicarb were in violation of FFDCA section 408. In 2004, this lawsuit was dismissed because the plaintiffs had not first presented their challenge to these tolerances to EPA in the form of section 408(d)(4) petition to revoke. (*New York v. EPA*, 350 F. Supp. 429 (S.D.N.Y. 2004)). The current petition was subsequently filed with EPA.

IV. The Challenged Tolerances

A. Alachlor

Alachlor is a selective herbicide used in agriculture for the control of broadleaf weeds and grasses. Alachlor is registered under FIFRA for use on corn, soybeans, sorghum, peanuts, and beans and 37 FFDCA tolerances are currently associated with those uses. (40 CFR 180.249).

In December 1998, EPA released a RED for alachlor finding it eligible for reregistration. (Ref. 6). The RED also reassessed alachlor's tolerances concluding that 22 met the requirements of section 408 but that 16 would have to be revised or revoked. (Id. at 184–187; Ref. 7). (The current number of tolerances for alachlor and the other five pesticides may not match the number of reassessed tolerances due to subsequent actions to establish or revoke tolerances as well as to a generic administrative action amending tolerance nomenclature. (68 FR 39428, July 1, 2003)). The RED found that alachlor posed chronic and cancer risks as a result of dietary exposure but not any acute risk. The RfD, or safe dose, for chronic exposure was based on a chronic dog study in which hemosiderosis and hemolytic anemia were observed. (Ref. 6 at 39). Cancer studies revealed that alachlor caused nasal, gastric, and thyroid tumors in the rat. A chronic dietary risk assessment found that exposure to alachlor from food and drinking water posed minimal risks. The subgroup facing the highest risk from food is non-nursing infants < 1 year at 0.5 percent of the RfD. (Id. at 85). For drinking water, the highest risk is posed to children 1–6 years at 2 percent of the RfD. (Id. at 87). The highest aggregate risk was 4 percent of the RfD for children 1–6 years. (Id. at 91). Cancer risks were found to be negligible. (Id. at 91–94). These risk assessments were based on moderately conservative exposure assumptions that relied on crop field trial data and information of the percentage of the crop treated with alachlor for some crops. (Id. at 83–84).

EPA removed the 10X children's safety factor based on its determination that (1) The toxicology database was complete; (2) the toxicology data showed no evidence of neurotoxicity and thus there was no need for a developmental neurotoxicity study for alachlor; (3) the toxicology data showed no evidence of increased susceptibility in the young; and (4) the exposure estimate was unlikely to understate exposure to infants and children. (Id. at 50). In the RED, EPA noted that alachlor is structurally similar to other chloroacetanilide pesticides (acetochlor, butachlor, propachlor, and metolachlor) and may share a common mechanism of toxicity with some or all of these pesticides. (Id. at 112). EPA indicated that no determination on this issue had been made at that time. (Id.). Subsequently, EPA did conclude that alachlor, acetochlor and butachlor share a common mechanism of toxicity with respect to the causation of nasal turbinate tumors. (Ref. 8). EPA has also now completed a cumulative cancer risk assessment for these pesticides that shows no risk of concern. (Ref. 9). Finally, the RED indicated that alachlor does have effects on the endocrine system in that it disrupts the hormone balance leading to the formation of thyroid tumors. (Ref. 6 at 31). Subsequently, EPA determined that these endocrine effects only occurred at high doses which were well above any exposure levels humans would face from pesticidal uses of alachlor. (Ref. 8).

B. Chlorothalonil

Chlorothalonil is a broad spectrum, non-systemic protectant pesticide mainly used as a fungicide to control fungal foliar diseases of vegetable, field, and ornamental crops. In connection with these uses there are 66 FFDCA tolerances currently established for chlorothalonil. (40 CFR 180.275).

In April 1999, EPA released a RED for chlorothalonil finding it eligible for reregistration so long as various uses were prohibited and numerous risk mitigation steps were taken. (Ref. 10 at v–vi). The RED also reassessed chlorothalonil's tolerances concluding that all met the requirements of section 408 except one that would have to be raised. Further, an additional tolerance was found to be necessary in connection with one use site. (Id. at 171–174; Ref. 7 at 58–59). The RED found that chlorothalonil posed acute, chronic and cancer risks as a result of dietary exposure. The RfD, or safe dose, for chronic exposure was based on a chronic rat study in which increased kidney weights and hyperplasia were observed. (Ref. 10 at 21). EPA evaluated acute risk based on the LOAEL from a subchronic rat study showing lesions and hyperplasia. (66 FR 56233, 56235, Nov. 7, 2001). Because no NOAEL was identified in this study EPA added an extra 3X safety factor. (Ref. 10 at 23). Cancer studies revealed that chlorothalonil caused renal adenomas and carcinomas in the rat and mouse. An aggregate chronic dietary risk assessment found that exposure to chlorothalonil from food and drinking water would utilize 68 percent of the RfD for children 1–6, the most highly-exposed subgroup. (Id. at 100). EPA concluded that there was a MOE of 310 for adults (the highest exposed subgroup) with regard to aggregate acute risk. (Id.). The target or safe MOE was 300. Cancer risks were found to be negligible. (Id. at 161–162). The acute and cancer risk assessments were based on relatively refined exposure assumptions including percent crop treated data on most crops and anticipated residue data based on field trial data or food monitoring data. The chronic risk assessment was more conservative in that it only relied upon percent crop treated information. (Id. at 36–41).

Other than retaining an additional 3X safety factor as to acute risks, EPA removed the 10X children's safety factor for chlorothalonil based on its determination that (1) the toxicology database was complete; (2) the toxicology data showed no evidence of increased susceptibility in the young; and (3) the exposure estimate was unlikely to understate exposure to infants and children. (Id. at 170; 66 FR at 56242). In the RED, EPA noted that chlorothalonil is a member of the polychlorinated fungicide class of pesticides which includes hexachlorobenzene, pentachlorophenol, and pentachloronitrobenzene. (Ref. 10 at

100). EPA indicated that no determination on the issue of common mechanism of toxicity had been made at that time. (Id.).

C. Methomyl

Methomyl is an insecticide registered on a wide variety of sites including field, vegetable, and orchard crops; turf (sod farms only); livestock quarters; commercial premises; and refuse containers. There are 78 FFDCA tolerances currently associated with these uses. (40 CFR 180.253).

In December 1998, EPA released a RED for methomyl finding it eligible for reregistration. (Ref. 11). The RED also reassessed methomyl's tolerances concluding that 65 met the requirements of section 408 but that 15 would have to be revised or revoked. (Id. at 103–111; Ref. 7 at 175–176). The RED found that methomyl posed chronic and acute risks as a result of dietary exposure. The RfD, or safe dose, for chronic exposure was based on a chronic dog study in which histopathological effects in the kidney were observed. (Ref. 11 at 24). EPA evaluated acute risk based on a rabbit developmental study that showed deaths in the dams on days 1–3 after dosing. (Id. at 25). Aggregate risks from methomyl were assessed taking into account that another pesticide, thiodicarb, degrades into methomyl and thus serves as another source of exposure to the compound. A chronic dietary risk assessment found that exposure to methomyl from food utilized no greater than 7 percent of the RfD for any subgroup. (Id. at 35). EPA concluded that there was a MOE of 417 for children 1–6 years (the highest exposed subgroup) with regard to acute risk from residues in food. (Id. at 37). Exposure to methomyl in drinking water was not expected to make either of these risk estimates exceed the level of concern. (Id. at 38). These risk assessments were based on moderately conservative exposure assumptions that relied on crop field trial data and information of the percentage of the crop treated with methomyl. (Id. at 35–36).

EPA reduced the 10X children's safety factor to 3X for methomyl. Although the data provided no indication of increased sensitivity of rats or rabbits to *in utero* or postnatal exposure to methomyl, there were data gaps for acute and subchronic neurotoxicity studies. (Id. at 24). In the RED, EPA indicated that no determination as to whether methomyl shared a common mechanism of toxicity with other substances had been made at that time. (Id. at 55–56). Subsequently, EPA did conclude that methomyl shares a common mechanism of toxicity with other *N*-methyl carbamate pesticides. (Ref. 8). EPA is re-examining the safety finding it made for methomyl in light of this conclusion. EPA has completed a preliminary cumulative risk assessment for the *N*-methyl carbamates. EPA expects to finish this cumulative risk assessment and make a safety determination as to all of the *N*-methyl carbamates in the near future.

D. Metribuzin

Metribuzin is a herbicide used on a wide range of sites, including vegetable and field crops, turf grasses (recreational areas), and non-crop areas, to selectively control certain broadleaf weeds and grassy weed species. In connection with these uses there are 61 FFDCA tolerances currently established for metribuzin (40 CFR 180.332).

In February 1999, EPA released a RED for metribuzin finding it eligible for reregistration based on various risk mitigation steps proposed by the registrant. (Ref. 12 at iv). The RED also reassessed metribuzin's tolerances concluding that 22 met the requirements of section 408 but that 38 would have to be revised or revoked. (Id. at 101–107; Ref. 7 at 187–188). The RED found that metribuzin posed acute and chronic risks as a result of dietary exposure. The RfD, or safe dose, for chronic exposure was based on a chronic rat study which showed increased thyroid weight, decreased lung weight, and increases of certain enzyme levels in blood. (Ref. 12 at 16). EPA evaluated acute risk based on the NOAEL from a developmental rabbit study showing decreased fetal body weight, increased number of runts, and increased incidence of extra and partial ribs. (Id. at 17). An aggregate chronic dietary risk assessment found that exposure to metribuzin from food and drinking water would utilize 79 percent of the RfD for children 1–6, the most highly-exposed subgroup. (Id. at 54). EPA concluded that there was a MOE of 1,200 for females 13–50 years (the highest exposed subgroup) with regard to aggregate acute risk. (Id. at 52). These risk assessments were based on the extremely conservative exposure assumptions that all commodities covered by the tolerances were treated with metribuzin and the residue levels were at the tolerance level. (Id. at 39–40).

EPA removed the 10X children's safety factor for metribuzin based on its determination that the toxicology database was complete and it showed no evidence of increased susceptibility in the young. (Id. at 51). In the RED, EPA indicated that no determination as to whether metribuzin shared a common mechanism of toxicity with other substances had been made at that time. (Id. at 55–56).

E. Thiodicarb

Thiodicarb is an insecticide used primarily on cotton, sweet corn, and soybeans. It is also registered for use on leafy vegetables, cole crops, ornamentals, and other minor use sites. In connection with these uses there are nine FFDCA tolerances currently established for thiodicarb. (40 CFR 180.407).

In December 1998, EPA released a RED for thiodicarb finding it eligible for reregistration. (Ref. 13). The RED also reassessed thiodicarb's tolerances concluding that 6 met the requirements of section 408 but that 34 would have to be revised or revoked. (Id. at at 89–91). The RED found that thiodicarb posed chronic, acute, and cancer risks as a result of dietary exposure. The RfD, or safe dose, for chronic exposure was based on a chronic rat study in which increased incidence of extramedullary hemopoiesis and decreased RBC cholinesterase were observed. (Ref. 13 at 20). EPA evaluated acute risk based on a rabbit developmental study that showed decreased body weight and increased developmental variations in the fetuses and a rat developmental study that found decreased body-weight gain in the dams. (Id. at 16, 21). Cancer studies showed that thiodicarb caused liver tumors in mice and testicular tumors in rats. Aggregate risks from thiodicarb were assessed taking into account that thiodicarb degrades into methomyl, another pesticide, and thus both pesticides serve as a source of exposure to the compound. A chronic dietary risk assessment found that exposure to thiodicarb from food utilized 104 percent of the RfD for the most highly-exposed subgroup, children 1–6 years. Although the exposure for this subgroup slightly exceeded the RfD, EPA concluded that this exposure estimate was significantly overstated because it assumed all treated crops had residues at the tolerance level. (Id. at 29). Cancer risks were found to be negligible. (Id. at 30). EPA concluded that there was a MOE of 1,680 for infants (the most highly-exposed subgroup) with regard to acute risk from residues in food. (Id. at 31). Exposure to thiodicarb in drinking water was not expected to make any of these risk estimates exceed the level of concern. (Id. at 33). The chronic risk assessment was based on very conservative exposure assumptions that relied on information of the percentage of the crop treated with thiodicarb and assumed residues were present at the tolerance level. (Id. at 29). The cancer

risk assessment and acute risk assessments used the less conservative approach of relying on percent crop treated data and anticipated residue data. (Id. at 30). Risk assessments for combined exposure to methomyl as a result of the use of thiodicarb and methomyl were identical to the risk assessments in the methomyl RED.

EPA reduced the 10X children's safety factor to 3X for thiodicarb. Although the data provided no indication of increased sensitivity of rats or rabbits to *in utero* or postnatal exposure to thiodicarb, there were data gaps for acute and subchronic neurotoxicity studies as to methomyl, a thiodicarb degradate. (Id. at 19). In the RED, EPA indicated that no determination as to whether thiodicarb shared a common mechanism of toxicity with other substances had been made at that time. (Id. at 55–56). Subsequently, EPA did conclude that thiodicarb shares a common mechanism of toxicity with other *N*-methyl carbamate pesticides. (Ref. 8). EPA is re-examining the safety finding it made for thiodicarb in light of this conclusion. EPA has completed a preliminary cumulative risk assessment for the *N*-methyl carbamates. EPA expects to finish this cumulative risk assessment and make a safety determination as to all of the *N*-methyl carbamates in the near future.

V. The Petition to Modify or Revoke

The States' petition requests that EPA modify or revoke all of the tolerances for alachlor, chlorothalonil, methomyl, metribuzin, and thiodicarb. (Ref. 1 at 1). These tolerances must be modified or revoked, the States assert, because they do not meet the safety standard in section 408 of the FFDCA. (Ref. 1 at 2). The States argue that the tolerances are unsafe because EPA's latest safety conclusion for these tolerances did not include the full 10X children's safety factor and, if that full 10X safety factor is included, EPA cannot make the required reasonable certainty of no harm determination.

The States claim that ''as a matter of law'' the full 10X children's safety factor must be retained for each of these pesticides because of missing data concerning developmental neurotoxicity, endocrine effects, and/or cumulative effects of pesticides having a common mechanism of toxicity. It is ''legally impermissible,'' the States assert, if any of these data are absent for EPA to conclude that there are ''reliable data'' to choose an additional safety factor other than 10X. (Ref. 1 at 2, 5, 9, 11). As statutory support for this allegation, the States cite several provisions in section 408. First, as to developmental neurotoxicity, the States point to section 408(b)(2)(C)'s requirement that EPA assess the risk to children based on ''available information concerning the special susceptibility of infants and children to the pesticide chemical residues, including neurological differences between infants and children and adults . . . .'' The States note that EPA has announced that it plans to require developmental neurotoxicity (''DNT'') studies on all pesticides that are neurotoxic. (Ref. 1 at 10 citing 64 FR 42945, August 6, 1999). Second, as to endocrine effects, the States cite both the provision in section 408(b)(2)(D)(vii) requiring consideration of ''such information as the Administrator may require on whether the pesticide chemical may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen or other endocrine effects'' and the requirement in section 408(p) for EPA to develop and implement an endocrine screening program. Finally, with regard to cumulative effects, the States reference the provision in section 408(b)(2)(D)(v) requiring consideration of ''available data on the cumulative effects of such residues and other substances that have a common mechanism of toxicity,'' and the requirement in section 408(b)(2)(C) mandating that EPA assess the risk to children based on similar considerations.

As to the individual pesticides, the States' allegations differ to some extent regarding developmental neurotoxicity data and cumulative effects data. The States claim that alachlor, methomyl, and thiodicarb are ''neurotoxin[s]'' and therefore, under EPA's own criterion, require a DNT study. (Ref. 1 at 14, 17, 19). No such claim is made as to chlorothalonil or metribuzin. As to cumulative effects, the States assert that for alachlor, methomyl, and thiodicarb, EPA has concluded that they share a common mechanism of toxicity with other substances, yet EPA has not assessed the risk posed by these pesticides' tolerances taking into account the cumulative effects from their respective common mechanism groups. (Ref. 1 at 13, 16–17, 19). For chlorothalonil, the States note that EPA has indicated that it may share a common mechanism with other pesticides in the same chemical class and argue that EPA has not determined whether in fact there is such a common mechanism. (Ref. 1 at 15). For metribuzin, the States allege that EPA has not evaluated whether it shares a common mechanism with other substances. (Ref. 1 at 18). As to endocrine effects, the States' claim is the same as to all five pesticides - endocrine effects data have not been submitted under the endocrine screening program for any of the pesticides.

Finally, the States present the following risk assessment figures for the five pesticides which the States claim would, if the full 10X safety factor was incorporated, exceed section 408's safety standard:

- Alachlor - exposure from residues in food equals 33 percent of the RfD for non-nursing infants, 17 percent for children 1–6, and 12 percent for children 7–12, (Ref. 1 at 14).
- Chlorothalonil - exposure from residues in food equals 60 percent of the RfD for non-nursing infants and children 1–6, and 32 percent of the RfD for the U.S. population, (Ref. 1 at 15–16).
- Methomyl - exposure from residues in food equals 67 percent of the RfD for non-nursing infants, 62 percent for children 1–6, and 34.6 percent for the U.S. population, (Ref. 1 at 17).
- Metribuzin - exposure from food equals 62 percent of the RfD for non-nursing infants, 75 percent for children 1–6 and 36 percent for the U.S. population, (Ref. 1 at 18–19).
- Thiodicarb - exposure from food equals 43 percent of the RfD for non-nursing infants, 104 percent of the RfD for children 1–6, and 68 percent for the U.S. population, (Ref. 1 at 20).

VI. Public Comment

A. In General

On March 9, 2005, EPA published a notice in the **Federal Register** announcing receipt of the States' petition to modify or revoke tolerances and requesting comments on the petition. (70 FR 11646, March 9, 2005). The notice included a short summary of the petition and referenced readers to EPA's electronic docket for a full copy of the petition. A period of 60 days was initially allowed for comment. EPA received two requests to extend the comment period. Because EPA could not publish notice of an extension prior to expiration of the 60 days, EPA reopened the comment period for 30 days on May 16, 2005. The comment period closed on June 15, 2005. (See 70 FR 25826, May 16, 2005). EPA received 13 comments on the petition. These comments are summarized below. EPA has not repeated comments in instances where they were made by more than one commenter.

B. Individual Comments

1. *CropLife America*. CropLife America (''CLA'') is a trade association

representing members of the pesticide industry. CLA provided extensive comments on the petition. (Ref. 14). CLA notes that, although the petition only concerned five pesticides, if the arguments in the petition are accepted it would have a ''far broader impact'' because the result would be that EPA would ''almost always [have] to apply the tenfold safety factor'' in pesticide tolerance decisions. (Id. at 3). CLA contends that routinely applying the 10X safety factor across the board would cause ''serious market disruption'' and not allow EPA to distinguish between ''conventional'' and reduced-risk pesticides.

According to CLA, the petitioners' assertion that the FQPA mandates an ''automatic'' retention of the 10X children's safety factor whenever there is a ''data gap'' is not supported by the statute or legislative history. (Id. at 5, 11). CLA points out that the statute does not use the term ''data gap'' but instead requires an additional safety factor to ''take into account the completeness of the data . . . .'' (Id. at 13). Moreover, CLA argues the statute gives EPA ''broad discretion'' to choose a different factor. Additionally, CLA claims that the statute bars application of the 10X factor to a pesticide due to the absence of data unless the registrant has first been given an opportunity to conduct and submit the study. (Id. at 17). Nonetheless, CLA admits that the additional 10X factor ''should be imposed . . . if the already available data give substantive reason for concern . . . .'' (Id. at 19).

As to data on endocrine effects, CLA notes that section 408(b)(2)(C) - the provision addressing the protection of infants and children - does not even address this issue. (Id. at 11). Further, even the general provisions of section 408 only require EPA to consider ''such information as the Administrator may require'' on endocrine effects. CLA concludes that ''[s]ince no data requirements pertaining to endocrine effects have been imposed, a data base cannot be said to be 'incomplete' because such endocrine data have not been generated.'' (Id. at 12). On cumulative effects, CLA asserts that the statute provides no data requirements; rather, EPA is directed to review ''available data'' on the issue. Thus, CLA argues that the database cannot be incomplete as to cumulative effects. (Id.)

The legislative history, CLA claims, supports its reading of the statute as granting EPA broad discretion in determining whether to apply the children's safety factor. CLA references portions of the National Research Council's report titled ''Pesticides in the Diets of Infants and Children'' and the legislative debate and reports which refer to the need for EPA ''consider'' an additional factor, and EPA's ''discretion'' and ''flexibility'' in choosing the appropriate factor to protect children. (Id. at 5–8).

CLA notes several examples of situations relevant to the current petition which demonstrate the wisdom of giving EPA discretion in applying the children's safety factor. CLA asserts that where there is no evidence that a pesticide causes neurotoxicity or developmental effects, the absence of a DNT study is unlikely to raise any concern regarding such effects. Additionally, where a cumulative assessment has not been performed, CLA argues there could be a number of circumstances where an additional 10X factor would be unnecessary because various exposure considerations would make any meaningful cumulation of effects unlikely. (Id. at 13–14).

Finally, CLA asserts that the databases for the five pesticides challenged in the petition are ''data-rich'' and support EPA's decision on the children's safety factor for these pesticides. Specifically as to alachlor, CLA challenges the States' claim that alachlor is a neurotoxin arguing this assertion is ''utterly baseless.'' (Id. at 22).

2. *Pesticide Policy Coalition*. The Pesticide Policy Coalition (''PPC'') is a group sponsored by organizations representing pesticide manufacturers, pesticide applicators, commodity groups, and food processors. (Ref. 15). The PPC's comments contain many of the same arguments presented by the CLA. Additional information is included, however, regarding the endocrine screening program and DNT studies.

The PPC asserts that the States are wrong in their claim that tolerance reassessments ''must include an assessment of [a pesticide's] endocrine effects in accordance with the prescribed endocrine effects (EE) screening program called for by FFDCA 408(p).'' (Id. at 8). This claim is inconsistent with sections 408(p) and 408(q), according to the PPC, because section 408(p) specifies ''an August 1999 date for starting the EE testing and [subsection 408(r) requires] . . . that a third of all tolerance reassessments be completed on the exact same date - three years after the date of enactment of the FQPA.'' (Id. at 8–9) (emphasis in original). The PPC notes that the tolerance reassessments which appear to have been the genesis of the States' petition ''were issued prior to that EE implementation date.'' (Id. at 9). Additionally, the PPC asserts that, even in the absence of endocrine screening tests, EPA has information bearing on endocrine effects from its existing toxicity database. (Id. at 8).

On DNT studies, the PPC argues that the States incorrectly assert that a DNT study is needed for all neurotoxic pesticides. EPA, according to the PPC, has now determined that in some circumstances other tests more appropriately address issues regarding developmental neuorotoxicity. (Id. at 10–11). Further, the PPC claims that DNT studies ''almost never affect the regulatory 'bottom line,''' and this information should be taken into account in determining the need for the children's safety factor. (Id. at 11).

3. *Monsanto Company*. Monsanto Company is the basic manufacturer and primary registrant for alachlor and its comments focused on that pesticide. (Ref. 16). Monsanto argues that EPA was justified in removing the children's safety factor for alachlor at the time of the alachlor RED given that the database was complete and there was no evidence of increased susceptibility in the young. (Id. at 3). Monsanto contends there is no data gap for a DNT study because EPA has not requested such a study for alachlor. No basis for requesting such a study is present, according to Monsanto, because it ''is unaware of any data indicating the alachlor is neurotoxic, even at lethal dose levels.'' (Id. at 4). Monsanto also disputes the States' assertion that alachlor is an endocrine disruptor. Although noting that alachlor has been found to cause thyroid tumors, Monsanto notes that ''significant increases in thyroid tumors occurred only at an excessive dose level that exceeded the Maximum Tolerance Dose, and occurred via a well-known mode of action that is generally not considered to be of concern at anticipated human exposure levels.'' (Id.). Monsanto submitted a report that discussed in more detail alachlor's potential for endocrine disruption. (Ref. 17). As to cumulative effects, Monsanto states that now that a decision on common mechanism concerning the chloroacetanilides has been made, it has conducted a cumulative assessment and the results show there is no cause for concern. (Ref. 18 at 4). Finally, Monsanto argues that the States misstated the risks presented by alachlor. The figures cited by the States, Monsanto notes, were from a worst-case assessment by EPA. A more refined assessment by EPA produced significantly lower risk numbers, according to Monsanto. In fact, Monsanto contends given these refined risk numbers the alachlor tolerances would still meet the safety standard

even if the children's safety factor is retained. (Id. at 5).

4. *GB Biosciences Corporation*. GB Biosciences is the basic manufacturer and primary registrant of chlorothalonil. It filed initial comments during the public comment period and submitted more detailed comments at a later date. (Ref. 18 and 19). GB Biosciences contends that a complete database on chlorothalonil was available to EPA at the time of the chlorothalonil RED and a 2001 chlorothalonil tolerance action. GB Biosciences states that this database indicates that further study of chlorothalonil through a DNT study is ''not justified.'' (Ref. 18 at 3). According to GB Biosciences, ''chlorothalonil has been shown in the numerous studies submitted by several registrants, including a subchronic neurotoxicity study, not to have any neurotoxic potential, even at doses that are clearly lethal in either short or long-term administration.'' (Ref. 19 at 5).

Further, GB Biosciences asserts that ''[t]he extensive database of mammalian and ecological toxicity studies that exists for chlorothalonil provides no evidence of potential to cause endocrine disruption.'' (Ref. 18 at 4). GB Biosciences notes that the type of studies needed for higher level (Tier II) endocrine screening are available for chlorothalonil. These studies include ''teratology studies performed in both rats and rabbits, and two well-conducted 2-generation reproduction studies with endocrine endpoints evaluated.'' (Ref. 19 at 6). According to GB Biosciences, ''[if] this chemical were an endocrine disruptor, it would have been obvious from the results of these studies, as well as evident in the numerous subchronic and chronic/carcinogenicity studies performed.'' (Id.). In these studies, ''any changes or perturbations in the hormone balance or maintenance of homeostasis would have been recognized, with endpoints such as tumors of the mammary gland, testicular or ovarian tumors or hyperplasia, decreased fertility or other reproductive indices in 2-generation reproduction studies at doses that are not toxic to the dams.'' (Id.). GB Biosciences asserts that the rat forestomach and kidney tumors seen in the chlorothalonil animal data ''are not indicative of any toxicity related to endocrine disruption.'' (Id.).

Finally, GB Biosciences argues that an examination of chlorothalonil and other similar pesticides in its class (polychlorinated pesticides) reveals that chlorothalonil does not share a common mechanism with these pesticides. GB Biosciences claims that of the polychlorinated pesticides only chlorothalonil and HCB result in kidney tumors. A close examination of these kidney tumors, according to GB Biosciences, shows that chlorothalonil and HCB work through different mechanisms. GB Biosciences argues that any potential common mechanism between chlorothalonil and HCB is irrelevant in any event since HCB has not been used as a pesticide for many years and only exists as a minor contaminant now in certain products. (Ref. 18 at 5).

5. *Bayer CropScience*. Bayer CropScience is the registrant for metribuzin and thiodicarb and its comments address both of these pesticides. (Ref. 20).

a. *Metribuzin*. Bayer contends that EPA's decision in the metribuzin RED that metribuzin did not cause cumulative effects with other substances was supported by reliable data because metribuzin is the only asymmetrical triazinone pesticide registered in the United States. (Id. at 5). Further, Bayer argues that ''the metribuzin database provides very robust data on potential endocrine effects from numerous studies'' addressing many parameters relevant to endocrine effects. (Id.). Finally, Bayer notes that EPA's risk assessment for metribuzin in the metribuzin RED was a worst-case assessment and asserts that a more refined assessment ''would result in an exposure well below EPA's level of concern even if an additional tenfold factor were applied.'' (Id.).

b. *Thiodicarb*. Bayer notes that a 3X FQPA safety factor was retained for thiodicarb in the thiodicarb RED due to outstanding studies on acute and sub-chronic neurotoxicity. (Id. at 6). These studies were submitted to EPA in 2000, according to Bayer, and ''show no unexpected or unreasonable neurotoxic effects.'' Thus, it is Bayer's view ''that the EPA extra 3X FQPA safety factor can now be removed from the risk assessment.'' (Id. at 7). Further, Bayer contends that based on the thiodicarb database ''there is no evidence that thiodicarb causes endocrine disruption.'' (Id. at 8). Bayer asserts that EPA is currently conducting a cumulative risk assessment for thiodicarb and other *N*-methyl carbamate pesticides but that this assessment ''has no bearing on the current petition.'' (Id. at 9). Finally, Bayer claims that, if a more refined risk assessment was performed for thiodicarb, it would demonstrate risks to be so low (in the range of 0.1 percent of the RfD) that applying an additional 10X factor would not matter in the safety determination. Bayer also claims that the States misunderstand the function of how risk assessment and the FQPA safety factor are used in evaluating the residue levels chosen as tolerance values. For example, Bayer states that the States are incorrect when they assert that the unacceptably high risks of these pesticides would require ''a reduction in the residue tolerance'' and that the tolerances ''must be recalculated applying the full tenfold safety factor.'' (Id. at 10). Risk determinations or safety factors are not used directly in selecting the values used in tolerances.

6. *DuPont Crop Protection*. Dupont Crop Protection is the basic manufacturer and primary registrant of methomyl. (Ref. 21). DuPont asserts that it has addressed the data gap for methomyl on neurotoxicity by submitting acute and subchronic neurotoxicity studies. (Id. at 2). Additionally, DuPont claims that the extensive database for methomyl contains ''no scientific evidence to suggest that methomyl induces a direct and adverse effect on endocrine function.'' (Id. at 3). In particular, DuPont argues that a review of the relevant studies shows that ''[i]n none of these studies was there a treatment-related effect on either organ weights or histopathology in tissues that would be indicative of endocrine system dysfunction.'' (Id.).

7. *NRDC*. NRDC submitted comments on behalf of various environmental organizations and individuals. (Ref. 22). Relative to the States' petition, NRDC asserted that the DNT study is more sensitive than other required studies and thus ''DNT testing is essential for assessing pesticide effects, not only as a measure of toxicity to the developing brain and nervous system, but also as a measure of developmental and reproductive effects generally.'' (Id. at 2). NRDC submitted various other comments concerning the children's safety factor that involved issues not raised in the States' petition (e.g., exposure of farm children to pesticides).

8. *Other comments*. The other comments received either repeated the arguments made by one of the commenters above, touted the benefits of one or more of the pesticides, or stated agreement with the petition without providing any supporting basis.

VII. Ruling on Petition

A. Introduction

This Order denies the States' petition to modify or revoke the tolerances as to the pesticides alachlor, chlorothalonil, and metribuzin. For the alachlor and metribuzin tolerances this denial is based on EPA's finding that, even if the additional 10X children's safety factor

was retained as to these tolerances, they would still meet the section 408(b) safety standard. The request for revocation or modification of the chlorothalonil tolerances is denied because EPA determined that, as to that pesticide, the grounds asserted for retaining the children's safety factor (lack of data on developmental neurotoxicity, endocrine effects, and cumulative effects) are without basis. This Order does not address methomyl and thiodicarb because EPA is currently re-evaluating the risk of these pesticides as part of the overall reassessment of the tolerances for carbamates.

This Unit of the Order is organized as follows: Unit VII.B. discusses EPA's reasons for not ruling on the petition's requests as to methomyl and thiodicarb; Unit VII.C. explains EPA's basis for denying the petition as to alachlor and metribuzin; and Unit VII.D. addresses EPA's conclusions regarding the alleged absence of data on developmental neurotoxicity, endocrine effects, and cumulative effects for chlorothalonil.

Before proceeding to the merits of the petition, several preliminary matters need to be addressed. First, the States initially raised their concerns regarding these pesticides in a 2003 lawsuit challenging the reassessment decisions for the pesticides. That lawsuit was dismissed because the States had not first presented their contentions to EPA in the form of a petition to revoke tolerances. (*New York v. EPA*, 350 F. Supp. 429 (S.D.N.Y. 2004)). The States have now presented such a petition to EPA but they continue to protest that EPA's regulation governing petitions to revoke is ''designed to be used by manufacturers seeking changes to tolerances on technical grounds'' and that they, as non-manufacturers ''cannot realistically make the factual assertions'' required under EPA's regulation. (Ref. 1 at 3, 5). EPA would clarify that the regulation in question, 40 CFR 180.32, does mandate that certain technical factors mostly relevant to pesticide manufacturers are ''reasonable grounds'' to seek modification or revocation of tolerances but the regulation does not, in any way, imply that these technical factors are the only reasonable grounds for seeking modification or revocation of a tolerance. Certainly, a petition, such as this one, asserting that a tolerance does not meet the safety standard would be an appropriate petition under section 408(d) and 40 CFR 180.32.

Second, the States' lawsuit was styled solely as a challenge to the tolerance reassessment decisions. The petition focuses heavily on the reassessment decision in arguing for modification or revocation but also cites matters arising after the reassessment decisions. EPA believes that this is appropriate. A section 408(d) petition to revoke or modify is the proper way to challenge a tolerance reassessment decision, and if such a petition follows immediately on the heels of a tolerance reassessment decision, the reassessment decision will likely be the sole focus in EPA's review of the petition. When several years have passed between the release of the tolerance reassessment decision and the filing of a petition to revoke or modify, however, the reassessment decision may be superseded in whole or in part by new information. In such circumstances, EPA believes it is appropriate to evaluate the petition in light of EPA's current knowledge regarding the risks of a pesticide.

Finally, it should be noted that EPA is treating this petition as a petition to revoke tolerances not to modify tolerances. The States argue that the children's safety factor should be retained for the objected-to tolerances and that, if the factor is retained, the safety finding cannot be made. Such a claim, if it could be substantiated, would be grounds for revocation of the tolerances. At times, the petition mentions reducing tolerance levels or recalculating tolerance levels to take into account the children's safety factor. As explained in Unit III.B.2., however, EPA determines appropriate tolerance levels (as opposed to the safety of tolerances) based on data bearing on the maximum pesticide residues that will appear on crops following use according to the FIFRA label. The petition presents no such data supporting a different tolerance level and therefore is treated solely as a petition to revoke.

B. Methomyl and Thiodicarb

Methomyl and thiodicarb are both *N*-methyl carbamates. This group of pesticides has been found to share a common mechanism of toxicity and EPA is now working on completing an assessment of the cumulative effects from the *N*-methyl carbamates, including methomyl and thiodicarb. A preliminary cumulative risk assessment has been prepared and released for public comment. The final cumulative risk assessment is expected in the near future.

EPA did complete reregistration and tolerance reassessment for methomyl and thiodicarb in 1998, shortly after the passage of FQPA. Subsequent to release of the REDs for these pesticides, EPA made the common mechanism determination for the *N*-methyl carbamates. Because methomyl and thiodicarb are *N*-methyl carbamates and are thus part of the cumulative risk assessment, EPA is revisiting the safety of the tolerances for these pesticides as part of the overall tolerance reassessment decision on *N*-methyl carbamates. Once EPA completes the *N*-methyl carbamate cumulative risk assessment, it will make a determination on whether all *N*-methyl carbamate pesticide tolerances meet the FFDCA section 408 standard. This determination will necessarily include the methomyl and thiodicarb tolerances. It would be disruptive of the overall *N*-methyl carbamate reassessment effort to separately respond to the States' petition regarding two of the *N*-methyl carbamates. Such a disruption would make it more difficult for EPA to comply with its statutory deadline for completing the tolerance reassessment process. Accordingly, EPA will not address the States' petition to revoke the methomyl and thiodicarb tolerances until the cumulative risk assessment for the *N*-methyl carbamates is completed and overall tolerance reassessment determinations are made.

C. Alachlor and Metribuzin

The States' petition is based on the premise that, EPA should retain the additional 10X safety factor for the five pesticides in question, the additional factor renders the tolerances for these pesticides unsafe. For two of the pesticides - alachlor and metribuzin - however, the States' logic collapses at its inception because retention of the 10X factor would not affect EPA's safety finding with regard to these pesticides and the States' petition as to those two pesticides is denied for that reason.

As to alachlor, the States maintain that EPA has assessed the risk in the alachlor RED as equaling 33 percent of the RfD for non-nursing infants, 17 percent for children 1–6, and 12 percent for children 7–12. The States correctly note that if an additional 10X safety factor was used in such assessments, the assessments would then indicate that exposure exceeded the RfD. Retaining an additional 10X factor would reduce the RfD by a factor of 10 and, correspondingly, estimated exposure as a percentage of the RfD would increase tenfold.

The States failed to take into account, however, that the RED also contained a revised risk assessment for alachlor that showed the highest aggregate risk estimate to be that exposure of children aged 1–6 is 4 percent of the RfD. (Ref. 6 at 91). Even incorporating an additional 10X safety factor into such a risk estimate would increase the risk estimate to no greater than 40 percent of the RfD, or still well within the safe level. Since completion of the RED, EPA

has conducted an assessment of the cumulative affects of alachlor and the other pesticides with which it shares a common mechanism of action. That assessment showed the cumulative risk to have a MOE of 7,700 for the most-exposed subgroup. (Ref. 9). Even applying an additional 10X factor in evaluating this risk would not raise concerns because the level of concern would be for a MOE falling below 1,000.

As to metribuzin, the States cite EPA's conclusion in the metribuzin RED that it poses a risk equaling 62 percent of the RfD for non-nursing infants, 75 percent for children 1–6 and 36 percent for the U.S. population. Again, the States correctly note that if an additional 10X safety factor was used in such assessments, the assessments would show that exposure exceeded the RfD. This risk assessment, however, was based on the worst case exposure assumptions that all crops on which metribuzin is registered are treated and that all commodities from those crops have metribuzin residues at the tolerance level. EPA is aware that such assumptions grossly overstate risk but EPA does not spend resources to conduct more realistic assessments if a risk assessment using these conservative assumptions shows no concerns. Because the States are now claiming that the additional 10X safety factor should be retained, EPA has conducted a revised risk assessment for metribuzin assuming that an additional 10X safety factor is needed.

This revised risk assessment uses relatively minor refinements to the worst case exposure assumptions used in the RED. (Ref. 23). For the acute risk assessment, EPA used tolerance level residues for most commodities, monitoring data for some commodities, and an anticipated residue value for milk. In addition to these refinements, the chronic risk assessment relied upon percent crop treated data for most commodities. Overall, the refinements were fairly conservative, and thus the assessment still overstates exposure. For example, monitoring data were used to estimate residue values in potatoes and potato products. U.S. Department of Agriculture monitoring data revealed 1,472 samplings of potatoes for metribuzin. Of those 1,472 samples, only one showed a detectable residue of metribuzin. Nonetheless, in its risk assessment, EPA assumed that all potatoes contained metribuzin at the level found in that one sample (0.05 parts per million). EPA also used monitoring data for beef and poultry products. Monitoring of these commodities revealed no detection of metribuzin in 3,299 samples. Yet, EPA assumed that all of these commodities had metribuzin present at the level of detection of the analytical method. The revised risk assessment - which contained an additional 10X safety factor - found the highest acute and chronic risks for any population subgroup to be 75 percent and 69 percent, respectively, of the RfD. Thus, even if an additional 10X safety factor is required for metribuzin, metribuzin still meets the safety standard in section 408.

Because the States are incorrect in their assertion that retaining the additional 10X factor for alachlor and metribuzin would demonstrate that their tolerances are unsafe, the States' petition is denied as to alachlor and metribuzin. It appears at this time that retention of the additional 10X factor may make a significant difference in the characterization of the safety of the chlorothalonil tolerances. For that reason, EPA addresses below the grounds asserted in the petition for retaining the additional 10X factor for the chlorothalonil tolerances.

D. Chlorothalonil

The States' petition seeks the revocation of tolerances for the named pesticides for EPA's alleged unlawful removal of the children's safety factor for these pesticides despite an alleged absence of DNT studies and data bearing on endocrine effects and cumulative effects from substances sharing a common mechanism of toxicity. Below each of these claims are examined in detail with regard to chlorothalonil. First, however, EPA explains its interpretation of the discretion granted it under the children's safety factor provision and the manner in which it has implemented the children's safety factor provision focusing on its current policy guidance document on the children's safety factor.

1. *The children's safety factor*—a. *The statutory provision*. The statutory requirements pertaining to the additional children's safety factor are contained in two sentences in section 408(b)(2)(C). The first sentence commands that as to ''threshold effects, for the purposes of [making the reasonable certainty of no harm finding], an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children.'' (21 U.S.C. 346a(b)(2)(C)). This sentence also explains that the purpose for this additional safety factor is ''to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children.'' (Id.). Switching course, the second sentence then countermands the mandatory language in the first sentence (''shall be applied'') and makes clear that, EPA has the authority to deviate from the requirement to apply an additional 10X safety factor. The second sentence reads ''[n]othwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such a margin will be safe for children.'' Importantly, other than requiring that EPA act only on the basis of reliable data, Congress did not impose an elevated standard upon EPA as a requirement for choosing a factor different than an additional factor of 10X. The substantive standard that Congress did include was that any factor different than the 10X factor be ''safe'' for infants and children. (Id.). This standard is equivalent to the overall substantive standard for approving tolerances. (21 U.S.C. 346a(b)(2)(A)). Essentially, the two sentences addressing the additional safety factor direct EPA, in determining whether a tolerance poses a reasonable certainty of no harm to children, to apply an additional 10X factor unless EPA concludes, based on reliable data, that a different factor provides a reasonable certainty of no harm to children. Viewed in this light, the children's safety factor provision gives EPA broad discretion in choosing the level of any additional safety factor, subject to the constraint that EPA must rely only on reliable data and the guidance that EPA should focus on the completeness of the database and potential pre- and post-natal toxicity.

b. *Legislative history*. The legislative history of this provision also recognizes that EPA should be accorded discretion concerning the size of any additional factor to protect children based on the circumstances surrounding each pesticide. In the House Commerce Committee Report, the committee urged EPA to construe the children's safety provision ''in futherance of the following recommendations of the National Research Council's Study, 'Pesticides in the Diets of Infants and Children.''' The committee then quoted two paragraphs from the Study including the conclusion that: ''Because there exist specific periods of vulnerability during postnatal development, the committee recommends that an uncertainty factor up to the tenfold factor traditionally used by EPA and [the Food and Drug Administration] for fetal developmental toxicity *should also be considered* when

there is evidence of postnatal developmental toxicity and when data from toxicity testing relative to children are incomplete.'' (H.Rep. 104–669, Part 2 at 43 (1996)) (emphasis added). This emphasis on the exercise of judgment by EPA was highlighted in a pre-enactment EPA letters to key legislators regarding how EPA interpreted the children's safety provision. In that letter EPA stated that it ''believe[d] that [the children's safety factor] provision is consistent with the recommendations in [the NRC Study] and would allow the Agency to ensure that pesticide tolerances are safe for children *in those situations* where an additional margin of safety is *necessary* to account for inadequate or otherwise incomplete data.'' (142 Cong. Rec. S8737 (July 24, 1996) (letter to Rep. Bliley included in the record by Sen. Lugar) (emphasis added)). EPA explicitly concluded that the children's safety factor provision ''provides the Agency with discretion, based on sound science, to set the margin of safety at an appropriate level to protect infants and children.'' (Id. at S8737–S8738).

c. *EPA policy and implementation of safety factor provision.* On January 31, 2002, EPA released its current science policy guidance on the children's safety factor. (Ref. 4) [This policy is hereinafter referred to as the ''Children's Safety Factor Policy'']. That policy had undergone an intensive and extended process of public comment as well as internal and external science peer review. An EPA-wide task force was established to consider the children's safety factor in March 1998. Taking into account reports issued by the task force on both toxicity and exposure issues, EPA's Office of Pesticide Programs (''OPP'') released a draft children's safety policy document in May 1999. That document was subject to an extended public comment period as well as review by the FIFRA Scientific Advisory Panel. (Id. at 5). Although EPA's overall weight-of-the-evidence approach for evaluating safety factor determinations has remained fairly consistent over the years, EPA's implementation of the approach, and the weight given certain considerations, has evolved as the Agency has gained experience in applying the safety factor provision in various circumstances. The January 31, 2002 policy reflects a continued evolution in EPA's implementation of the safety factor provision.

The Children's Safety Factor Policy emphasizes throughout that EPA interprets the children's safety factor provision as establishing a presumption in favor of application of 10X safety factor for the protection of infants and children in addition to the traditional inter- and intra-species safety factors. (Id. at 4, 11, 50, A–5). Further, EPA notes that the children's safety factor provision permits a different safety factor to be substituted for this default 10X factor only if reliable data are available to show that the different factor will protect the safety of infants and children. (Id.). Given the wealth of data available on pesticides, however, EPA indicates a preference for making an individualized determination of a protective safety factor if possible. (Id. at 12). EPA states that use of the default factor could under- or over-protect infants and children due to the wide variety of issues addressed by the children's safety factor. (Id.). EPA notes that ''[i]ndividual assessments may result in the use of additional factors greater or less than, or equal to 10X, or no additional factor at all.'' (Id.).

In making such individual assessments regarding the magnitude of the safety factor, EPA stresses the importance of focusing on the statutory language that ties the children's safety factor to concerns regarding potential pre- and post-natal toxicity and the completeness of the toxicity and exposure databases. (Id. at 12–13). As to the completeness of the toxicity database, EPA recommends use of a weight-of-the-evidence approach which considers not only the presence or absence of data generally required under EPA regulations and guidelines but also the availability of ''any other data needed to evaluate potential risks to children.'' (Id. at 23). Under this weight-of-the-evidence approach, the fact that data are missing is not outcome determinative with regard to retention of the children's safety factor. Rather, when data are absent, EPA indicates that the principal inquiry of the weight-of-the-evidence evaluation would center on whether the missing data would significantly affect calculation of a safe exposure level (commonly referred to as the Reference Dose (''RfD'')). (Id. at 24–25; accord 67 FR 60950, 60955, September 27, 2002) (finding no additional safety factor necessary for triticonazole despite lack of DNT study because the ''DNT [study] is unlikely to affect the manner in which triticonazole is regulated.'')). When the missing data are data above and beyond general regulatory requirements, EPA indicates that the weight of evidence would generally only support the need for an additional safety factor where the data ''is being required for 'cause,' that is, if a significant concern is raised based upon a review of existing information, not simply because a data requirement has been levied to expand OPP's general knowledge.'' (Ref. 4 at 26). The extent to which the policy stresses the need for EPA's evaluation of the completeness of the database to focus directly on whether missing data might possibly lower an existing RfD was a change in emphasis from past actions.

In evaluating the completeness of the exposure database, EPA explains that a weight-of-the-evidence approach should be used to determine the confidence level EPA has as to whether the exposure assessment ''is either highly accurate or based upon sufficiently conservative input that it does not underestimate those exposures that are critical for assessing the risks to infants and children.'' (Id. at 36). EPA describes why its methods for calculating exposure through various routes and aggregating exposure over those routes generally produce conservative exposure estimates - i.e., health-protective estimates due to overestimation of exposure. (Id. at 43–47). Nonetheless, EPA emphasizes the importance of verifying that the tendency for its methods to overestimate exposure in fact were adequately protective in each individual assessment. (Id. at 48–49).

As to potential pre- and post-natal toxicity, the Children's Safety Factor Policy lists a variety of factors that should be considered in evaluating the degree of concern regarding any identified pre- or post-natal toxicity. (Id. at 31). As with the completeness of the toxicity database, EPA emphasizes that the analysis should focus on whether any identified pre- or post-natal toxicity raises uncertainty as to whether the chosen RfD is protective of infants and children. (Id. at 35). Once again, the presence of pre- or post-natal toxicity, by itself, is not regarded as determinative as to size of the children's safety factor. Rather, EPA stresses the importance of evaluating all of the data under a weight of evidence approach focusing on the safety of infants and children. (Id.). This attention on the overall database also indicated a shift in emphasis for EPA's implementation of the children's safety factor provision as previous decisions had often treated a finding of increased sensitivity in the young as almost necessitating some additional safety factor.

EPA's experience in making decisions under the 2002 policy is that while for many pesticides the safety factor determination has not changed, for others the safety factors may go up or down. To generalize, in situations where the database is incomplete, EPA's heightened emphasis on whether the

missing data may affect the assessment of risk has tended to make it more likely that EPA will retain the full 10X children's safety factor. (See, e.g., 70 FR 7876, 7882, February 16, 2005) (avermectin - 10X factor retained due to lack of DNT study and acute and subchronic neuorotoxicity studies and residual toxicological concerns as to safety of young; 70 FR 7886, 7891, February 16, 2005) (clothianidim - 10X factor retained due to lack of developmental immunotoxicity study; 69 FR 58058, 58062–58063, September 29, 2004) (fenamidone - 10X factor retained due to lack of DNT study); but see 69 FR 52182, 52187, August 25, 2004) (folpet - 10X removed despite lack of DNT study because the DNT study is unlikely to change RfD). On the other hand, EPA's weight-of-the-evidence evaluation of any identified increased sensitivity in the young has tended to have the opposite effect. Rather than retaining the 10X factor simply because increased sensitivity is found, EPA has evaluated whether, in the context of the entire database, there exists a clearly-defined no effect threshold for the more sensitive effects in the young (i.e. is the effect ''well-characterized'') and whether EPA's RfD selection has provided an adequate margin of safety to protect against the effects seen in the young. In circumstances where the increased sensitivity is well-characterized and the RfD otherwise provides at least a 100X margin of safety for these effects, EPA has concluded it is safe to remove the additional children's safety factor. (See, e.g., 69 FR 63083, 63092–63093, October 29, 2004) (pyraclostrobin - 10X factor removed because additional sensitivity well-characterized and an adequate margin of safety); 69 FR 58290, 58295, September 30, 2004) (cyazofamid - 10X factor removed because additional sensitivity well-characterized and an adequate margin of safety); but see 69 FR 62602, 62610, October 27, 2004) (deltamethrin - 10X factor lowered but not removed taking into consideration level at which additional sensitivity was observed)). As these decisions evidence, the determination on the children's safety factor is heavily dependent on the results from the toxicity studies specific to the pesticide in question. (See, e.g., 70 FR 14535, 14541–14542, March 23, 2005) (dinotefuran - 10X factor retained as to some risk assessments due to the lack of a developmental immunotoxicity study; no additional factor on any risk assessment found necessary to address lack of a DNT study).

2. *The Developmental Neurotoxicity Study and chlorothalonil*. The States claim that several of the pesticides named in the petition are ''neurotoxins'' and that, therefore, a DNT study is required and EPA must retain the children's safety factor until the DNT study is submitted. As to the alleged legal requirement to retain the children's safety factor due to the absence of a DNT study, the States argue ''the statute requires that a tolerance safety determination include consideration of . . . the special neurological susceptibility of infants and children as reflected in developmental neurotoxicity studies.'' (Ref. 1 at 9).

Precisely what the States are arguing here is somewhat unclear. To the extent they are claiming that the statute requires that pesticides be evaluated in a DNT study, their argument is without a basis. Although the statute does require EPA to consider the ''special susceptibility of infants and children to pesticide chemical residues, including neurological differences between infants and children and adults . . .,'' (21 U.S.C. 346a(b)(2)(C)(i)(II)), it does not specify any particular study that must be reviewed, leaving the matter to EPA's discretion. In fact, all of the five core toxicological studies required for agricultural pesticides (developmental toxicity study in two species, 2-generation reproduction study in rats, and chronic toxicity study in two species) include an evaluation of potential neurological effects. (Ref. 24 at 2).

It appears more likely that the States are arguing that EPA has concluded that a DNT study is required for neurotoxins. (Ref. 1 at 10). The States, however, do not claim that chlorothalonil is a neurotoxin. EPA agrees that the evidence does not show chlorothalonil to be neurotoxic and has accordingly not required a DNT for this pesticide. (Ref. 24 at 2–3). Therefore, this portion of the States' petition does not support its claim that the additional 10X factor should be retained as to chlorothalonil.

Moreover, even had the States claimed that a DNT is required as to chlorothalonil, that allegation alone would not have been enough to demonstrate that the 10X factor should be retained. In the Children's Safety Factor Policy, EPA makes clear that, like any other missing study, the absence of the DNT study does not trigger a mandatory requirement to retain the default 10X value. Rather, whether the additional safety factor is retained depends on an individualized assessment centering on the question of whether ''a DNT study is likely to identify a new hazard or effects at lower dose levels of the pesticide that could significantly change the outcome of its risk assessment . . . .'' (Ref. 4 at 27). For this reason, EPA denied objections to various tolerance rulemakings filed by the Natural Resources Defense Council (NRDC) regarding DNT studies and the children's safety factor. There, DNT studies had been required but not yet submitted. EPA rejected NRDC's argument that the potential for a DNT study to identify harmful effects at lower levels than seen in other studies alone requires that the children's safety factor be maintained. EPA wrote:

> The statute specifically grants EPA discretion to apply a different additional safety factor where EPA can conclude based on reliable data that the different factor is safe for infants and children. NRDC has made no argument that would justify an across-the-board conclusion that in the absence of a DNT study an individual examination of the existing data pertaining to a pesticide cannot provide a reliable basis for concluding that a different safety factor would be safe for infants and children. NRDC's claim that a DNT study may lower EPA's RfD (which EPA does not disagree with) is not by itself sufficient to bar EPA from making a case-by-case inquiry into the safety of a different additional safety factor for the protection of infants and children in the absence of such a study.

(70 FR 46706, 46724 (August 10, 2005)). Because NRDC made no pesticide-specific allegations regarding the challenged pesticides, EPA dismissed NRDC's objections to a lowering of the children's safety factor.

3. *Endocrine effects*. The States note that the statute requires EPA to consider, in making safety determinations as to tolerances, whether a pesticide has an effect that mimics estrogen or has other endocrine effects, (see 21 U.S.C. 346a(b)(2)(D)(viii)), and to establish an endocrine screening program, (see 21 U.S.C. 346a(p)). The States claim that, as a matter of law, because assessments under the endocrine screening program have not been completed, EPA must retain the children's safety factor as to the pesticides in the petition (and presumably for all other pesticides as well). The States are incorrect. The statute imposes no mandatory bar on, or other limitation of EPA's discretion regarding, adjustment or removal of the children's safety factor pending completion of the endocrine screening program. Further, EPA has acted reasonably in not rigidly tying its safety factor decisions to completion of the endocrine screening program given the available data it has on the potential for pesticides in general, and chlorothalonil in particular, to cause adverse endocrine effects.

a. *The States' position is contradicted by the statute and legislative history*. As discussed above, the children's safety factor does not apply in some type of automatic manner whenever any data gap is identified. Rather, the statute, in clear and unmistakable language, grants EPA discretion to make a fact-based determination of whether a safety factor different than the 10X default value is safe for children:

> Notwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children.

21 U.S.C. 346a(b)(2)(C). There is nothing in FFDCA section 408(p) concerning the endocrine screening program that contradicts the discretion given EPA in the children's safety factor provision. In fact, subsection (p)(6) expressly addresses ''Agency Action'' required on the basis of the endocrine screening program and that provision mentions only agency action upon the finding of an endocrine effect, not actions, such as retaining the children's safety factor, that might be mandated by the mere establishment of the program. 21 U.S.C. 346a(p)(6). If Congress had intended that the mere establishment of the endocrine screening program should have the dramatic and far-reaching effect of requiring EPA to apply automatically an additional 10X safety factor for each and every pesticide for the several years needed to complete the screening program, it is surprising that this intent finds neither mention in the statutory language nor any comment in the legislative history.

This lack of a connection between the endocrine screening provision and the children's safety factor provision is understandable given the legislative origins of the endocrine screening program. The endocrine screening provision was not a well-integrated component in the bills comprising the long history of the legislative debate over revision of section 408. Rather, the endocrine screening provision arose in a context outside of FFDCA section 408, and even outside the context of pesticide regulation. The endocrine screening provision first appeared as an amendment to an unenacted bill updating the Safe Drinking Water Act (''SDWA'') in 1994. (S. 2019, 103rd Cong., 2d Sess, 20(l) (June 15, 1994)). It was again appended to amendments to the SDWA in 1995 although no final action was taken on the bill that year. (S. 1316, 104th Cong., 1st Sess., 28(g) (December 4, 1995)). It was only at the last minute that the endocrine screening program language proposed for the SDWA was inserted in the FQPA, (compare H.R. 1627, 104th Cong., 2nd Sess., 142 Cong. Rec. H8127 (July 23, 1996) with H.R. 1627, 104th Cong., 1st Sess. (May 12, 1995)), and much more modest language on endocrine screening included in amendments to the SDWA passed contemporaneously with the FQPA. (See S. 1316, 104th Cong., 2nd Sess. 404 (July 18, 1996) (full estrogenic screening program present in SDWA bill only 2 weeks before passage of FQPA); H.R. 3604, 104th Cong., 2nd Sess. (June 18, 1996) (same)).

In sum, under section 408(b)(2)(C) EPA clearly has the discretion to determine, in any given case, whether it has reliable data to choose a factor different than the 10X default value. Not only is there no statutory language supporting the States' argument in favor of automatic retention of the 10X until completion of the endocrine screening program but the legislative history is in no way supportive of construing the enactment of the program as intended to have such a dramatic impact. Further, since the enactment of the FQPA, EPA's contemporaneous and consistent approach to the endocrine screening program has been to treat that information-gathering exercise as not imposing some type of statutorily-prescribed, automatic injunction barring removal of the children's safety factor until completion of information-gathering under the program.

b. *Endocrine screening program builds upon the existing pesticide database bearing on endocrine effects*. The endocrine screening program was not created in a vacuum. Rather, the endocrine screening program, developed in consultation with knowledgeable scientists from academia, government, industry, and environmental groups and a wide range of interested stakeholders, builds upon work performed by EPA's Office of Pesticide Programs in examining the potential adverse endocrine effects of pesticides. Most of the critical tests that are projected to be used in the endocrine disruptor screening program are built on tests that have been developed and used for years in evaluating the safety of pesticides. Thus, while the endocrine screening program will further extend the Agency's understanding of the potential for pesticides and other substances to cause adverse endocrine effects, EPA already has substantial information on the degree to which pesticides cause such effects. These available data allow EPA to make weight-of-the-evidence assessments of a pesticide's ability to cause adverse effects due to endocrine disruption.

As described in detail in Unit III.D., EPA's endocrine disruptor screening program closely follows recommendations made to EPA by the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), a task force comprised of members representing the commercial chemical and pesticides industries, Federal and State agencies, worker protection and labor organizations, environmental and public health groups, and research scientists. 63 FR 71542, 71544 (December 28, 1998). The EDSTAC presented a comprehensive report in August 1998 addressing both the scope and elements of the endocrine screening program. The EDSTAC's recommendations were largely adopted by EPA.

As recommended by EDSTAC, EPA adopted a two-tier testing regime with the first tier involving screening ''to identify substances that have the potential to interact with the endocrine system'' and the second tier involving testing ''to determine whether the substance causes adverse effects, identify the adverse effects caused by the substance, and establish a quantitative relationship between the dose and the adverse effect.'' (Id. at 71545). ''The outcome of Tier 2 is designed to be conclusive in relation to the outcome of Tier 1.'' (Id. at 71554–71555). EPA also accepted the EDSTAC's detailed recommendations concerning the assays for Tier 1 screening and Tier 2 testing including a battery of short-term *in vitro* and *in vivo* assays for the Tier 1 screening exercise and five longer-term reproduction studies for Tier 2 testing that, with one exception, ''are routinely performed for pesticides with widespread outdoor exposures that are expected to affect reproduction.'' (Id. at 71555). EPA is examining, pursuant to the suggestion of the EDSTAC, modifications to these studies to enhance their ability to detect endocrine effects.

The primary proposed Tier 2 study relevant to endocrine effects on humans is the 2-generation reproductive toxicity study in rats. This is one of the core studies required for all food-use pesticides since 1984. (40 CFR 158.340(a)). In this reproduction study, ''potential hormonal effects can be detected through behavioral changes, ability to become pregnant, duration of gestation, signs of difficult or prolonged parturition, apparent sex ratio (as ascertained by anogenital distances) of the offspring, feminization or masculinization of offspring, number of pups, stillbirths, gross pathology and histopathology of the vagina, uterus, ovaries, testis, epididymis, seminal

vesicles, prostate, and any other identified target organs.'' 63 FR at 71555. In fact, EPA, in 1998, in discussing this study's use in Tier 2, identified 39 endpoints examined in this study relevant to estrogenic, androgenic, or thyroid effects. At that time, EPA noted that it was evaluating whether to add another 10 endocrine-related endpoints to the study protocol to enhance the utility of the study to detect endocrine effects. Id. at 71555–71556. Despite the ongoing evaluation of additional endpoints, EPA has concluded that ''the existing 2-generation mammalian assay is valid for the identification and characterization of reproductive and developmental effects, including those due to endocrine disruption, based on the long history of its use, the endorsement of the 1998 test guideline by the FIFRA Scientific Advisory Panel, and acceptance by member countries of the Organizations for Economic Cooperation and Development (OECD).'' (Ref. 25).

Although the 2-generation rat reproduction study currently is considered the definitive mammalian study to evaluate the adverse outcomes of endocrine disruptors for the endocrine screening program, it is not the only study routinely required or submitted for pesticides that provides information on potential endocrine effects. Information regarding endocrine effects is available from the other standard required toxicity studies including the subchronic bioassays (rat and dog), chronic bioassays (rat and dog), the cancer bioassays (rat and mouse), and prenatal development toxicity studies (usually the rat and rabbit). The subchronic, chronic, and cancer bioassays evaluate, among other things, the clinical signs and symptoms of the test animals exposed to a pesticide. In addition, at the conclusion of the test, animals are sacrificed and their organs are removed, weighed and subjected microscopically to examination for evidence of any pathology. The organs that play a critical role in the endocrine system (e.g., testes, epididymides, uterus, ovaries, mammary glands, and thyroid with parathyroid) are included in this evaluation. If an endocrine tissue (e.g., thyroid, testes, mammary gland) is identified as a target organ (particularly for carcinogenesis) in the standard toxicity studies, often the pesticide registrant will submit special studies that measure circulating levels of certain hormones (e.g., thyroid, luteinizing hormone, estrogen, or testosterone) to identify the mode of action. The required standard prenatal developmental toxicity studies would also detect the consequences of endocrine influences on fertility and pregnancy (e.g., litter size and loss) and development (e.g., fetal viability, altered sex ratios, and morphology). For example, developmental anomalies indicative of endocrine disruption would be assessed and include hypospadias, anogenital distance, and undescended testis. If a DNT study is required for a pesticide, that study will provide further information concerning potential endocrine effects. The DNT study involves exposure of the test animals from gestation through lactation and observation of effects on neurological function including motor activity, auditory startle, learning and memory and neuropathology at various ages through postnatal day 60. Additionally, DNT studies include evaluations of such potential endocrine-mediated effects such as effects on postnatal growth, reproduction and on developmental landmarks of puberty.

For food-use pesticides, therefore, EPA generally has an substantial database bearing on potential adverse endocrine effects. Not only does EPA require a 2-generation reproduction study in rats for such pesticides, but also requires data in multiple species on subchronic and chronic toxicity and developmental toxicity which bear on, among other things, potential endocrine effects, including effects beyond those examined in the 2-generation reproduction study. Thus, EPA believes that in many instances the totality of the information gleaned from current data required for pesticides used on food will make it is possible to develop a meaningful weight-of-the-evidence determination on the potential of the pesticide to adversely effect the endocrine system.

c. *Data bearing on chlorothalonil.* EPA has multiple data sets on chlorothalonil submitted both prior to and subsequent to the 1998 reregistration eligibility decision for chlorothalonil. This database includes subchronic and chronic toxicity testing in multiple species, developmental toxicity testing in multiple species, and 2-generation rat reproduction tests, including a 2-generation rat reproduction test under the most recent testing guidelines. None of these tests show any evidence of endocrine effects. Rather, the main toxic effects associated with exposure to chlorothalonil appear to be gastric lesions and kidney toxicity. As explained in more detail in the following unit, these two adverse effects occur through a non-hormonally-mediated mechanism. The gastric lesions are due to chlorothalonil's irritant effect on the stomach causing forestomach lesions. The kidney toxicity is produced as a result of enzymatic reactions in the kidney that cause perturbation of mitochondrial respiration, osmotic changes, and vacuolar degeneration.

Accordingly, EPA concludes that it has adequate reliable data on the potential of chlorothalonil to disrupt the endocrine system to support its decision that it will be safe for children to remove the additional 10X safety factor.

4. *Cumulative effects.* The States assert that ''as a matter of law'', EPA must retain the children's safety factor for each of the pesticides due to an alleged lack of data on cumulative effects from substances sharing a common mechanism of toxicity. With regard to chlorothalonil in particular, the States note that EPA acknowledged in the RED that chlorothalonil is a member of the polychlorinated fungicide class of pesticides but had not issued a determination on common mechanism by the time the States filed their petition. (Ref. 1 at 15). The States argue that EPA ''did not have reliable data on which to base a deviation from the tenfold factor'' because it lacked, among other things, data on the cumulative risk of chlorothalonil and other pesticides with a common mechanism of toxicity. (Id. at 16).

The States are incorrect. First, as discussed above, FFDCA does not require the children's safety factor to be applied automatically whenever any data gap is identified. EPA has discretion to establish an appropriate safety factor based on the particular facts related to a chemical. Second, as discussed below, available reliable data indicate that there is no common mechanism of toxicity for chlorothalonil with other members of the polychlorinated fungicide class of pesticides so a cumulative risk assessment is not appropriate and removal of the children's safety factor is authorized.

a. *Agency approach to conducting cumulative risk assessments.* Section 408(b)(2)(C)(i)(III) of the FFDCA directs EPA to assess risk of pesticide chemical residues to infants and children based on ''available evidence concerning the cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity.'' 21 U.S.C. 346a(b)(2)(C)(i)(III). The Agency's process for determining whether a substance has a cumulative effect includes two primary steps: determining whether a substance has a common mechanism of toxicity with another

chemical and if so, then conducting a cumulative effects risk assessment.

The EPA defines a common mechanism of toxicity as ''two or more pesticide chemicals or other substances that cause a common toxic effect to human health by the same, or essentially the same, sequence of major biochemical events. Hence, the underlying basis of the toxicity is the same, or essentially the same, for each chemical.'' (Ref. 26 at 4). To determine whether substances have a common mechanism of toxicity, EPA first identifies a preliminary grouping of substances that might cause a common toxic effect based on factors such as structural similarity, mechanism of pesticidal action, general mechanism of mammalian toxicity, and particular toxic effect. After conducting a detailed evaluation of available toxicological data for each substance and determining the mechanism by which each substance causes a common toxic effect, the Agency selects a common mechanism group based on similarities in the nature and sequence of the major biochemical events that cause toxicity. (See generally Ref. 24).

Once EPA concludes that a group of pesticides have a common mechanism of toxicity, EPA conducts a cumulative effects risk assessment. Depending upon the number of substances in the group, the extent of the pesticide use, the level of risk posed by the individual members in the group, and the levels of residues, EPA will determine whether a screening-level or more refined comprehensive cumulative effects risk assessment is appropriate. (See generally Ref. 27). EPA evaluates a range of data to conduct the cumulative effects risk assessment, including consideration of the relevant timeframe for the common mechanism effect, the pathways of exposure, the amount of exposure, and the population of concern, including any important subpopulations (e.g., children). In its final characterization of the cumulative effects risk, EPA determines the need for any uncertainty and safety factors based on any uncertainties identified during the risk assessment process or any need to protect against risks to exposed populations and important subgroups who may be at disproportionate risk (e.g., children).

b. *Common mechanism of toxicity evaluation of chlorothalonil and other polychlorinated fungicides*. In the chlorothalonil RED, chlorothalonil was mentioned as a member of the polychlorinated fungicide class of pesticides. (Ref. 10 at 100). Other members of this class include hexachlorobenzene (HCB), pentachlorophenol (PCP), and pentachloronitrobenzene (PCNB). This class was loosely assembled based only on structural similarities between chlorothalonil and other chemicals and mention of the class was not intended to demonstrate that these pesticides shared a common mechanism of action. Subsequent to the promulgation of the chlorothalonil RED, EPA has gained experience in making common mechanism of toxicity determinations and has released a policy guidance regarding how common mechanism questions should be approached. (Ref. 26). After reviewing the available data on chlorothalonil and the other polychlorinated fungicides, EPA can now conclude that chlorothalonil does not share a common mechanism of toxicity with these pesticides.

The available data demonstrate that chlorothalonil produces cancer effects (i.e., renal (kidney) tubular adenomas and carcinomas and papillomas of the forestomach in rats) as well as noncancerous effects (i.e., gastric lesions and kidney toxicity). (Ref. 24 at 5–8). Chlorothalonil induces renal tumors and kidney toxicity by bioactivating cysteine conjugates which leads to the production of chlorothalonil's thiol metabolites. These metabolites disrupt mitochondrial respiration in the kidney resulting in irritation, cytotoxicity, cell necrosis, increased cell proliferation, and restorative hyperplasia. The noncancerous kidney toxicity occurs during this process prior to the end result, which is adenomas in the tubular cells of the kidneys. (See Ref. 28). Similarly, chlorothalonil causes forestomach tumors and gastric lesions through a non-genotoxic mechanism involving irritation, cytotoxicity, cell necrosis, increased cell proliferation, and restorative hyperplasia.

None of the other chemicals in the polychlorinated fungicide class cause forestomach tumors and only one, HCB, causes renal tumors. HCB's toxicological profile, however, is far different than chlorothalonil's. HCB's primary target organ is the liver. HCB causes liver damage and tumors through disruption of the enzymes producing heme (an essential component of hemoglobin) leading to the build up of a heme-precusor, porphyrins, which can be toxic in excessive amounts. This condition is commonly referred to as porphyria, and hepatic (liver) porphryia is characterized by, in addition to liver damage, neurological effects. Although the liver is the organ most sensitive to HCB exposure; some studies have shown that HCB can cause renal toxicity and tumors. HCB, however, does not produce these renal effects by the same biochemical mechanism of action as chlorothalonil. HCB studies show that renal tumors may result from an accumulation of protein droplets in the kidney caused by an accumulation of a kidney cell substance called alpha-2U-globulin or an accumulation of porphyrins in the urine. There is no evidence that chlorothalonil leads to the accumulation of either of these substances. Further, metabolism studies with HCB show no evidence that HCB results in the production of cysteine conjugates and their byproducts, which lead to the renal toxicity seen with chlorothalonil.

Based on the foregoing, the available data show that chlorothalonil does not have a common mechanism of toxicity with any of the chemicals in the polychlorinated fungicide class. FFDCA does not require EPA to conduct a cumulative effects risk assessment for chemicals that do not have a common mechanism of toxicity. Therefore, EPA concludes that it has adequate reliable data on the potential cumulative effects of chlorothalonil to support its decision that it will be safe for children to remove the additional 10X safety factor.

5. *Conclusion*. Contrary to the States' contentions, EPA does not lack reliable data on chlorothalonil pertaining to neurotoxicity, endocrine effects, or cumulative effects from substances with a common mechanism of toxicity. Therefore, the States' objection to the removal of the children's safety factor has not been substantiated. Because the States' argument that the chlorothalonil tolerances are unsafe rested wholly on their assertion that retention of the children's safety factor was required, their petition to revoke the chlorothalonil tolerances is denied.

VIII. Response to Comments on the Petition to Revoke

Many points raised in comments from the pesticide industry groups and individual pesticide manufacturers have been specifically relied upon by EPA in its decision. To the extent these commenters addressed issues not addressed in this Order or presented arguments that were not necessary to reach in responding to the petition, EPA expresses no opinion on such comments. One such issue, however, deserves brief mention. GB Biosciences contested the States' claim regarding the potential cumulative effects of chlorothalonil and HCB by pointing out that HCB is only a minor contaminant of certain pesticides and, thus, it is relatively meaningless whether chlorothalonil and HCB share a common mechanism because cumulative exposure to chlorothalonil

and HCB would not be substantially greater than chlorothalonil alone. (Ref. 18 at 5). This assertion appears to have some force but EPA did not analyze it closely due to its conclusion that chlorothalonil and HCB operate by different mechanisms.

Some of the comments made by CLA have previously been submitted in the public participation procedures EPA used in developing the various FQPA science policies, including the children's safety policy. EPA reaffirms its earlier responses to such comments. (See Ref. 29). Further, EPA notes its disagreement with CLA's claim that a pesticide database cannot be incomplete with regard to endocrine effects because EPA has not imposed data requirements pursuant to the endocrine screening program. This claim is no more correct than the States' opposite assertion - that all pesticide databases are incomplete and require retention of the 10X factor because EPA has not imposed data requirements under the endocrine screening program. EPA's standard data requirements on pesticides address many endocrine-related issues and to the extent any of those data are missing, the relative incompleteness of the database relative to endocrine effects would have to be taken into account in making a decision on the children's safety factor.

NRDC's comment on the sensitivity of the DNT study was previously addressed by EPA in its Order denying NRDC's objections to various tolerances. See 70 FR 46706, 46722–46724 (August 10, 2005). NRDC's other comments concerned matters (e.g., exposure of farm children to pesticides) that were not raised in the States' petition and thus are not relevant to EPA's response to that petition.

Comments citing the alleged benefits of some of the pesticides named in the petition are not relevant to the petition because benefit considerations are strictly circumscribed under section 408 and have no applicability to the threshold risk issues involved in the petition. See 21 U.S.C. 346a(b)(2)(B).

IX. Regulatory Assessment Requirements

As indicated previously, this action announces the Agency's order denying, in part, a petition filed under section 408(d) of FFDCA. As such, this action is an adjudication and not a rule. The regulatory assessment requirements imposed on rulemaking do not, therefore, apply to this action.

X. Submission to Congress and the Comptroller General

The Congressional Review Act, (5 U.S.C. 801 et seq.), as added by the Small Business Regulatory Enforcement Fairness Act of 1996, does not apply because this action is not a rule for purposes of 5 U.S.C. 804(3).

XI. References

1. Petition of New York, California, Connecticut and Massachusetts for Modification of Tolerances for Pesticide Chemical Residues Established in Reregistration Eligibility Determinations for the Following Chemicals: Alachlor; Chlorothalonil; Methomyl; Metribuzin; Thiodicarb (December 17, 2004) (petition addressed to Michael O. Leavitt, Administrator, United States Environmental Protection Agency).

2. U.S. EPA, A User's Guide to Available EPA Information on Assessing Exposure to Pesticides in Food 11 (March 2000) [hereinafter cited as ''User's Guide''].

3. U.S. EPA, Residue Chemistry Test Guidelines: OPPTS 860.1500 Crop Field Trials 1 (August 1996).

4. Office of Pesticide Programs, US EPA, Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessment 13–16 (January 31, 2002) (available at *http://www.epa.gov/oppfead1/trac/science/determ.pdf*).

5. US EPA, Endocrine Disruptor Screening and Testing Advisory Committee Final Report (August 1998) (available at *http://www.epa.gov/scipoly/oscpendo/edspoverview/finalrpt.htm*).

6. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Reregistration Eligibility Decision: Alachlor (December 1998).

7. US EPA, Permanent Tolerances by Pesticide: Aug. 1996 TIS 13–14 (August 2002) (available at *http://www.epa.gov/oppsrrd1/tolerance/pdf__files/TolUniv8–05–2002.PDF*).

8. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Memorandum from Marcia E. Mulkey to Lois Rossi, A Common Mechanism of Toxicity Determination for Chloroacetanilide Pesticides (July 10, 2001).

9. Office of Prevention, Pesticides, and Toxic Substances, Memorandum from Alberto Proetzel to Felicia Fort, ACETOCHLOR/ALACHLOR: Cumulative Risk Assessment for the Chloroacetanilides (March 8, 2006).

10. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Reregistration Eligibility Decision: Chlorothalonil (April 1999).

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12. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Reregistration Eligibility Decision: Metribuzin (February 1998).

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14. Croplife America, Comments of CropLife America on the Petition of New York, California, Connecticut, and Massachusetts for Modification of Tolerances for Certain Pesticides (June 2005).

15. Pesticide Policy Coalition, Comments on Petition of Attorney Generals of New York, California, Connecticut and Massachusetts to Revoke or Modify Tolerances (June 15, 2005).

16. Monsanto Company, Docket ID Number OPP–2005–0050 (April 28, 2005).

17. Monsanto Company, Alachlor: Evaluation of the Potential for Endocrine Disruption (December 20, 2002).

18. GB Biosciences Corp., Docket ID Number OPP–2005–0050 (June 14, 2005).

19. GB Biosciences Corp., Chlorothalonil White Paper on Neurotoxicity and Endocrine Disruption (December 20, 2005).

20. Bayer Crop Science, Comments by Bayer CropScience Specific to the Named Chemicals Metribuzin (EPA 738–R–97–066) and Thiodicarb (EPA 738–R–98–022) (June 15, 2005).

21. DuPont Crop Protection, Re: Petition of New York, California, Connecticut, and Massachusetts for Modification of Tolerances for Certain Pesticides (June 9, 2005).

22. NRDC, Re: Petition of New York, California, Connecticut, and Massachusetts to Modify Tolerances for Alachlor, Chlorothalonil, Methomyl, Metribuzin, and Thiodicarb (May 9, 2005).

23. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Memorandum from Douglas Dotson to Paula Deschamp, Metribuzin Acute and Chronic Dietary Exposure Assessments (April 17, 2006).

24. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Memorandum from P.V. Shah to Pete Caulkins, HED Response to Questions Raised by SRRD Regarding Chlorothalonil (June 22, 2006).

25. Office of Prevention, Pesticides, and Toxic Substances, US EPA, Letter from Clifford Gabriel to Erik Olson, Attachment B (March 8, 2005).

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29. Office of Pesticide Programs, US EPA, Office of Pesticide Programs' Policy on the Determination of the Appropriate FQPA Safety Factor(s) For Use in the Tolerance Setting Process: Response to Comments (February 28, 2002) (available at *http://www.epa.gov/oppfead1/trac/science/fqpa__resp.pdf*).

List of Subjects

Environmental protection, pesticides, and pest.

Dated: July 24, 2006.

James Jones,

Director, Office of Pesticide Programs.

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