

Telephone: (202) 707-8380. Telefax: (202) 707-8366.

**SUPPLEMENTARY INFORMATION:** The Copyright Office makes a non-substantive correcting amendment to the final rule governing exemption to prohibition on circumvention of copyright protection systems for access control technologies which was published July 27, 2010.

#### List of Subjects in 37 CFR 201

Copyright, Exemptions to prohibition against circumvention.

#### Correction

For the reason set forth in the preamble, 37 CFR part 201 is corrected by making the following technical amendment:

#### PART 201—GENERAL PROVISIONS

■ 1. The authority citation for part 201 continues to read as follows:

**Authority:** 17 U.S.C. 702

■ 2. Amend § 201.40 (b) introductory text by removing the word “five”.

Dated: July 28, 2010

**Marybeth Peters,**

*Register of Copyrights.*

[FR Doc. 2010-19007 Filed 8-5-10; 8:45 am]

**BILLING CODE 1410-30-S**

## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 180

[EPA-HQ-OPP-2005-0190; FRL-8836-8]

#### Pymetrozine; Regulation Denying NRDC's Objections on Remand

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Final Regulation.

**SUMMARY:** In this regulation, EPA again denies objections by the Natural Resources Defense Council (NRDC) to an action establishing tolerance regulations for the pesticide pymetrozine under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA). EPA's previous denial of NRDC's objections, published in the **Federal Register** on August 10, 2005, was remanded to EPA by the U.S. Court of Appeals, Ninth Circuit, for further explanation of EPA's decision on the application of the FFDCA's requirement concerning an additional tenfold safety factor for the protection of infants and children to these pesticide tolerances. In the challenged action, EPA had applied a reduced additional safety factor to several risk assessments for

pymetrozine. EPA has reviewed its decision on the children's safety factor in light of the current data on pymetrozine and now determined that the full additional children's safety factor should be applied in assessing the risk of the pymetrozine tolerances. However, EPA still denies NRDC's objections because the increase in the children's safety factor does not change EPA's conclusion that the tolerances are safe. EPA's explanation for its decisions on the children's safety factor and the safety of pymetrozine tolerances are included in this regulation.

**DATES:** This regulation is effective August 6, 2010. Objections and requests for hearings must be received on or before October 5, 2010, 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-2004-0190. To access the electronic docket, go to <http://www.regulations.gov>, and search for the docket number. Follow the instructions on the regulations.gov website to view the docket index or access available documents. All documents in the docket are listed in the docket index available in regulations.gov. Although listed in the index, some information is not publicly available, e.g., Confidential Business Information (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 Regulatory Public Docket in Rm. S-4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. The Docket Facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket Facility telephone number is (703) 305-5805.

**FOR FURTHER INFORMATION CONTACT:** Meredith Laws, Registration Division (7510P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 304-7038; e-mail address: [laws.meredith@epa.gov](mailto:laws.meredith@epa.gov).

**SUPPLEMENTARY INFORMATION:**

## I. General Information

### A. Does this Action Apply to Me?

In this document EPA denies objections by the NRDC to EPA's establishment of certain pesticide tolerances. This action may also be of interest to agricultural producers, food manufacturers, or pesticide manufacturers. Potentially affected entities may include, but are not limited to those engaged in the following activities:

- Crop production (NAICS code 111), e.g., agricultural workers; greenhouse, nursery, and floriculture workers; farmers.
- Animal production (NAICS code 112), e.g., cattle ranchers and farmers, dairy cattle farmers, livestock farmers.
- Food manufacturing (NAICS code 311), e.g., agricultural workers; farmers; greenhouse, nursery, and floriculture workers; ranchers; pesticide applicators.
- Pesticide manufacturing (NAICS code 32532), e.g., agricultural workers; commercial applicators; farmers; greenhouse, nursery, and floriculture workers; residential users.

This listing is not intended to be exhaustive, but rather to provide 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. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

### 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 EPA's tolerance regulations at 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 FFDCA, 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. 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-2005-0190 in the subject line on the first page of your submission. All requests must be in writing, and must be received by the Hearing Clerk as required by 40 CFR part 178 on or before October 5, 2010.

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 this copy, identified by docket ID number EPA-HQ-OPP-2005-0190, 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 Bldg.), 2777 S. Crystal Dr., Arlington, VA. Deliveries are only accepted during the Docket Facility'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 Facility telephone number is (703) 305-5805.

## II. Introduction

### A. What Action Is the Agency Taking?

This action is being taken in response to a remand to EPA of a final order denying objections filed by the NRDC to regulations establishing pesticide tolerances for pymetrozine under section 408 of the FFDCA, 21 U.S.C. 346a. (70 FR 46706, August 10, 2005); (Ref. 1). The order was remanded to EPA by the U.S. Court of Appeals, Ninth Circuit, for an explanation of the basis for EPA's decision on the FFDCA's provision requiring a presumptive additional tenfold (10X) safety factor for the protection of infants and children. (*NCAP v. EPA*, 544 F.3d 1043, 1052 (9th Cir. 2008)). Specifically, the court held that EPA did not provide "enough information" on why in evaluating the risk of pymetrozine it chose to deviate from this presumptive safety factor.

(Id.). In response to the remand, EPA is again denying the objections. In light of new data received on pymetrozine, EPA has now determined that the presumptive safety factor for infants and children should be retained; however, the objections are denied because retention of this additional safety factor does not show the pymetrozine tolerances to be unsafe.

Because EPA has taken new information into account in issuing this decision upon remand, EPA is issuing the remand decision as a regulation under FFDCA section 408(d)(4)(i). Any person may file objections to a FFDCA section 408(d)(4)(i) regulation with EPA and request a hearing on those objections. (Id.). If this decision was issued as a revised final order on NRDC's objections under FFDCA section 408(g)(2)(C), (21 U.S.C. 346a(g)(2)(C)), then any party who wished to contest EPA's determination would have no opportunity to submit factual contentions to the record concerning the new information prior to seeking judicial review.

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

EPA's authority for issuing pesticide tolerances is contained in FFDCA section 408(d) and the statutory provisions governing the administrative review process for tolerances is in FFDCA section 408(g)(2). (21 U.S.C. 346a(d) and (g)(2)).

## III. Statutory and Regulatory Background

In this Unit, EPA provides background on the relevant statutes and regulations governing NRDC's objections as well as on pertinent Agency policies and practices. Unit III.A. summarizes the requirements and procedures in section 408 of the FFDCA and applicable regulations pertaining to pesticide tolerances. Unit III.B. provides an overview of EPA's risk assessment process. It contains an explanation of how EPA identifies the hazards posed by pesticides, how EPA determines the level of exposure to pesticides that pose a concern ("level of concern"), how EPA measures human exposure to pesticides, and how hazard, level of concern conclusions, and human exposure estimates are combined to evaluate risk. Further, this unit presents background information on the EPA's policy with regard to the statutory safety factor for the protection of infants and children.

### A. FFDCA

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 (USDA). 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 and additional protections for infants and children. (Public Law 104-170, 110 Stat. 1489 (1996)).

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)). The statute explains that aggregate exposure to a pesticide includes "dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources." (21 U.S.C. 346a(b)(2)(D)(vi)).

In making the safety determination for a tolerance, risks to infants and children are given special consideration. Specifically, section 408(b)(2)(C) creates a presumptive additional safety factor for the protection of infants and children. It 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 document 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, a tolerance 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 establishing, amending, or revoking the tolerance or denying the petition, any person may file objections with EPA and seek an evidentiary hearing on those objections. (21 U.S.C. 346a(g)(2)). Objections and hearing requests must be filed within 60 days after date of publication in the **Federal Register**. (Id.). EPA's final order on the objections is subject to judicial review. (21 U.S.C. 346a(h)(1)).

#### B. EPA Risk Assessment for Tolerances – Policy and Practice

1. *The safety determination-risk assessment.* To assess risk of a pesticide tolerance, EPA combines information on pesticide toxicity with information regarding the route, magnitude, and duration of exposure to the pesticide. The risk assessment process involves four distinct steps:

- Identification of the toxicological hazards posed by a pesticide;
- Determination of the “level of concern” with respect to human exposure to the pesticide;
- Estimation of human exposure to the pesticide; and
- Characterization of the risk posed to humans by the pesticide based on comparison of human exposure to the level of concern.

a. *Hazard identification.* In evaluating toxicity or hazard, EPA reviews toxicity studies, primarily in laboratory animals, to identify any adverse effects on the test subjects. Animal studies typically involve investigating a broad range of endpoints including gross and microscopic effects on organs and tissues, functional effects on body organs and systems, effects on blood parameters (such as red blood cell count, hemoglobin concentration, hematocrit, and a measure of clotting potential), effects on the concentrations of normal blood chemicals (including glucose, total cholesterol, urea nitrogen, creatinine, total protein, total bilirubin, albumin, hormones, and enzymes such as alkaline phosphatase, alanine aminotransferase and cholinesterases),

and behavioral or other gross effects identified through clinical observation and measurement. EPA examines whether adverse effects are caused by either short-term (e.g., acute) or longer-term (e.g., chronic) pesticide exposure and the effects of pre-natal and post-natal exposure in animals.

EPA also considers whether the adverse effect has a threshold — a level below which exposure has no appreciable chance of causing the 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 4–9). Not all carcinogens, however, pose a risk at any exposure level (i.e., “a non-threshold effect or risk”). Advances in the understanding of the mode of action of carcinogenesis have increasingly led EPA to conclude that some pesticides that cause carcinogenic effects in animal studies only cause such effects above a certain threshold of exposure.

b. *Level of concern/dose-response analysis.* Once a pesticide's potential hazards are identified, EPA determines a toxicological level of concern for evaluating the risk posed by human exposure to the pesticide. In this step of the risk assessment process, EPA essentially evaluates the levels of exposure to the pesticide at which effects might occur. An important aspect of this determination is assessing the relationship between exposure (dose) and response. The assessment of this relationship is often referred to as the dose-response analysis. EPA follows differing approaches to identifying a level of concern for threshold and non-threshold hazards.

i. *Threshold effects.* In examining the dose-response relationship for a pesticide's threshold effects, EPA evaluates an array of toxicity 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 effect levels (NOAEL). Generally, EPA will use the lowest NOAEL from the available studies as a starting point (called the Point of Departure) in estimating the level of concern for humans. (Ref. 2 at 9 (The Point of Departure “is simply the toxic dose that serves as the ‘starting point’ in extrapolating a risk to the human population.”)). At times, however, EPA will use a LOAEL from a study as the Point of Departure when no NOAEL is identified in that study and the LOAEL is close to, or lower than, other relevant NOAELs. The Point of

Departure is in turn used in choosing a level of concern. EPA will make separate determinations as to the Points of Departure, and correspondingly levels of concern, for both short and long exposure periods as well as for the different routes of exposure (oral, dermal, and inhalation).

In estimating and describing the level of concern, the Point of Departure is at times used differently depending on whether the risk assessment addresses dietary or non-dietary exposures. (Pymetrozine is not expected to result in any meaningful non-dietary exposure and thus risk assessment of non-dietary exposure is not further discussed in this document.) For dietary risks, EPA uses the Point of Departure to calculate an safe or acceptable level of exposure designated as the reference dose (RfD). The RfD is calculated by dividing the Point of Departure by applicable safety or uncertainty factors. Typically, EPA uses a baseline safety/uncertainty factor of 100X. That value includes a factor of ten (10X) where EPA is using data from laboratory animals to reflect potentially greater sensitivity in humans than animals and a factor of 10X to account for potential variations in sensitivity among members of the human population as well as other unknowns. Additional safety factors may be added to address data deficiencies or concerns raised by the existing data. 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. This FQPA additional safety factor largely replaces pre-FQPA EPA practice regarding additional safety factors. (Ref. 3 at 4–11).

In implementing FFDCa section 408, EPA's Office of Pesticide Programs, 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 assessments. (Ref. 3 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. Today, RfDs and PADs are generally calculated for both acute and chronic dietary risks although traditionally a RfD or PAD was only calculated for chronic dietary risks. Throughout this document general references to EPA's

calculated safe dose are denoted as a RfD/PAD.

ii. *Non-threshold effects.* For risk assessments for non-threshold effects, EPA does not use the RfD/PAD approach to choose a level of concern if quantification of the risk is deemed appropriate. Rather, EPA calculates the slope of the dose-response curve for the non-threshold effects from relevant studies using a linear, low-dose extrapolation model that assumes that any amount of exposure will lead to some degree of risk. This dose-response analysis will be used in the risk characterization stage to estimate the risk to humans of the non-threshold effect. Linear, low-dose extrapolation is typically used as the default approach for estimating the risk to carcinogens, unless there are mode of action data indicating a threshold response (or nonlinearity).

c. *Estimating human exposure.* Risk is a function of both hazard and exposure. Thus, equally important to the risk assessment process as determining the hazards posed by a pesticide and the toxicological level of concern for those hazards 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)).

i. *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 USDA. (Ref. 2 at 12). Information on residue values comes from a range of sources including crop field trials, data on pesticide reduction (or concentration) due to processing, cooking, 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 (i.e., Tier 1), assesses exposure using the worst case assumptions that 100 percent of the crops for which tolerances exist or are proposed are treated with the pesticide and 100 percent of the food from those crops contain pesticide residues at the tolerance level. (Id. at 11). When such an assessment shows no risks of concern, a more complex risk

assessment is unnecessary. By avoiding a more complex risk assessment, EPA's resources are conserved and regulated parties are spared the cost of any additional studies that may be needed. If, however, a Tier 1 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." EPA refinement of an exposure assessment "can have dramatic effects on the level of exposure predicted, reducing worst case estimates by 1 or 2 orders of magnitude or more." (73 FR 42683, 42687, July 23, 2008). More information on how EPA refines estimates of exposure from pesticides in food can be found in the following EPA publication, "A User's Guide to Available EPA Information on Assessing Exposure to Pesticides in Food." (Ref. 2; see also 73 FR at 42687).

ii. *Exposure from water.* EPA may use either or both field monitoring data and mathematical water exposure models to generate pesticide exposure estimates in drinking water. Monitoring and modeling are both important tools for estimating pesticide concentrations in water and can provide different types of information. Monitoring data can provide estimates of pesticide concentrations in water that are representative of specific agricultural or residential pesticide practices and under environmental conditions associated with a sampling design. Although monitoring data can provide a direct measure of the concentration of a pesticide in water, it does not always provide a reliable estimate of exposure because sampling may not occur in areas with the highest pesticide use, and/or the sampling may not occur when the pesticides are being used.

In estimating pesticide exposure levels in drinking water, EPA most frequently uses mathematical water exposure models. EPA's models are based on extensive monitoring data and detailed information on soil properties, crop characteristics, and weather patterns. (69 FR 30042, 30054–30065 (May 26, 2004)). These models calculate estimated environmental concentrations of pesticides using laboratory data that describe how fast the pesticide breaks down to other chemicals and how it moves in the environment. These concentrations can be estimated continuously over long periods of time, and for places that are of most interest

for any particular pesticide. Modeling is a useful tool for characterizing vulnerable sites, and can be used to estimate peak concentrations from infrequent, large storms.

Typically EPA uses a two-tiered approach to modeling pesticide concentrations in surface and ground water. The first tier model uses high-end and worst-case assumptions as a screen to identify pesticides that will not result in residues in water that pose a concern. If the first tier model suggests that pesticide levels in water may be unacceptably high, a more refined model is used as a second tier assessment. Second tier models substitute more detailed information for the high-end or worst-case assumptions used in first tier models. For example, a second tier model may incorporate information on the maximum percentage of acreage surrounding a drinking water reservoir that may be devoted to agriculture instead of assuming that 100 percent of the watershed is, in fact, farmland.

iii. *Residential exposures.* Generally, in assessing residential exposure to pesticides EPA relies on its Residential Standard Operating Procedures (SOPs). (Ref. 4). The SOPs establish models for estimating application and post-application exposures in a residential setting where pesticide-specific monitoring data are not available. SOPs have been developed for many common exposure scenarios including pesticide treatment of lawns, garden plants, trees, swimming pools, pets, and indoor surfaces including crack and crevice treatments. The SOPs are based on existing monitoring and survey data including information on activity patterns, particularly for children. Where available, EPA relies on pesticide-specific data in estimating residential exposures.

d. *Risk characterization.* The final step in the risk assessment is risk characterization. In this step, EPA combines information from the first three steps (hazard identification, level of concern/dose-response analysis, and human exposure assessment) to quantitatively estimate the risks posed by a pesticide. Separate characterizations of risk are conducted for different durations of exposure. Additionally, separate and, where appropriate, aggregate characterizations of risk are conducted for the different routes of exposure (dietary and non-dietary).

For threshold dietary risks, EPA typically estimates risk by expressing human exposure as a percentage of the RfD/PAD. Exposures lower than 100 percent of the RfD/PAD are generally

not of concern. Under current procedures, EPA aggregates pesticide exposure from food and drinking water prior to comparing exposure to the RfD/PAD.

2. *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 the use of traditional 10X safety factors to account for potential differences between animals and humans when relying on studies in animals (inter-species safety factor) and potential differences among humans (intra-species safety factor) as well as the use of FQPA's additional 10X children's safety factor.

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. 3 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 listed 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).

#### **IV. Challenged Tolerance Regulation for Pymetrozine**

1. *In general.* NRDC challenged a December 27, 2001, action establishing tolerances for pymetrozine on cotton seed; cotton gin byproducts; fruiting, cucurbit, leafy, and Brassica vegetables; turnip greens; hops; and pecans. (66 FR 66786, December 27, 2001). Given pymetrozine's exposure pattern and toxicological characteristics, EPA determined that pymetrozine potentially presented acute, short-term, chronic, and cancer risks and EPA quantitatively assessed these risks in making its safety determination. (Id. at 66791–66792). All of these risks were found to be below the Agency's level of concern. (Id.).

2. *Children's safety factor determination.* For pymetrozine, EPA concluded there was uncertainty regarding its effects on the young because a DNT was outstanding and a

NOAEL had not been identified in an acute neurotoxicity study. (66 FR at 66791; 64 FR 52438, 52444, September 29, 1999). EPA determined, however, that these uncertainties were partially offset by a number of factors. First, EPA noted that there was no increased sensitivity in young animals observed in the pre- and post-natal studies conducted with pymetrozine, and that these studies showed no evidence of abnormalities in the fetal nervous system. (Ref. 5 at 5). Second, the evidence on pymetrozine's neurotoxicity was mixed. Although the acute neurotoxicity study had identified behavioral effects at 125 milligrams per kilogram of body weight per day (mg/kg bw/day), the subchronic neurotoxicity only showed "indefinite evidence" of neurotoxicity at significantly higher doses (201 mg/kg/day for males, 228 mg/kg/day for females). (Id. at 2). Third, exposure data were deemed adequate not to underestimate exposure. (Id. at 5). Weighing all of this evidence, EPA determined that the safety of infants and children would be protected by an additional 3X safety factor applied to all risk assessments; (66 FR at 55791) and a second additional 3X safety factor for assessing acute risks to the general population, including infants and children. The second additional safety factor was only applied to the acute assessment because it was only in an acute neurotoxicity study that a NOAEL had not been identified. (64 FR at 52444). Given the two 3X safety factors for acute risk, EPA essentially retained the full 10X FQPA safety factor for the acute risk assessment. The second additional 3X safety factor was not retained as to the acute assessment for women of child-bearing age because this assessment was based on an acute study in which a NOAEL was obtained. (Id.).

#### **V. Subsequent Tolerance Action for Pymetrozine**

Since December 2001, EPA has established an additional tolerance for pymetrozine on asparagus. (70 FR 43292, July 27, 2005). Because section 408 requires EPA, in setting a pesticide tolerance, to consider aggregate exposure to the pesticide, "including dietary exposure under . . . all other tolerances for the pesticide chemical residue," in this subsequent action EPA took into account exposure to pymetrozine under challenged tolerances established on December 27, 2001 (cotton seed; cotton gin byproducts; fruiting, cucurbit, leafy, and Brassica vegetables; turnip greens; hops; and pecans). In its action on the asparagus tolerance in 2005, EPA concluded that the additional exposure

from the new tolerance, when aggregated with exposure under existing tolerances, was safe. (70 FR at 43297).

With regard to the children's safety factor in this subsequent action, EPA relied on a revised analysis taking into account its Children's Safety Factor Policy, which had not been released at the time of the December 27, 2001 tolerance action. This revised analysis focused on how the expected dose level in the requested DNT study compared to the existing Points of Departure for acute and chronic risks. The dose levels in the DNT study are generally guided by the results of the two-generation study in rats because it is a study involving the young and is conducted in the same species as the DNT study. Noting that the Points of Departure for acute risk were generally in the same order of magnitude of the NOAEL in the reproduction study, EPA concluded that full additional 10X safety factor should be retained for acute risk assessments because the DNT study could potentially lower the existing Point of Departure significantly and thus EPA lacked reliable data to choose a factor other than the default value. EPA reasoned that if the DNT study showed adverse effects at the lowest dose tested (presumably a dose in the range of the current Point of Departure), then a revised Point of Departure would be tenfold lower than the existing Point of Departure once EPA compensated for a lack of NOAEL in the DNT study. The opposite conclusion was reached for chronic risks because the Point of Departure for chronic risk assessment was already 30X lower than the expected low dose in the DNT study. Due to this significant difference in the chronic Point of Departure and the expected low dose in the DNT study, the results of the DNT study were unlikely to affect the chronic Point of Departure and thus an additional safety factor was not needed to protect infants and children in the absence of the DNT study. (Ref. 6).

#### **VI. Summary of NRDC Objections, Administrative Review of the Objections, and Judicial Review of EPA's Order Denying the Objections**

##### *A. NRDC's Objections*

On four occasions in the first half of 2002, the NRDC and various other parties filed objections with EPA to final rules under section 408 of the FFDCA, (21 U.S.C. 346a), establishing pesticide tolerances for various pesticides. The objections applied to 14 pesticides and 112 separate pesticide tolerances. The challenged tolerances included the tolerances for pymetrozine addressed in

today's regulation. The objections to the pymetrozine tolerances were filed on February 25, 2002, and grouped with objections to tolerances for halosulfuron-methyl.

Although NRDC's petitions raised dozens of issues, most of the issues related to two main claims: (1) That EPA had not properly applied the additional 10X safety factor for the protection of infants and children in section 408(b)(2)(C); and (2) that EPA had not accurately assessed the aggregate exposure of farm children to pesticide residues. Many of the issues were not fact-specific to the challenged tolerances but rather represented a generic challenge to EPA's implementation of the FQPA.

Two specific issues raised by NRDC are worthy of greater description because they later figured in the judicial review of EPA's disposition of the objections. First, as to several of the pesticides, NRDC argued that EPA had unlawfully removed the 10X children's safety factor because EPA had required that a DNT study be submitted for the pesticides but such study had not yet been completed. Specifically as to pymetrozine, NRDC asserted that:

Even though . . . DNT results are required and overdue, EPA has established new tolerances for pymetrozine. In doing so, EPA failed to apply the required 10X safety factor for children that is intended to compensate for just such data gaps.

(Ref. 1 at 4). Second, NRDC argued that EPA could not lawfully remove the children's safety factor as to all of the challenged pesticides because EPA relied on drinking water exposure models to estimate pesticide exposure levels in water instead of "collect[ing] pesticide-specific data on water-based exposure." (Ref. 7 at 5; Ref. 8 at 6). According to NRDC, drinking water models, as a definitional matter, could not supply the "reliable data" needed to choose a children's safety factor differing from the presumptive value. (Ref. 7 at 4–6; Ref. 8 at 6).

#### B. EPA's Denial of the Objections

EPA denied NRDC's objections in two separate orders. The first was issued on May 26, 2004, and addressed only the tolerances for imidacloprid. (69 FR 30042, May 26, 2004). The second was released on August 10, 2005 and addressed the tolerances for the remaining 14 pesticides. (70 FR 46706, August 10, 2005). The second order relied heavily on the imidacloprid order because in the process of resolving the claims pertaining to imidacloprid, EPA resolved many of NRDC's generic

attacks on EPA's interpretation of the FQPA. (70 FR at 46711, 46716, 46725, 46726, 46730).

As to the DNT study and the children's safety factor, EPA rejected "NRDC's contention that an EPA finding that a DNT study is needed in evaluating the risks posed by the pesticide is outcome-determinative as regards to retaining the children's safety factor until such time as the DNT study is submitted and reviewed." (70 FR at 46724). EPA carefully reviewed all of the evidence cited by NRDC regarding the DNT study and concluded that NRDC had not shown that the DNT was so critical to the protection of children that in the absence of that study EPA was conclusively precluded from exercising its statutory authority to make a case-by-case determination regarding the appropriate children's safety factor. EPA specifically did not address the specific factual considerations relating to its individual children's safety factor decisions as to pymetrozine (and the other pesticides), noting that "NRDC has offered no pesticide-specific arguments as to the pesticides in this proceeding as to why the absence of a DNT study requires the retention of the default 10X additional factor." (Id.)

With regard to whether reliance on drinking water models precluded lowering of the children's safety factor, EPA exhaustively reviewed the underlying factual basis for its models, the scientific peer review they had received, and how the models had worked in practice. EPA concluded that "they are based on reliable data and have produced estimates that EPA can reliably conclude will not underestimate exposure to pesticides in drinking water." (70 FR at 46726). Accordingly, NRDC's claim that only actual pesticide-specific water monitoring data could provide "reliable data" on the levels of pesticides in drinking water was rejected.

#### C. Judicial Review

1. *NRDC's petition for review.* In August, 2005, NRDC and the Northwest Coalition for Alternatives to Pesticides (NCAP) filed petitions for review of EPA's August 10, 2005 order. NRDC had not challenged the May 26, 2004 imidacloprid order. The petitions were filed in the Second and Ninth Circuits and the matter was assigned to the Ninth Circuit. The consolidated petitions sought review as to EPA's denial of NRDC's objections as they pertained to the tolerances of the following seven pesticides: acetamiprid, fenhexamid, halosulfuron-methyl,

isoxadifen-ethyl, mepiquat, pymetrozine, and zeta-cypermethrin.

NRDC/NCAP's brief argued that EPA had unlawfully removed or lowered the children's safety factor as to these seven pesticides and that EPA's establishment of tolerances for the seven pesticides was arbitrary and capricious. (Ref. 9). As to the contentions regarding the children's safety factor, NRDC/NCAP made several independent claims as to why EPA's action was unlawful. These claims were:

- a. As to acetamiprid, halosulfuron-methyl, mepiquat, pymetrozine, and zeta-cypermethrin, EPA had no discretion to alter the children's safety factor because it had determined that a DNT study was specifically needed to address concerns regarding these pesticides (DNT studies were not required on fenhexamid and isoxadifen-ethyl);
- b. EPA's decision on the children's safety factor could not be upheld because EPA provided "no pesticide-specific response to NRDC's objections with respect to the missing DNT studies, and does not offer any explanation or justification for the agency's departure from the tenfold children's safety factor for these five pesticides;"
- c. EPA lacked the reliable data on pesticide exposure levels in drinking water for each of the pesticides and such data are necessary to justify altering the children's safety factor; and
- d. EPA must retain the children's safety factor for each of the pesticides because data showed that they resulted in pre- or post-natal toxicity.

NRDC/NCAP argued that EPA's decision was arbitrary and capricious because EPA determined that additional data were needed on the pesticides but had not waited for submission of that data before establishing the pesticide tolerances and because EPA had not offered a sufficient explanation of its decisions on the children's safety factor.

2. *The Ninth Circuit's decision.* On September 19, 2008, the Ninth Circuit unanimously determined that:

- a. It was not arbitrary and capricious for EPA to have established the tolerances for acetamiprid, mepiquat, and pymetrozine without waiting for DNT studies for these pesticides;
- b. EPA had offered a reasoned explanation for why, as a general matter, the children's safety factor could be reduced in the absence of a DNT study; and
- c. It was reasonable for EPA to rely

in drinking water models in estimating pesticide levels in water in making children's safety factor determinations.

(*NCAP v. EPA*, 544 F.3d 1043, 1044–1051 (9th Cir. 2008)). Additionally, by a 2-to-1 vote, the court remanded to EPA its decision on the children's safety factor for acetamiprid, mepiquat, and pymetrozine. The majority found that EPA's order on NRDC's objections had not adequately explained the pesticide-specific reasons for removing or reducing the children's safety factor as to these pesticides in the absence of a required DNT study. (Id. at 1052). Without elaborating, the court dismissed all other issues raised by NRDC/NCAP. (Id. at 1053).

Although NRDC/NCAP's petition for review concerned seven pesticides, the court only remanded to EPA the tolerance decisions on acetamiprid, mepiquat, and pymetrozine. The petition for review was denied as to the other four pesticides because the remand only pertained to pesticides for which there was a question concerning EPA's pesticide-specific choice of a children's safety factor in the absence of a required DNT study. As to fenhexamid and isoxadifen-ethyl, a DNT study had not been required by EPA. For halosulfuron-methyl and zeta-cypermethrin tolerances, a DNT study had been required and had not been submitted at the time of the tolerance action; however, by the time of the oral argument, the circumstances had changed. As to zeta-cypermethrin, the DNT study had been submitted and reviewed by EPA and EPA had established further tolerances in reliance on the DNT study. As to halosulfuron-methyl, EPA had withdrawn the requirement for a DNT study. EPA notified the court that there was no longer a live controversy as to the tolerances for halosulfuron-methyl and zeta-cypermethrin and NRDC/NCAP and the court agreed the petition was moot as to these pesticides. (544 F.3d at 1048 n.4; Refs. 10 and 11).

## VII. Revised Regulation on Remand

On remand, EPA has determined that NRDC's objections should again be denied because the remanded objections do not show that the pymetrozine tolerances are not safe. EPA has now received and reviewed a DNT study on pymetrozine. The results of the DNT study, when considered in combination with the rest of the pymetrozine database, convince EPA that the 10X children's safety factor should be retained for pymetrozine. EPA evaluated the risk of pymetrozine, taking into account the additional 10X children's

safety factor and has concluded that pymetrozine tolerances are safe. A summary of EPA's reasons for retaining the 10X children's safety factor and of EPA's risk assessment is provided below.

### A. DNT Study for Pymetrozine

A DNT study with pymetrozine was performed in Wistar-derived rats. (Ref. 12). Dose levels in the study were 0 (control), 100, 500, or 2,500 parts per million (ppm). To translate these doses to humans they are expressed in terms of the daily dose in milligrams of pymetrozine per kilogram of body weight of the experimental animals. Additionally, because of significant body weight changes between fetuses during the period of gestation and post-natal animals during lactation, that weight change is incorporated into the expression of dose by using separate dose calculations for gestation and lactation. Expressed in these terms, the doses in the pymetrozine DNT study were 0/0 (gestation/lactation), 8.1/16.8, 38.7/82.6, and 173.1 milligrams/kilogram of body weight/day (mg/kg/day). No dose is provided for the high dose group of lactation animals because higher than expected mortality was observed during littering, resulting in an insufficient number of litters. Therefore, the study was terminated for the high dose group prior to lactation.

Effects in pups, as well as maternal animals, were evaluated through both in-life and post-mortem observations. To investigate potential neurotoxic effects, the in-life observations included monitoring of motor activity, testing of acoustic startle response, learning and memory evaluation, and use of a functional observation battery (FOB). The FOB is a noninvasive procedure designed to detect gross functional deficits resulting from exposure to chemicals and to better quantify neurotoxic effects detected in other studies. The FOB consists of six types of observations: home cage, handling, open field, sensory, neuromuscular, and physiological responses. Post-mortem evaluation included examination of the major portions of the central and peripheral nervous system for any sign of neuropathology.

The primary effect seen in the maternal animals was loss of the litter. At the 38.7 mg/kg/day dose, total litter loss was experienced between birth and post-natal-day 5 by 5 out of 29 treated maternal animals (17.2%) compared to 2 out of 30 controls (6.7%). On gestation day 24, one maternal animal with staining around the nose was sacrificed due to difficult parturition, and another animal was pale. Food consumption

was decreased ( $\downarrow$ 21%; statistical significance of  $p \leq 0.01$ ) during lactation days 1–5. However, body weights at this dose were comparable to controls throughout treatment. At the 8.1/16.8 mg/kg/day dose, no treatment-related effects were seen on litter loss, survival, clinical signs, body weight, body weight gain, food consumption, or reproductive performances. EPA determined that the maternal LOAEL is 38.7 mg/kg/day and the maternal NOAEL is 8.1 mg/kg/day.

Pymetrozine caused a dose-dependent increase in the number of pups dying during post-natal-days 1–5; 57 pups at 8.1/16.8 mg/kg/day, 95 pups at 38.7/82.6 mg/kg/day, and 151 pups at 173.1 mg/kg/day, compared to 48 pups in the controls. This was due to the increase in the number of whole litter losses at 8.1/16.8 mg/kg/day (3 litters), 38.7/82.6 mg/kg/day (5 litters), and 173.1 mg/kg/day (4 litters) compared to controls (2 litters). When whole litter losses are excluded, no treatment-related findings were observed on litter size or viability.

Treatment had no adverse effects on pup body weight, body weight gain, food consumption, developmental landmarks, clinical signs, FOB, motor activity, auditory startle reflex, learning and memory, or brain weights. However, measurement of brain morphometry showed the following differences ( $p \leq 0.05$ ) from controls: (i) increased thickness of the corpus callosum in the 38.7/82.6 mg/kg/day males on post-natal-day 12 ( $\uparrow$ 15%) and in the 8.1/16.8 mg/kg/day males on post-natal-day 63 ( $\uparrow$ 4–13%); (ii) increased thickness of the inner granular and molecular layers of the pre-pyramidal fissure in the cerebellum in the 38.7/82.6 mg/kg/day males on post-natal-day 63 ( $\uparrow$ 4–19%); and (iii) increased thickness of the dorsal cortex in the 8.1/16.8 mg/kg/day females on post-natal-day 12 ( $\uparrow$ 4–10%).

EPA determined that the offspring LOAEL is 8.1 mg/kg/day, the lowest dose tested, based on morphometric changes in the brains of female pups on post-natal-day 12 and male pups on post-natal-day 63. The offspring NOAEL was not established.

### B. Children's Safety Factor Decision for Pymetrozine

In evaluating the children's safety factor for pymetrozine, EPA considered the completeness of the toxicity and exposure databases as well as the potential for pymetrozine to cause pre- or post-natal toxicity, particularly where such toxicity indicates increased sensitivity in juvenile animals compared to adult animals. (Ref. 13)

1. *Toxicity database.* With the receipt of the DNT study, the toxicity database

for pymetrozine is complete in terms of the requirements in place at the time of the challenged pymetrozine tolerance action in 2001. However, since that time, EPA has amended data requirements pertaining to registration of pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act, (7 U.S.C. 136 et seq.), and establishment of tolerances under the FFDCA. (72 FR 60934, October 26, 2007). Several new requirements apply to agricultural pesticides such as pymetrozine but the only new data requirement for pymetrozine that has not yet been fulfilled is the requirement for an immunotoxicity study.

In the absence of this study, EPA examined the pymetrozine database to evaluate pymetrozine's immunotoxic potential. EPA concluded that the liver is the primary target organ of pymetrozine and that apparent immunotoxic effects are the result of exceedingly high doses.

Potential immune organ effects include atrophy of the thymus in the subchronic rat and dog studies at 360 and 54 mg/kg/day, respectively; decreased thymus weight in the chronic mouse study at 675 mg/kg/day; increased leucocytes in the subchronic rat study at 360 mg/kg/day; and hyperplasia of the splenic lymphocyte follicles in the reproduction study at 136.9 mg/kg/day. Clear NOAELs were identified for these potential immunotoxic effects at higher doses than the endpoint that was selected for risk assessment, i.e., the 8.1 mg/kg/day LOAEL from the DNT study based on brain morphometric changes in the offspring. Lymphocytic infiltration in the prostate and thyroid was observed at 14 mg/kg/day in the subchronic dog study but these organs are not a primary part of the immune system and the lymphocytic infiltration is considered an immune system reaction to other toxic effects on these organs and not an immunotoxic effect.

The Agency does not believe that conducting a functional immunotoxicity study will result in a lower Point of Departure than the endpoint currently selected for overall risk assessment (i.e. the extrapolated NOAEL from the DNT study—see discussion below in Unit VII.C.1.a.) based on:

- a. The only potential immunotoxic responses occurred at doses greater than the endpoint selected for risk assessment,
- b. Clear NOAELs were identified for the potential immunotoxic effects, again at doses greater than the endpoint selected for risk assessment; and
- c. The lymphohistocytic effects were determined not to be

immunotoxic effects but a reaction to other toxic effects.

The other concern with the toxicity database is that a NOAEL was not identified for juvenile animals in the DNT study. The LOAEL in that study was based on differences from controls in the measurement of brain morphometrics. The concern with this effect, however, is lessened somewhat here in that no effects were seen in other barometers of effects on developmental neurology such as developmental landmarks, clinical signs, FOB, motor activity, auditory startle reflex, learning and memory, or brain weights.

*2. Potential pre- and post-natal toxicity.* No indications of qualitative or quantitative sensitivity in the young were seen in the developmental studies in rats and rabbits or in the two generation reproduction study in rats. NOAELs were identified for all effects in the young seen in these studies. On the other hand, EPA has assumed that quantitative sensitivity was detected in the DNT study in rats given that toxicity was observed in the juveniles (brain morphometric changes) in the absence of maternal toxicity. This is a conservative assumption on EPA's part in that the maternal animals' brains were not examined for morphometric changes.

*3. Exposure database.* EPA's exposure estimate is based mainly on a 2005 exposure assessment performed for the last pymetrozine tolerance action. (70 FR 43292, July 27, 2005). For the acute exposure assessment, EPA used the very conservative approach of assuming pymetrozine was used on all foods with a tolerance and residues were at the tolerance level. The chronic exposure assessment is more refined in that for most crops EPA relied on average values from pesticide residue field trials for all commodities and data on the percentage of crops that are treated with pymetrozine for most of the more heavily-consumed commodities.

Because several years have passed since the 2005 pymetrozine tolerance action, EPA updated the percent crop treated data in assessing exposure. Although pymetrozine is licensed for use on ornamentals, EPA expects exposure to the public, including children, from this use to be negligible because pymetrozine may only be applied by commercial applicators (hence, no applicator exposure for the public) and post-application contact with ornamentals is infrequent and brief compared with, for example, turf.

*4. Conclusion.* The primary factor of concern from the above is the weakness in the toxicity database due to the failure to identify a NOAEL in the DNT

study. This deficiency is heightened by the fact that, although pre- and post-natal animals were generally not more sensitive than adults, the DNT study showed quantitative sensitivity in rat pups due to the identification of adverse brain morphometric changes in rat pups at a dose that did not cause maternal toxicity. Although the brain morphometric effects seen at the LOAEL in the DNT study were not confirmed by other barometers of developmental neurotoxicity, the absence of a NOAEL for these effects creates sufficient uncertainty that reliable data are not available to revise the default 10X children's safety factor. Therefore, EPA is retaining the full 10X children's safety factor in assessing risk based on the DNT study. As discussed in Unit VII.C.1. below, the DNT study provides the Point of Departure for both acute and chronic risk assessments. Retention of the full children's safety factor reduces any concerns from lack of an immunotoxicity study as the NOAELs from the potential immunotoxic organ effects are all greater than 1000X higher than the level of concern (aPAD and cPAD) when the 10X children's safety factor is taken into account. Despite the lack of a NOAEL in the DNT study and the increased sensitivity in juveniles shown in that study, EPA does not believe that the weight of the evidence supports an additional safety factor higher than 10X given that the brain morphometric effects seen at the LOAEL in the DNT study were not confirmed by any other measures of neurological effect.

### *C. Risk Assessment and Safety Determination for Pymetrozine*

Given the new data on developmental neurotoxicity and EPA's revised children's safety factor determination, EPA has recalculated the risks of pymetrozine taking this information into account. EPA last assessed the risks of pymetrozine in connection with a tolerance rulemaking for pymetrozine on asparagus in 2005. (70 FR 43292, July 27, 2005). The new information affects the hazard identification and dose-response aspects of the risk assessment for acute and chronic non-cancer risk. EPA has also updated the exposure assessment performed for the 2005 assessment because exposure information is needed in completing a revised acute and chronic risk assessment.

*1. Hazard identification/dose response—*a. *Point of Departure.* As previously explained, EPA chooses a Point of Departure from toxicology studies for use in calculating a safe level of exposure to humans. This safe level

of exposure is called a Reference Dose (RfD) or Population-Adjusted Dose (PAD). In the 2002 tolerance rulemaking, EPA used the following Points of Departure: for acute risk to the general population (including infants and children) a LOAEL of 125 mg/kg/day from the acute neurotoxicity study in rats; for acute risk to pre-natal infants (focusing on exposure to females of child-bearing age) a NOAEL of 10 mg/kg/day from the rabbit developmental study; and for chronic risk to the general population (including infants and children) a NOAEL of 0.377 from the chronic toxicity study in rats. The same Points of Departure were used in risk assessment for the 2005 rulemaking.

The Points of Departure have been changed based on a review of the DNT study. EPA determined that the LOAEL of 8.1 mg/kg/day from the DNT study (no NOAEL was established) would be used as the Point of Departure for both acute risk (all population groups including infants and children and women of child-bearing age) and chronic risk (again, all population groups). As described above, the effect seen at the LOAEL was changes in brain morphometrics in the offspring. The LOAEL from the DNT study was chosen for the Point of Departure for assessing acute risk because it is lower than either of the two doses previously used (the LOAEL from the acute neurotoxicity study and the NOAEL from the rabbit developmental study). Selection of this LOAEL for the Point of Departure for

acute risk assessment is conservative because the brain morphometric changes were observed in the absence of impacts on other parameters, including developmental landmarks, clinical signs, FOB, motor activity, acoustic startle response, learning and memory, or brain weight. It is additionally conservative because EPA has assumed that these brain changes could occur from a single dose.

The Agency is using the LOAEL from the DNT study as the Point of Departure for chronic risk because brain morphometric changes may be the result of single or multiple doses and this LOAEL produces the most protective cPAD. Previously, EPA used the NOAEL from the chronic rat study as the Point of Departure but the LOAEL from that study is based on hepatic hypertrophy and EPA no longer considers hepatic hypertrophy in the absence of liver pathology or changes in relevant clinical chemistry parameters to be an adverse effect. Hepatocellular hypertrophy is often an adaptive and reversible effect in response to the presence of a chemical (i.e. induction of microsomal enzymes in the liver). Although there are other NOAELs in the pymetrozine database at or slightly below the LOAEL from the DNT study, once an additional safety factor (see above) is retained to address the lack of a NOAEL in the DNT study, reliance on the LOAEL from this study produces the most protective cPAD.

b. *Dose response.* To calculate both the aPAD and cPAD, EPA divided the LOAEL from the DNT study by 1,000, representing a 10X factor to account for inter-species variability, a 10X factor to account for intra-species variability, and an additional 10X safety factor for the protection of infants and children due to the lack of a NOAEL in the DNT study. As noted above, the retention of the full 10X children's safety factor is conservative given the fact that the brain morphometric changes were noted in the absence of any confirming clinical or neuropathological signs.

2. *Exposure.* As explained in Unit VII.B. above, EPA relied on the exposure assessment for the 2005 pymetrozine tolerance rulemaking updated to incorporate more recent percent crop treated information. Residue levels in drinking water were estimated for that exposure assessment based upon EPA's screening level drinking water models. This assessment is very conservative with regard to acute exposure, and, while more refined for chronic exposure, still retains significant conservatism. (Refs. 13 and 14).

3. *Safety Determination.* Table 1 below shows how exposure to pymetrozine residues in food and drinking water compared to the aPAD and cPAD for the general population and major population subgroups based on age. The highest subgroups for acute and chronic exposure are shown in bold.

TABLE 1—SUMMARY OF COMBINED DIETARY (FOOD + DRINKING WATER) EXPOSURE AND RISK ESTIMATES FOR PYMETROZINE

Population Subgroup	Acute (95th Percentile)		Chronic	
	Exposure (mg/kg/day)	% aPAD	Exposure(mg/kg/day)	% cPAD
General U.S. Population	0.002831	35	0.000237	2.9
All Infants (1 year old)	0.003882	48	0.000707	<b>8.7</b>
Children 1–2 years old	0.004368	<b>54</b>	0.000350	4.3
Children 3–5 years old	0.004034	50	0.000329	4.1
Children 4–12 years old	0.003027	37	0.000224	2.8
Youth 13–19 years old	0.002312	28	0.000174	2.2
Adults 24–49 years old	0.002698	33	0.000222	2.7
Adults 50+ years old	0.002669	33	0.000235	2.9
Females 13–49 years old	0.002625	32	0.000217	2.7

Given the data and analysis underlying the derivation of the pymetrozine aPAD and cPAD and the pymetrozine exposure assessment, EPA

concludes that its finding that exposure for the highest exposed population subgroup is below the aPAD and cPAD shows that there is a reasonable

certainty of no harm from aggregate exposure to pymetrozine for all population subgroups including infants and children. (Refs. 13 and 14).

#### D. Conclusion

Because EPA's revised risk assessment – which incorporates both the DNT study and the 10X children's safety factor – shows pymetrozine exposure to be safe, NRDC's objection to the establishment of the pymetrozine tolerances is denied.

#### VIII. Regulatory Assessment Requirements

This final rule reaffirms, over objections, tolerances established under section 408(d) of FFDCA in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled *Regulatory Planning and Review* (58 FR 51735, October 4, 1993). Because this final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled *Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, nor does it require any special considerations under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under section 408(d) of FFDCA, such as the tolerance in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*) do not apply.

This final rule directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of section 408(n)(4) of FFDCA. As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined

that Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 9, 2000) do not apply to this final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Public Law 104–4).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), Public Law 104–113, section 12(d) (15 U.S.C. 272 note).

#### IX. Congressional Review Act

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, generally provides that before a rule may take effect, the agency promulgating the rule must submit a rule report to each House of the Congress and to the Comptroller General of the United States. Here, the underlying rule establishing pymetrozine tolerances is currently in effect. (See 66 FR 66786, December 27, 2001). The EPA order denying objections to that rule, however, has been remanded to EPA for a further explanation of the basis for EPA's decision on the objections. Importantly, the court remanded the matter to EPA without vacating the underlying rule. Today's action reaffirming the prior rule responds to the judicial remand and does not affect the status of the underlying rule. EPA will submit a report containing today's action reaffirming the pymetrozine tolerance regulation and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of this final rule in the **Federal Register**. The reaffirmed pymetrozine tolerance regulation is not a "major rule" as defined by 5 U.S.C. 804(2).

#### X. References

1. Objections to the Establishment of Tolerances for Pesticide Chemical Residues: Halosulfuron-methyl and Pymetrozine Tolerances (filed February 25, 2002).
2. USEPA, A User's Guide to Available EPA Information on Assessing Exposure to Pesticides in Food (June 21, 2000).
3. Office of Pesticide Programs, USEPA, Office of Pesticide Programs' Policy on the Determination of the Appropriate FQPA Safety Factor(s) For

Use in the Tolerance Setting Process (February 28, 2002).

4. Office of Pesticide Programs, USEPA, Standard Operating Procedures (SOPs) for Residential Exposure Assessments (Draft December 19, 1997).

5. Office Of Prevention, Pesticides and Toxic Substances, USEPA, Memorandum from Brenda Tarplee to Michael Doherty, Pymetrozine - Report of the FQPA Safety Factor Committee (July 21, 1999).

6. Office Of Prevention, Pesticides and Toxic Substances, USEPA, Memorandum from Brenda Tarplee to Michael Doherty, Pymetrozine - 3rd Report of the Hazard Identification Assessment Review Committee (February 9, 2003).

7. NRDC, Objections to the Establishment of Tolerances for Pesticide Chemical Residues: Isoxadifen-ethyl, Acetamiprid, Propiconazole, Furlazole, Fenhexamid, and Fluazinam Tolerances (filed May 20, 2002).

8. NRDC, Objections to the Establishment of Tolerances for Pesticide Chemical Residues: Imidacloprid, Mepiquat, Bifenazate, Zeta-cypermethrin, and Difluzenuron Tolerances (filed March 19, 2002).

9. Petitioners' Brief, *NCAP v. EPA*, Case Nos. 75255, 76807 (9th Cir. March 6, 2006).

10. Letter from Kent E. Hanson, U.S. Department of Justice to Cathy Catterson, Clerk of the Court, United States Court of Appeals, Ninth Circuit, Notice of Supplemental Authority in *Northwest Coalition for Alternatives to Pesticides v. EPA*, Nos. 04–75255 & 04–76807 (May 25, 2007).

11. Letter from Aaron Colangelo, U.S. Department of Justice to Cathy Catterson, Clerk of the Court, United States Court of Appeals, Ninth Circuit, Response to EPA's Notice of Supplemental Authority in *Northwest Coalition for Alternatives to Pesticides v. EPA*, Nos. 04–75255 & 04–76807 (May 29, 2007).

12. Office Of Prevention, Pesticides and Toxic Substances, USEPA, Memorandum from Robert J. Mitkus to Daniel Peacock, Pymetrozine – Review of Developmental Neurotoxicity Study in Rats (July 13, 2005).

13. Office Of Prevention, Pesticides and Toxic Substances, USEPA, Memorandum from Christina Swartz to Daniel B. Peacock and Meredith F. Laws, Pymetrozine. Updated Aggregate Human Health Risk Assessment (April 2, 2010).

14. Office Of Prevention, Pesticides and Toxic Substances, USEPA, Memorandum from Christina Swartz to Daniel B. Peacock and Meredith F.

Laws, Pymetrozine – Acute, Chronic and Cancer Combined Dietary (Food + Drinking Water) Exposure and Risk Assessments (April 2, 2010).

#### List of Subjects in 40 CFR Part 180

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

Dated: July 27, 2010.

Steven Bradbury,

Director, Office of Pesticide Programs.

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## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 180

[EPA-HQ-OPP-2005-0190; FRL-8836-7]

#### Acetamiprid, Mepiquat; Order Denying NRDC's Objections on Remand: Environmental Protection Agency

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Final order.

**SUMMARY:** In this order, EPA again denies objections by the Natural Resources Defense Council (NRDC) to actions establishing tolerance regulations for the pesticides acetamiprid and mepiquat under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA). EPA's previous denial of NRDC's objections, published in the **Federal Register** on August 10, 2005, was remanded to EPA by the U.S. Court of Appeals, Ninth Circuit, for further explanation of EPA's decision on the application of the FFDCA's requirement concerning an additional safety factor for the protection of infants and children to these pesticide tolerances. On remand, EPA is denying NRDC's objections because the objections are now either moot or not sufficient to justify the relief requested.

**DATES:** This order is effective August 6, 2010.

**ADDRESSES:** EPA has established a docket for this action under docket identification (ID) number EPA-HQ-OPP-2005-0190. To access the electronic docket, go to <http://www.regulations.gov>, and search for the docket number. Follow the instructions on the [www.regulations.gov](http://www.regulations.gov) website to view the docket index or access available documents. All documents in the docket are listed in the docket index available in [regulations.gov](http://www.regulations.gov). Although listed in

the index, some information is not publicly available, e.g., Confidential Business Information (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 Regulatory Public Docket in Rm. S-4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. The Docket Facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket Facility telephone number is (703) 305-5805.

#### FOR FURTHER INFORMATION CONTACT:

Meredith Laws, Registration Division (7510P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 308-7038; e-mail address: [laws.meredith@epa.gov](mailto:laws.meredith@epa.gov).

#### SUPPLEMENTARY INFORMATION:

##### I. General Information

###### A. Does this Action Apply to Me?

In this document EPA denies objections by the Natural Resources Defense Council ("NRDC") to EPA's to establishment of certain pesticide tolerances. This action may also be of interest to agricultural producers, food manufacturers, or pesticide manufacturers. Potentially affected entities may include, but are not limited to those engaged in the following activities:

- Crop production (NAICS code 111), e.g., agricultural workers; greenhouse, nursery, and floriculture workers; farmers.
- Animal production (NAICS code 112), e.g., cattle ranchers and farmers, dairy cattle farmers, livestock farmers.
- Food manufacturing (NAICS code 311), e.g., agricultural workers; greenhouse, nursery, and floriculture workers; ranchers; pesticide applicators.
- Pesticide manufacturing (NAICS code 32532), e.g., agricultural workers; commercial applicators; farmers; greenhouse, nursery, and floriculture workers; residential users.

This listing is not intended to be exhaustive, but rather to provide 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 NAICS codes have been provided to assist you and others in determining whether this action might

apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

###### 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 EPA's tolerance regulations at 40 CFR part 180 through the Government Printing Office's pilot e-CFR site at <http://www.gpoaccess.gov/ecfr>.

## II. Introduction

### A. What Action Is the Agency Taking?

In this order, EPA denies objections filed by the NRDC to regulations establishing pesticide tolerances for acetamiprid and mepiquat under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a. EPA previously denied NRDC's objections in an order dated August 10, 2005. (70 FR 46706 (August 10, 2005)). NRDC sought judicial review of the August, 2005 order, and the U.S. Court of Appeals, Ninth Circuit, remanded the order to EPA on the sole ground that EPA had not provided an adequate explanation as to one aspect of its decision. (NCAP v. EPA, 544 F.3d 1043, 1052 (9th Cir. 2008)). Specifically, the court held that EPA did not provide "enough information" on why it chose to deviate from the presumptive ten-fold (10X) additional safety factor for the protection of infants and children in FFDCA section 408(b)(2)(C). (Id.). In response to the remand, EPA is again denying the objections; however, EPA has not provided further information on its decision on the children's safety factor because that issue is now either moot or not outcome-determinative with regard to the challenged tolerances.

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

EPA's authority for issuing pesticide tolerances is contained in FFDCA section 408(d) and the statutory provisions governing the administrative review process for tolerances is in FFDCA section 408(g)(2). (21 U.S.C. 346a(d) and (g)(2)).