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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2007-1005; FRL-9997-06]

Chlorpyrifos; Final Order Denying Objections to March 2017 Petition Denial Order

AGENCY: Environmental Protection Agency (EPA).

ACTION: Order.

SUMMARY: In this Order, EPA denies the objections to EPA's March 29, 2017 order denying a 2007 petition from the Pesticide Action Network North America (PANNA) and the Natural Resources Defense Council (NRDC) to revoke all tolerances and cancel all registrations for the insecticide chlorpyrifos. This order is issued under section 408(g)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FFDCA) and constitutes final agency action on the 2007 petition. The objections were filed by Earthjustice on behalf of 12 public interest groups, the North Coast Rivers Alliance, and the States of New York, Washington, California, Massachusetts, Maine, Maryland, and Vermont.

DATES: This Order is effective [INSERT DATE OF PUBLICATION IN THE ***Federal Register***].

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2007-1005, is available at *http://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the

Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805. Please review the visitor instructions and additional information about the docket available at *http://www.epa.gov/dockets*.

FOR FURTHER INFORMATION CONTACT: Pesticide Re-Evaluation Division (7508P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (703) 347-0206; email address: *OPPChlorpyrifosInquiries@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

In this document, EPA denies all objections in response to a March 29, 2017 order denying the 2007 PANNA and NRDC petition requesting that EPA revoke all tolerances and cancel all pesticide product registrations for chlorpyrifos. In addition to the Petitioners, this action may be of interest to agricultural producers, food manufacturers or pesticide manufacturers, and others interested in food safety issues generally. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

· 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.

B. What Action Is the Agency Taking?

In this order, EPA denies objections to EPA's order of March 29, 2017 (the Denial Order), in which EPA denied a 2007 petition (the Petition) from PANNA and NRDC (the Petitioners) that requested that EPA revoke all tolerances for the pesticide chlorpyrifos established under FFDCA section 408. (Ref. 1) The Petition also sought the cancellation of all chlorpyrifos pesticide product registrations under section 6 the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136d.

The Petition raised the following claims regarding both EPA's 2006 FIFRA reregistration decision and active registrations of chlorpyrifos in support of the request for tolerance revocations and product cancellations:

1. EPA has ignored genetic evidence of vulnerable populations.

2. EPA has needlessly delayed a decision regarding endocrine disrupting effects.

3. EPA has ignored data regarding cancer risks.

4. EPA's 2006 cumulative risk assessment (CRA) for the organophosphates misrepresented risks and failed to apply FQPA 10X safety factor. (Note: For convenience's sake, the legal requirements regarding the additional safety margin for infants and children in FFDCA section 408(b)(2)(C) are referred to throughout this response as the "FQPA 10X safety factor" or simply the "FQPA safety factor." Due to Congress' focus on both pre- and post-natal toxicity, EPA has interpreted this additional safety factor as pertaining to risks to infants and children that arise due to pre-natal exposure as well as to exposure during childhood years.)

5. EPA has over-relied on registrant data.

6. EPA has failed to properly address the exporting hazard in foreign countries from chlorpyrifos.

7. EPA has failed to quantitatively incorporate data demonstrating long-lasting effects from early life exposure to chlorpyrifos in children.

8. EPA has disregarded data demonstrating that there is no evidence of a safe level of exposure during pre-birth and early life stages.

9. EPA has failed to cite or quantitatively incorporate studies and clinical reports suggesting potential adverse effects below 10% cholinesterase inhibition.

10. EPA has failed to incorporate inhalation routes of exposure.

EPA's Denial Order denied the Petition in full (82 FR 16581). Prior to issuing that order, EPA provided the Petitioners with two interim responses on July 16, 2012 and July 15, 2014. The July 16, 2012 response denied claim 6 (export hazard) completely, and that portion of the response was a final agency action. The remainder of the July 16, 2012 response and the July 15, 2014 response expressed EPA's intention to deny six other petition claims (1-5 and 10). (Note: In the 2012 response, EPA did, however, inform Petitioners of its approval of label mitigation (in the form of rate reductions and spray drift buffers) to reduce bystander risks, including risks from inhalation exposure, which in effect partially granted Petition claim 10.) EPA made clear in both the 2012 and 2014 responses that, absent a request from Petitioners, EPA's denial of those six claims would not be made final until EPA finalized its response to the entire Petition. Petitioners made no such request, and EPA therefore finalized its response to those claims in the Denial Order.

The remaining Petition claims (7-9) all related to same issue: whether the potential exists

for chlorpyrifos to cause neurodevelopmental effects in children at exposure levels below EPA's existing regulatory standard (10% cholinesterase inhibition). Because these claims raised novel, highly complex scientific issues, EPA originally decided it would be appropriate to address these issues in connection with the registration review of chlorpyrifos under FIFRA section 3(g) and decided to expedite that review, intending to finalize it several years in advance of the October 1, 2022 registration review deadline. EPA decided as a policy matter that it would address the Petition claims raising these matters on a similar timeframe. Although EPA had expedited its registration review to address these issues, the Petitioners were not satisfied with EPA's progress in responding to the Petition, and they brought legal action in the Ninth Circuit Court of Appeals to compel EPA to either issue an order denying the Petition or to grant the Petition by initiating the tolerance revocation process. Following several rounds of litigation (see discussion of the litigation in Unit III. of this Order), EPA was ordered by the Ninth Circuit to issue either a tolerance revocation rule or an order denying the Petition by March 31, 2017. *In re Pesticide Action Network of North America v. EPA*, 840 F.3d (9th Cir. 2016). Accordingly, in compliance with the court's order, the Denial Order also finalized EPA's response on claims 7-9. As to those claims, EPA concluded that, despite several years of study, the science addressing neurodevelopmental effects remains unresolved and that further evaluation of the science during the remaining time for completion of registration review was warranted regarding whether the potential exists for adverse neurodevelopmental effects to occur from current human exposures to chlorpyrifos. EPA therefore denied the remaining Petition claims, concluding that it was not required to complete -- and would not complete -- the human health portion of the registration review or any associated tolerance revocation of chlorpyrifos without resolution of those issues during the ongoing FIFRA registration review of chlorpyrifos.

In June 2017, several public interest groups and states filed objections to the Denial Order pursuant to the procedures in FFDCA section 408(g)(2). Specifically, Earthjustice submitted objections on behalf of the following 12 public interest groups: Petitioners PANNA and NRDC, United Farm Workers, California Rural Legal Assistance Foundation, Farmworker Association of Florida, Farmworker Justice, GreenLatinos, Labor Council for Latin American Advancement, League of United Latin American Citizens, Learning Disabilities Association of America, National Hispanic Medical Association and Pineros y Campesinos Unidos del Noroeste. Another public interest group, the North Coast River Alliance, submitted separate objections. With respect to the states, New York, Washington, California, Massachusetts, Maine, Maryland, and Vermont submitted a joint set of objections (Ref. 2).

The objections focus on three main topics: (1) The Objectors assert that the FFDCA requires EPA apply to the FFDCA safety standard in reviewing any petition to revoke tolerances and that EPA's decision to deny the Petition failed to apply that standard; (2) The Objectors contend that the record before EPA demonstrates that chlorpyrifos results in unsafe drinking water exposures and adverse neurodevelopmental effects and that EPA must therefore issue a final rule revoking all chlorpyrifos tolerances; and (3) The Objectors claim that EPA committed procedural error in failing to respond to comments, and they specifically point to comments related to neurodevelopmental effects, inhalation risk, and Dow AgroSciences' physiologically based pharmacokinetic model (PBPK model) used in EPA's risk assessment. Dow AgroSciences, which is now Corteva AgriScience, will be referred to as Corteva throughout the remainder of this Order.

On June 5, 2017, the same the day the Objectors were required to submit their objections to EPA, the League of United Latin American Citizens (LULAC) and the other 11 public interest

Objectors represented by Earthjustice filed suit in the U.S. Court of Appeals for the 9th Circuit directly challenging the Denial Order, asserting that the court could review the order directly, even in the absence of EPA's final order under FFDCA section 408(g)(2)(C) responding to the objections they had just submitted. *LULAC, et al. v. Wheeler, et al.*, No. 17-71636. In their pleadings, Petitioners alternatively asked the court to issue a mandamus order compelling EPA to respond to the June 2017 objections within 60 days. On August 9, 2018, a three-judge panel of the 9th Circuit vacated the Denial Order and ordered EPA to revoke all chlorpyrifos tolerances and cancel all chlorpyrifos registrations within 60 days. *Id.*, 899 F.3d 814. EPA sought rehearing of that decision before an *en banc* panel of the 9th Circuit, a request that was granted on February 6, 2019, effectively vacating the August 9, 2018 panel decision. On April 19, 2019, the *en banc* panel granted the request for mandamus and directed EPA to respond to the objections not later than 90 days from that date. The court did not otherwise address the claims in the case.

After reviewing the objections, EPA has determined that the objections related to Petition claims regarding neurodevelopmental toxicity must be denied because the objections and the underlying Petition are not supported by valid, complete, and reliable evidence sufficient to meet the Petitioners' burden under the FFDCA, as set forth in EPA's implementing regulations. Further, for reasons stated in the Denial Order, EPA has concluded that it is also appropriate to deny the objections related to new issues raised after EPA's 2006 tolerance reassessment and reregistration of chlorpyrifos. These issues are being addressed according to the schedule for EPA's ongoing registration review of chlorpyrifos. EPA is also denying all claims related to drinking water risk and the use of the Corteva PBPK model in EPA's 2014 risk assessment and 2015 proposed rule because these claims were not made in the Petition and the objections process cannot be used to raise new issues and restart the petition process. Finally, EPA is

denying the objections claiming procedural error, as EPA is not required to respond to comments made during the rulemaking process in this adjudication denying petition objections. Any response to comments will be completed in connection with EPA's final action in registration review.

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

The procedure for filing objections to EPA's final rule or order issued under FFDCA section 408(d) and EPA's authority for acting on such objections is contained in FFDCA section 408(g) (21 U.S.C. 346a(g)) and EPA's regulations at 40 CFR part 178.

II. Statutory and Regulatory Background

In this unit, EPA provides background on the relevant statutes and regulations governing the objections as well as on pertinent Agency policies and practices.

A. FFDCA and FIFRA Standards

EPA establishes maximum residue limits, or ''tolerances,'' for pesticide residues in food and feed commodities under FFDCA section 408. Without a tolerance or an exemption from the requirement of a tolerance, food containing a pesticide residue is ''adulterated'' under FFDCA section 402 and may not be legally moved in interstate commerce. FFDCA section 408 was substantially rewritten by the Food Quality Protection Act of 1996 (FQPA) (Public Law 104–170, 110 Stat. 1489 (1996)), which established a detailed safety standard for pesticides and integrated EPA's regulation of pesticide food residues under the FFDCA with EPA's registration and re-evaluation of pesticides under FIFRA. The standard to establish, leave in effect, modify, or revoke a tolerance is stated in FFDCA section 408(b)(2)(A)(i). "The Administrator may establish or leave in effect a tolerance for a pesticide chemical residue in or on a food only if the Administrator determines that the tolerance is safe." *Id.* "The Administrator shall modify or

revoke a tolerance if the Administrator determines it is not safe." *Id.* ''Safe'' is defined by FFDCA section 408(b)(2)(A)(ii) 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.'' Among the factors that must be addressed in making a safety determination, FFDCA section 408(b)(2)(D) directs EPA to consider "validity, completeness, and reliability of the available data from studies of the pesticide chemical and pesticide chemical residue."

Risks to infants and children are given special consideration. Specifically, FFDCA section 408(b)(2)(C)(i)(II) requires that EPA assess the risk of pesticides 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, and effects of *in utero* exposure to pesticide chemicals . . . ." (21 U.S.C. 346a(b)(2)(C)(i)(II)). This provision also creates a presumption that EPA will use an additional safety factor for the protection of infants and children. Specifically, 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.*

While the FFDCA authorizes the establishment of legal limits for pesticide residues in food, FIFRA section 3(a) requires the approval of pesticides prior to their sale and distribution 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. 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 for pesticide uses that result in residues in or on food, (*see* FIFRA section 2(bb)), and directing that EPA coordinate, to the extent practicable, revocations of tolerances with pesticide cancellations under FIFRA. (*see* FFDCA section 408(l)(1)). FIFRA section 4 directed EPA to determine whether pesticides first registered prior to 1984 should be reregistered, including whether any associated FFDCA tolerances are safe and should be left in effect (*see* FIFRA section 4(g)(2)(E)). FFDCA section 408(q) directed EPA to complete that tolerance reassessment (which included the reassessment of all chlorpyrifos tolerances) by 2006. Following the completion of FIFRA reregistration and tolerance reassessment, FIFRA section 3(g) requires EPA to re-evaluate pesticides under the FIFRA standard – which includes a determination whether to leave in effect existing FFDCA tolerances --every 15 years under a program known as "registration review." The deadline for completing the current registration review for chlorpyrifos is October 1, 2022.

B. Procedures for Establishing, Modifying, or Revoking Tolerances

Tolerances are established, modified, 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, modify, or revoke a tolerance by means of filing a petition with EPA. (*See* FFDCA section 408(d)(1)). EPA publishes in the ***Federal Register*** a notice of the petition filing and requests public comment. After reviewing the petition and submitted comments, FFDCA section 408(d)(4) provides that EPA may issue a final rule establishing,

modifying, or revoking the tolerance; issue a proposed rule to do the same; or issue an order denying the petition.

Once EPA takes action granting or denying the petition, FFDCA section 408(g)(2) allows any party to file objections with EPA and seek an evidentiary hearing on those objections. Objections and hearing requests must be filed within 60 days after the date on which EPA issues its rule or order under FFDCA section 408(d). A party may not raise issues in objections unless they were part of the petition and an objecting party must state objections to the EPA decision and not just repeat the allegations in its petition. *Corn Growers v. EPA*, 613 F.3d 266 (D.C. Cir. 2010), cert. denied, 131 S. Ct. 2931 (2011). EPA's final order on the objections, issued under FFDCA section 408(g)(2)(C), is subject to judicial review. (21 U.S.C. 346a(h)(1)).

III. Chlorpyrifos Regulatory Background

Chlorpyrifos (0,0-diethyl-0-3,5,6-trichloro-2-pyridyl phosphorothioate) is a broad-spectrum, chlorinated organophosphate (OP) insecticide that has been registered for use in the United States since 1965. By pounds of active ingredient, it is the most widely used conventional insecticide in the country. Currently registered use sites include a large variety of food crops (e.g., tree fruits and nuts; many types of small fruits and vegetables, including vegetable seed treatments; grain/oilseed crops; cotton), and non-food use settings (e.g., ornamental and agricultural seed production; non-residential turf; industrial sites/rights of way; greenhouse and nursery production; sod farms; pulpwood production; public health; and wood protection). For some of these crops, chlorpyrifos is currently the only cost-effective choice for control of certain insect pests. In 2000, the chlorpyrifos registrants reached an agreement with EPA to voluntarily cancel all residential use products except those registered for ant and roach baits in child-resistant packaging and fire ant mound treatments (e.g., 65 FR 76233 (Dec. 6,

2000); 66 FR 47481 (Sept. 12, 2001).

The OPs are a group of closely related pesticides that affect functioning of the nervous system. The OPs were included in the Agency's first priority group of pesticides to be reviewed under FQPA. In 2006, EPA completed FIFRA section 4 reregistration and FFDCA tolerance reassessment for chlorpyrifos and the OP class of pesticides and determined those tolerances were safe and should be left in effect (Ref. 3). Having completed reregistration and tolerance reassessment, EPA is required to complete the next re-evaluation of chlorpyrifos under the FIFRA section 3(g) registration review program by October 1, 2022. Given ongoing scientific developments in the study of the OPs generally, in March 2009 EPA announced its decision to prioritize the FIFRA section 3(g) registration review of chlorpyrifos by opening a public docket and releasing a preliminary work plan to complete the chlorpyrifos registration review by 2015 – 7 years in advance of the date required by law.

The registration review of chlorpyrifos has proven to be far more complex than originally anticipated. The OPs presented EPA with numerous novel scientific issues that the agency has taken to multiple FIFRA Scientific Advisory Panel (SAP) meetings since the completion of reregistration in 2006. (Note: The SAP is a federal advisory committee created by FIFRA section 25(d) and serves as EPA's primary source of peer review for significant regulatory and policy matters involving pesticides.) Many of these complex scientific issues formed the basis of the 2007 petition filed by PANNA and NRDC, specifically issues related to potential human health risks associated with volatilization and neurodevelopmental effects. During the registration review process, EPA reviews the currently available body of scientific data, including animal and epidemiology data, and the assessment of potential risks from various routes of exposure. Therefore, when EPA began the registration review for chlorpyrifos in March 2009, the Agency

indicated that the Agency had decided to address the Petition on a similar timeframe to EPA's expedited registration review schedule.

Although EPA has expedited the chlorpyrifos registration review to address the novel scientific issues raised by the Petition in advance of the statutory deadline, the complexity of the issues has precluded EPA from finishing this review according to the Agency's original timeframe. The Petitioners were dissatisfied with the pace of EPA's response efforts and sued EPA in federal court on three separate occasions to compel a faster response to the Petition. As explained in Unit I. of this Order, EPA addressed 7 of the 10 claims asserted in the Petition by either denying the claim, issuing a preliminary denial or approving label mitigation to address the claims, but notwithstanding these efforts, on August 10, 2015, the court issued a mandamus order directing EPA to "issue either a proposed or final revocation rule or a full and final response to the administrative Petition by October 31, 2015." *In re Pesticide Action Network of North America v. EPA*, 798 F.3d (9th Cir. 2015).

In response to that order, EPA issued a proposed rule to revoke all chlorpyrifos tolerances on October 30, 2015 (published in the ***Federal Register*** on November 6, 2015 (80 FR 69080)), based on its unfinished registration review risk assessment. EPA acknowledged it had insufficient time to complete its drinking water assessment and its review of data addressing the potential for neurodevelopmental effects.

On December 10, 2015, the Ninth Circuit issued a further order requiring EPA to complete any final rule (or petition denial) and fully respond to the Petition by December 30, 2016. On June 30, 2016, EPA sought a six-month extension to that deadline in order to allow EPA to fully consider the most recent views of the FIFRA SAP with respect to chlorpyrifos toxicology. The FIFRA SAP report was finalized and made available for EPA consideration on

July 20, 2016 (Ref. 4). On August 12, 2016, the court rejected EPA's request for an extension and ordered EPA to complete its final action by March 31, 2017 (effectively granting EPA a three-month extension). On November 17, 2016, EPA published a notice of data availability (NODA) seeking public comment on both EPA's revised risk and water assessments and reopening the comment period on the proposal to revoke all chlorpyrifos tolerances (81 FR 81049). The comment period for the NODA closed on January 17, 2017.

Following the close of the comment period on the NODA, EPA issued the Denial Order on March 29, 2017, as described in Unit I. of this Order. As noted, in June 2017, EPA received objections to the Denial Order from both public interest groups and states, and some of those same organizations simultaneously filed suit in the Ninth Circuit seeking to challenge the Denial Order in advance of EPA's response to the submitted objections. That litigation is summarized in Unit I. of this Order.

IV. The Petition and EPA's Petition Response

As explained in Unit I. of this Order, PANNA and NRDC submitted the Petition in 2007, raising 10 claims in support of their request that EPA revoke all chlorpyrifos tolerances under the FFDCA and cancel all chlorpyrifos registrations under FIFRA. EPA's Denial Order denied the Petition in full. The following is a summary of EPA's response in the Denial Order to the 10 Petition claims.

A. Claim 1: Genetic Evidence of Vulnerable Populations

The Petitioners claimed that as part of EPA's 2006 reregistration and tolerance reassessment decision the Agency failed to calculate an appropriate intra-species uncertainty factor (i.e., within human variability) for chlorpyrifos in both its aggregate and cumulative risk assessments (CRA). They asserted that certain data (the "Furlong study") addressing intra-

species variability in the behavior of the detoxifying enzyme paraoxonase (PON1), indicates that the Agency should have applied an intra-species safety factor "of at least 150X in the aggregate and cumulative assessments" rather than the 10X factor EPA applied.

In the Denial Order, EPA explained that it carefully considered the issue of PON1 variability and determined that data addressing PON1 in isolation are not appropriate for use alone in deriving an intra-species uncertainty factor and that the issue is more appropriately handled using a PBPK model. Further, the derivation of an intra-species factor of over 150X advocated by the Petitioners is based on combining values from humanized mice with human measured values with a range from highest to lowest; the Furlong study derivation is inappropriate and inconsistent with international risk assessment practice. In addition, the 2008 FIFRA SAP did not support the PON1 data used in isolation. Finally, Petitioners' statement that the Furlong study supports an intra-species uncertainty factor of at least 150X likely overstates potential variability. EPA therefore denied this aspect of the Petition.

B. Claim 2: Endocrine Disrupting Effects

Petitioners summarized a number of studies evaluating the effects of chlorpyrifos on the endocrine system, asserting that, taken together, the studies "suggest that chlorpyrifos may be an endocrine disrupting chemical, capable of interfering with multiple hormones controlling reproduction and neurodevelopment."

EPA denied this claim because the Petition did not explain whether and how endocrine effects should form the basis of a decision to revoke tolerances. The basis for seeking revocation of a tolerance is a showing that the pesticide is not "safe." Petitioners neither asserted that EPA should revoke tolerances because effects on the endocrine system render the tolerances unsafe, nor did Petitioners submit a factual analysis demonstrating that aggregate exposure to

chlorpyrifos presents an unsafe risk to humans based on effects on the endocrine system.

EPA noted that while the cited studies provide qualitative information that exposure to chlorpyrifos may be associated with effects on the androgen and thyroid hormonal pathways, these data alone do not demonstrate that current human exposures from existing tolerances are unsafe. Further, EPA explained that in June 2015, it completed an Endocrine Disruption Screening Program weight-of-evidence conclusion for chlorpyrifos. That analysis evaluated all observed effects induced, the magnitude and pattern of responses observed across studies, taxa, and sexes, and the Agency also considered the conditions under which effects occurred, in particular whether or not endocrine-related responses occurred at dose(s) that also resulted in general systemic or overt toxicity. The Agency concluded that, based on weight-of-evidence considerations, further testing was not recommended for chlorpyrifos since there was no evidence of potential interaction with the estrogen, androgen, and thyroid pathways.

C. Claim 3: Cancer Risks

Petitioners claim that the Agency "ignored" a December 2004 National Institutes of Health Agricultural Health Study showing that the incidence of lung cancer has a statistically significant association with chlorpyrifos exposure. Petitioners did not otherwise explain whether and how these data support the revocation of tolerances or the cancellation of pesticide registrations. Specifically, Petitioners did not present any fact-based argument demonstrating that aggregate exposure to chlorpyrifos poses an unsafe carcinogenic risk. Accordingly, EPA denied the Petition to revoke chlorpyrifos tolerances or cancel chlorpyrifos registrations to the extent the Petition relies on claims pertaining to carcinogenicity. EPA went on to note, however, that while there is initial suggestive epidemiological evidence of an association between chlorpyrifos and lung cancer, it is reasonable to conclude chlorpyrifos is not a carcinogen in view

of the lack of carcinogenicity in the rodent bioassays and the lack of a genotoxic or mutagenic potential.

D. Claim 4: CRA Misrepresents Risks, Failed to Apply FQPA 10X Safety Factor

Petitioners asserted that EPA relied on limited data and inaccurate interpretations of a specific study (the "Zheng study") to support its decision to remove the FQPA safety factor in the 2006 OP cumulative risk assessment (CRA). Petitioners claimed the Zheng study showed an obvious difference between juvenile and adult responses to chlorpyrifos that supported retention of the 10X safety factor for chlorpyrifos in the CRA. EPA concluded that Petitioners' assertions did not provide a sufficient basis for revoking chlorpyrifos tolerances. The Petitioners' claim that the data EPA relied upon support a different FQPA safety factor for chlorpyrifos in the CRA did not amount to a showing that chlorpyrifos tolerances are unsafe as Petitioners did not present a factual analysis demonstrating that the lack of a 10X safety factor in the CRA for chlorpyrifos poses unsafe cumulative exposures to the OPs. For this reason, EPA denied the Petitioners' request to revoke chlorpyrifos tolerances or cancel chlorpyrifos registrations on the basis of the FQPA safety factor in the CRA.

Despite the inadequacy of Petitioners' FQPA CRA safety factor claims, EPA nonetheless examined the evidence Petitioners cited regarding the Zheng study. EPA acknowledged that in that study, pups appeared to be more sensitive than adults at the tested high dose. However, at the low-dose end of the response curve, relevant for human exposures, little to no difference was observed. This result is consistent with a comparative cholinesterase study submitted by Corteva that specifically compared the dose-response relationship in juvenile and adult rats and found no basis for concluding that juveniles are more sensitive, further supporting EPA's use of an FQPA safety factor of 1X for the AChE inhibition endpoint used in the 2006 OP CRA.

E. Claim 5: Over-Reliance on Registrant Data

Petitioners asserted that in reregistering chlorpyrifos EPA "cherry picked" data, "ignoring robust, peer-reviewed data in favor of weak, industry-sponsored data to determine that chlorpyrifos could be re-registered and food tolerances be retained." As such, Petitioners argued that the Agency's reassessment decision is not scientifically defensible. EPA concluded that this Petition claim was not purported to be an independent basis for revoking chlorpyrifos tolerances or cancelling chlorpyrifos registrations but simply support for Petitioners' arguments in other parts of the Petition. While Petitioners claim that EPA ignored robust, peer-reviewed data in favor of weak, industry-sponsored data for the reregistration of chlorpyrifos, Petitioners did not cite to any studies other than those used to support their other claims. In general, Petitioners did not provide any studies in the Petition that EPA failed to evaluate. Since the specific studies cited by Petitioners were not associated with this claim, but rather their other claims, EPA's response to the specific studies were, therefore, addressed in its responses to Petitioners' other claims. EPA went on to explain, however, that the Agency does not ignore robust, peer-reviewed data in favor of industry-sponsored data and that EPA has a public and well-documented set of procedures that it applies to the use and significance of all data utilized to inform risk management decisions. EPA does rely on registrant-generated data submitted in response to FIFRA and FFDCA requirements, as these data are conducted and evaluated in accordance with a series of internationally harmonized and scientifically peer-reviewed study protocols designed to maintain a high standard of scientific quality and reproducibility. But EPA does not end its review there. To further inform the Agency's risk assessment, EPA is committed to the consideration of other sources of information such as data identified in the open, peer-reviewed literature and information submitted by the public as part of the regulatory

evaluation of a pesticide.

F. Claim 6: EPA Failed to Properly Address the Exporting Hazard in Foreign Countries from Chlorpyrifos

In the July 16, 2012 interim Petition response, EPA issued a final denial of this claim, as it was not a claim subject to the FFDCA, which provides for an administrative objections process following the denial of a petition. EPA explained in the interim response that it lacked authority to address the risks chlorpyrifos may pose to workers in foreign countries who may not utilize worker protection equipment that the United States requires. Further, EPA noted that it has no authority to ban the export of pesticides to foreign countries regardless of whether those pesticides may be lawfully used in the United States. Accordingly, EPA denied this claim, and that denial constituted final agency action.

G. Claims 7-9: EPA failed to quantitatively incorporate data demonstrating long-lasting effects from early life exposure to chlorpyrifos in children; EPA disregarded data demonstrating that there is no evidence of a safe level of exposure during pre-birth and early life stages; and EPA failed to cite or quantitatively incorporate studies and clinical reports suggesting potential adverse effects below 10% cholinesterase inhibition.

The Petitioners asserted that human epidemiology and rodent developmental neurotoxicity data suggest that pre-natal and early life exposure to chlorpyrifos can result in long-lasting, possibly permanent damage to the nervous system and that these effects are likely occurring at exposure levels below 10% cholinesterase inhibition, EPA's existing regulatory standard for chlorpyrifos and other OPs. They assert that EPA has therefore used the wrong endpoint as a basis for regulation and that, taking into account the full spectrum of toxicity, chlorpyrifos does not meet the FFDCA safety standard or the FIFRA standard for registration.

EPA grouped these claims together because they fundamentally all raised the same issue: whether the potential exists for chlorpyrifos to cause neurodevelopmental effects in infants and children from exposures (either to mothers during pregnancy or directly to infants and children) that are lower than those resulting in 10% cholinesterase inhibition – the basis for EPA's long-standing point of departure (POD) in regulating chlorpyrifos and other OPs. EPA noted that these claims were not challenges to EPA's 2006 reregistration decision for chlorpyrifos, but rather, new challenges to EPA's ongoing approval of chlorpyrifos under FIFRA and the FFDCA because they rely in large measure on data published after EPA completed both its 2001 chlorpyrifos Interim Reregistration Decision and the 2006 OP CRA that concluded the reregistration process for chlorpyrifos and all other OPs. As matters that largely came to light after the completion of reregistration, EPA made clear that these Petition issues are being addressed as part of the registration review of chlorpyrifos – the next round of re-evaluation under FIFRA section 3(g). The Denial Order noted that the question of OP neurodevelopmental toxicity was, and remains, an issue at the cutting edge of science, involving significant uncertainties.

During registration review, EPA conducted an in-depth analysis of the available OP and chlorpyrifos biomonitoring data and of the available epidemiologic studies from three major children's health cohort studies in the U.S., specifically from the Columbia Center for Children's Environmental Health (CCCEH), Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), and Mt. Sinai. EPA three times, in 2008, 2012, and 2016 has presented approaches and proposals to the FIFRA SAP for evaluating this epidemiologic data exploring the possible connection between *in utero* and early childhood exposure to chlorpyrifos and adverse neurodevelopmental effects. The SAP's reports have rendered numerous recommendations for

additional study and sometimes conflicting advice for how EPA should consider (or not consider) the epidemiology data in conducting EPA's registration review human health risk assessment for chlorpyrifos and served to underscore that the science on this question is not resolved and would benefit from additional inquiry. Indeed, EPA explained in the Denial Order that the comments received by EPA indicate that there are considerable areas of uncertainty with regard to what the epidemiology data show and deep disagreement over how those data should be considered in EPA's risk assessment. In August 2016, the Ninth Circuit made clear, however, that EPA was to provide a final response to the Petition by March 31, 2017, and that no more extensions would be granted -- regardless of whether the science remains unsettled and irrespective of whatever options may exist for resolution of these issues during the registration review process.

While EPA acknowledged its obligation to respond to the Petition as required by the court, EPA noted that the court's order did not and could not compel EPA to complete the registration review of chlorpyrifos and the issues required for that determination in advance of the October 1, 2022 deadline provided in FIFRA section 3(g), 7 U.S.C. 136a(g). Although past EPA Administrators had proposed to attempt to complete that review several years in advance of the statutory deadline (and respond to the Petition on the same time frame), it was not possible to fully address these registration issues earlier than the registration review period. As a result, EPA concluded that it needed to adjust the schedule for chlorpyrifos so that it could complete its review of the science addressing neurodevelopmental effects prior to making a final registration review decision whether to retain, limit, or remove chlorpyrifos from the market. Accordingly, EPA denied the Petition claims and stated its intention to complete a full and appropriate review of the neurodevelopmental data before either finalizing the proposed rule of October 30, 2015, or

taking an alternative regulatory path.

EPA explained that that denial of the Petition on these grounds provided was consistent with governing law because the petition provision in FFDCA section 408(d) does not address the timing for responding to a petition, nor does it limit the extent to which EPA may coordinate or stage its petition responses with the registration review provisions of FIFRA section 3(g). Provided EPA completes registration review by October 1, 2022, Congress otherwise gave the EPA Administrator the discretion under FIFRA to determine the schedule and timing for completing the review of the over 1000 pesticide active ingredients currently subject to evaluation under FIFRA section 3(g). EPA may lawfully re-prioritize the registration review schedule developed by earlier administrations provided that decision is consistent with law and an appropriate exercise of discretion. *See Federal Communications Commission v. Fox Television Stations*, 129 S.Ct. 1800 (2009) (Administrative Procedure Act does not require that a policy change be justified by reasons more substantial than those required to adopt a policy in the first instance). Nothing in FIFRA section 3(g) precludes EPA from altering a previously established registration review schedule. Given the absence of a clear statutory directive, FIFRA and the FFDCA provide EPA with discretion to take into account EPA's registration review of a pesticide in determining how and when the Agency responds to FFDCA petitions to revoke tolerances. As outlined previously, given the importance of this matter and the fact that critical questions remained regarding the significance of the data addressing neurodevelopmental effects, EPA asserted that there is good reason to extend the registration review of chlorpyrifos and therefore to deny the Petition. To find otherwise would effectively give petitioners under the FFDCA the authority to re-order scheduling decisions regarding the FIFRA registration review process that Congress has vested in the Administrator.

H. Claim 10: Inhalation Exposure from Volatilization

Petitioners assert that when EPA completed its 2006 OP CRA, EPA failed to consider and incorporate significant exposures to chlorpyrifos-contaminated air that exist for some populations in communities where chlorpyrifos is applied. Petitioners assert that these exposures exceeded safe levels when considering cholinesterase inhibition as a POD and that developmental neurotoxicity may occur at even lower exposure levels than those resulting in cholinesterase inhibition.

To the extent Petitioners are asserting that human exposure to chlorpyrifos spray drift and volatilized chlorpyrifos present neurodevelopmental risks for infants and children, EPA denied this claim for the reasons stated in EPA's response to claims 7-9.

With respect to Petitioners' claim that exposures to spray drift and volatilized chlorpyrifos present a risk from cholinesterase inhibition, EPA denied the Petition for the reasons identified in EPA's Spray Drift Mitigation Decision of July 16, 2012, and EPA's interim response of July 15, 2014, addressing chlorpyrifos volatilization. Specifically, in the Spray Drift Mitigation Decision, EPA determined that the chlorpyrifos registrants' adoption of label mitigation (in the form of label use rate reductions and no-spray buffer zones) eliminated risk from cholinesterase inhibition as a result of spray drift. As for risks presented by volatilized chlorpyrifos that may occur following application, EPA's July 15, 2014 interim response to the Petition explained that vapor-phase inhalation studies for both chlorpyrifos and chlorpyrifos-oxon made clear that neither vapor-phase chlorpyrifos nor chlorpyrifos oxon presents a risk of cholinesterase inhibition.

V. Objections

The three separate sets of objections to the Denial Order filed with EPA in June 2017

raise similar concerns and can be reduced to the following three primary arguments:

· The Objectors argue that EPA's Denial Order applied the wrong legal standard. (Note: All persons filing objections will be referred to as "Objectors.") They assert that neither "scientific uncertainty" nor the October 2022 deadline for registration review under FIFRA section 3(g), nor the widespread agricultural use of chlorpyrifos, provide a basis for denying petitions to revoke. They claim that EPA has unlawfully left chlorpyrifos tolerances in place without making the safety finding required by the FFDCA.

· The Objectors assert that EPA has previously found that chlorpyrifos tolerances are unsafe and has not disavowed those findings. Specifically, they claim that EPA has found that chlorpyrifos results in unsafe drinking water exposures and results in adverse neurodevelopmental effects to children and that EPA must therefore revoke the tolerances.

· The Objectors argue that EPA's Denial Order committed a procedural error by failing to address significant concerns raised in the comments on EPA's 2014 risk assessment and 2015 proposed revocation that EPA's assessment fails to protect children. In particular, the Objectors focus on concerns raised in comments asserting that (1) EPA's use of 10% cholinesterase as a regulatory standard is not protective for effects to children's developing brains; (2) EPA has not properly accounted for effects from inhalation of chlorpyrifos from spray drift and volatilization; and (3) EPA inappropriately used the Corteva PBPK model to reduce inter- and intra-species safety factors because the model is ethically and scientifically deficient.

VI. Corteva's Comments on the Objections

Corteva, the primary registrant of chlorpyrifos products registered for use in agriculture, submitted a response to the objections on August 27, 2018, raising specific detailed scientific concerns with the objections (Ref. 4). In addition, Corteva states that there is nothing in the

FFDCA suggesting that statute requires EPA to make a safety finding in order to deny a response to a petition and that the FFDCA's implementing regulations place the burden on a petitioner to prove that a pesticide is unsafe. Corteva argues that to find otherwise would lead to the result that EPA is required to renew its safety finding every time a petition is filed, irrespective of the strength and quality of the evidence cited and regardless of whether EPA is engaged in an ongoing scientific review of issues addressed in the petition through FIFRA registration review.

VII. EPA's Response to Objections

EPA's responses to the specific objections summarized in Unit V. are provided in this unit.

A. *Claims Regarding the Legal Standard for Reviewing Petitions to Revoke*

Before addressing the specific legal objections, EPA notes that the Objectors' concerns focus primarily on EPA's denial of Petition claims 7-10 as they relate to the potential for adverse neurodevelopmental effects to children from exposure to chlorpyrifos in food, drinking water, and from spray drift. These concerns fundamentally relate to issues EPA is evaluating in its current registration review of chlorpyrifos. EPA is in the process of completing revised risk assessments to address new data and advancements in risk assessment methodology since EPA's 2006 safety finding for chlorpyrifos as part of FIFRA section 4 reregistration and FFDCA section 408(q) tolerance reassessment to review tolerances for pesticide residues in effect (Ref. 3). The Objectors have not materially challenged EPA's denial of Petition claims that related to matters before EPA at the time of EPA's 2006 safety finding. Specifically, they have not raised objections to the denial of claims relating to the genetic evidence for human vulnerability with respect to the detoxifying enzyme paraoxonase, endocrine-related effects, or carcinogenicity (claims 1-3). Nor have Objectors challenged most aspects of EPA's conclusions in the Denial

Order respecting the potential for current chlorpyrifos exposures to result in acetyl cholinesterase inhibition – the regulatory POD used in EPA's 2006 reregistration and tolerance reassessment decisions.

In sum, the objections are focused on EPA's ongoing work in FIFRA registration review to evaluate more recent information addressing the risk of adverse neurodevelopmental effects. With respect to these claims, EPA has concluded, after many years of attempting to obtain information necessary to validate this information, that the objections and the underlying petition fail to provide evidence of neurodevelopmental effects that is sufficiently valid, complete, and reliable at this time to meet the burden petitioners for revocation bear in presenting a case that tolerances are unsafe, pursuant to the standard under FFDCA section 408(b)(2). In addition, as provided in the Denial Order, EPA has concluded that it is also appropriate to deny the petition to allow EPA to complete its assessment of the potential for adverse neurodevelopmental outcomes in connection with the ongoing chlorpyrifos FIFRA registration review.

1. *Burden of coming forward with valid, complete, and reliable evidence.* In response to the Objectors' claims that EPA applied an incorrect legal standard in denying the Petition, EPA disagrees that the FFDCA requires EPA to make a new safety determination in response to every petition to revoke under FFDCA section 408(d) or that it must revoke tolerances in the absence of making a renewed safety determination in response to a petition. Petitioners cite the FFDCA safety definition and the findings EPA must make to establish a tolerance or leave a tolerance in effect when reassessing the safety of tolerance under FFDCA section 408(q) and FIFRA section 3(g). None of their arguments, however, specifically focus on the FFDCA section 408(d) petition process to modify or revoke a tolerance and EPA's implementing procedural regulations that require persons seeking tolerance revocation to come forward with evidence sufficient to support

a finding that the applicable safety standard has not been met. In other words, even if one were to assume, *arguendo*, that the same safety standard applies to EPA action on a petition to revoke a tolerance as applies to the Agency's initial establishment of a tolerance, that is a separate issue from the evidentiary burden a petitioner must meet to support its position. As explained in this unit, in this case, EPA reasonably construes the FFDCA and the Agency's implementing regulations to require petitioners seeking withdrawal of a tolerance to support this request with valid, complete and reliable data that set forth why the tolerances are unsafe, a burden Petitioners here have failed to meet.

By way of background, it is important to note that while Congress addressed the requirements for petitions to establish a tolerance with considerable specificity, *see* FFDCA section 408(d)(2)(A), it by contrast expressly left the specific requirements for petitions to modify or revoke a tolerance to EPA's rulemaking discretion. Id., FFDCA section 408(d)(2)(B). In turn, EPA's long-standing regulations require petitions seeking modification or revocation of a tolerance based on "new data" to furnish that data in the same form required for petitions seeking to establish tolerances, to the extent applicable. 40 CFR 180.32(b) ("New data should be furnished in the form specified in 180.7(b) [pertaining to "[p]etitions proposing tolerances"] for submitting petitions, as applicable."). Thus, Congress expressly conferred discretion on EPA to specify the requirements for withdrawal of an existing tolerance, and EPA's long-standing regulations require a petitioner seeking revocation to meet the same standard of data reliability as a petitioner seeking to establish a tolerance.

FFDCA section 408(b)(2)(D)(i) requires that all actions of the Administrator to establish, modify, leave in effect, or revoke tolerances must consider, among other factors, "the validity, completeness, and reliability of the available data from studies of the pesticide chemical and

pesticide chemical residue." Consistent with this obligation, EPA regulations provide that a petitioner has a burden to provide "reasonable grounds" for revocation, including an assertion of facts to justify the modification or revocation of the tolerance (40 CFR 180.32(b)). Further, the regulations also make clear that persons seeking revocation have an initial evidentiary burden that must be met before the question of whether the applicable safety standard under FFDCA section 408(b)(2) is met is properly placed before EPA. *See* 40 CFR 179.91 (Party requesting revocation hearing has initial burden of going forward with evidence). This longstanding interpretation of the statute and the procedures Congress established is permissible and entitled to substantial deference. *Sebelius v. Auburn Reg'l Med. Ctr.*, 133 S. Ct. 817, 826–827 (2013) (citing *National Cable & Telecomm. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967, 980 (2005)). Notably, this regulation mirrors EPA's implementing FIFRA hearing regulations at 40 CFR 164.80(a), which likewise make clear that a person seeking cancellation or suspension must present the case that the standards for those actions have been met.

Recently, in *Ellis v. Housenger*, 252 F. Supp. 3d 800, 809 (N.D. Cal. 2017), the U.S. District for the Northern District of California interpreted those regulations, explaining that the FIFRA hearing regulations place the burden on the proponent of a regulatory action to present an affirmative case for action, and that initial burden is properly applied to petitions seeking immediate action. Similarly, before the question whether the applicable safety standard under FFDCA section 408(b)(2) is met is properly placed before the EPA, petitioners must first meet their burden of coming forward with sufficient evidence to show that pesticide tolerances to be modified or revoked are not safe.

EPA concludes that Petitioners have not met that burden. Petitioners have not presented evidence to establish that chlorpyrifos tolerances must be revoked because of the risk of

neurodevelopmental effects at levels lower than EPA's currently regulatory standard. After several years and numerous, significant efforts to evaluate the petition claims related to neurodevelopmental toxicity, including communications with study authors and researchers in an effort to obtain underlying data and validate and replicate reported results, EPA concludes that the information yet presented by Petitioners is not sufficiently valid, complete, and reliable to support abandoning the use of AChE inhibition as the critical effect for regulatory purposes under the FFDCA section 408.

Cholinesterase inhibition and the cholinergic effects (i.e., the physiological or behavioral changes) caused by organophosphorous pesticides, including chlorpyrifos, have long been the endpoints that EPA and nearly every other pesticide regulatory body in the world have used in assessing potential human health hazards. EPA has regarded data showing cholinesterase inhibition in brain, red blood cell (RBC), or plasma, and data on physiological or behavioral changes as critical effects for regulatory purposes. Guideline animal toxicity studies have historically been used in support of the 10% RBC acetylcholinesterase (AChE) inhibition point of departure (POD) for chlorpyrifos in EPA risk assessments.

EPA's 2006 Registration Eligibility Decision (RED) for chlorpyrifos relied on AChE inhibition results from laboratory animals for deriving the POD. Although not acknowledged by the Petitioners and Objectors, in conducting risk assessments in support of the chlorpyrifos RED, EPA also considered the emerging new information from laboratory studies that identified potential concern for increased sensitivity and susceptibility for the young from neurodevelopmental effects unrelated to AChE inhibition. At that time, EPA did not believe those studies support a neurodevelopmental POD for quantitative risk assessment, but it did provide the support for EPA's retention of the FQPA 10X factor in the 2001 chlorpyrifos IRED

(Ref. 5).

While Petitioners and Objectors are correct that EPA did not retain the FQPA 10X for chlorpyrifos in the OPs 2006 cumulative risk assessment, that assessment dealt only with the established common mechanism of toxicity for the OPs – AChE inhibition – not with potential hazards that relate to the OPs individually. Accordingly, EPA did not reduce the 10X safety factor as it relates to chlorpyrifos specifically in its 2006 tolerance reassessment and reregistration determination that chlorpyrifos tolerances are safe. To the extent the Objectors are therefore arguing that EPA must, at a minimum, retain the FQPA 10X factor for chlorpyrifos because of the potential for neurodevelopmental effects, those objections are denied as moot. EPA's most recent assessment of the chlorpyrifos tolerances that was challenged in the Petition did retain the FQPA 10X, in part because of neurodevelopmental studies.

The Petition and the objections also argue, however, that EPA should not simply retain the FQPA 10X safety factor but should revoke chlorpyrifos tolerances because of evidence showing the potential for neurodevelopmental effects to occur well below EPA's existing regulatory standard. In sum, they believe EPA should be using the results of existing epidemiologic data to set a regulatory POD for chlorpyrifos at levels that would require EPA to revoke all chlorpyrifos tolerances.

EPA has, since the issuance of the 2006 RED, consistently concluded that the available data support a conclusion of increased sensitivity of the young to the neurotoxic effects of chlorpyrifos and for the susceptibility of the developing brain to chlorpyrifos. This conclusion comes from an evaluation across multiples lines of evidence including mechanistic studies and newer *in vivo* laboratory animal studies, but particularly with the available epidemiology reports along with feedback from the 2012 and 2016 FIFRA SAP meetings. As noted, EPA has retained

the FQPA 10X safety factor on these grounds. However, EPA and the FIFRA SAP have also consistently cited the lack of robustness of these data for deriving a POD for neurodevelopmental effects given (1) the absence of a clear mechanism of action for chlorpyrifos in the developing brain; (2) the dosing regimen in *in vivo* studies that differs from internationally accepted protocols; and (3) the lack of any meaningful raw data from the epidemiologic data that are the centerpiece of this area of inquiry.

The lack of a mechanistic understanding for effects on the developing brain precludes EPA from validly or reliably assessing potential differences (and similarities) between laboratory animals and humans with respect to dose-response and temporal windows of susceptibility. In the absence of this information, EPA has no valid or reliable ways to bridge the scientific interpretation of the laboratory studies and epidemiology studies with chlorpyrifos. In addition, the dosing regimen used in the *in vivo* studies means the data are not sufficiently valid, complete and reliable for regulatory purposes given the problems they present for the quantitative interpretation and extrapolation of the results. Specifically, the *in vivo* laboratory animal studies generally use fewer days of dosing that are aimed at specific periods of rodent fetal or early post-natal development compared to internationally adopted guideline studies which are intended to cover both pre- and post-gestational periods. The degree to which these shorter dosing periods coincide with comparable windows of susceptibility in human brain development is unclear. In addition, except for some studies conducted recently, most of the *in vivo* laboratory studies use doses that are higher than doses that cause 10% RBC AChE inhibition. These studies are therefore are not useful quantitatively to evaluate whether EPA's current regulatory standard is or is not sufficient to preclude the potential for neurodevelopmental effects.

Finally, and most significantly, despite numerous requests over the last decade, the

authors of the epidemiologic studies that provide potentially the most relevant information regarding effects to humans have never provided the underlying data from their studies to EPA to allow EPA and others to independently verify the validity and reliability of the results reported in their published articles. EPA believes it is necessary to first replicate the statistical analyses used in the studies to ensure their accuracy. In addition, EPA wants to examine the raw data used in the analysis to ensure appropriate handling of data points and in potentially conducting alternative statistical analyses. For example, EPA would want to evaluate the elimination of certain study participants from the CCCEH study that were deemed to be outliers in order to determine whether their exclusion was proper and how it may have affected the results. The lack of publicly available raw data does not necessarily preclude EPA from reliance on such information for the purpose of risk assessment. Given the long history and internationally harmonized use of acetylcholinesterase inhibition as the point of departure for chlorpyrifos, however, EPA reasonably requires more complete information regarding the studies in the published articles to establish a POD and that threshold has not been met in this instance. Due to these limitations, EPA does not believe the Petition, or the objections make the case for EPA to establish a POD based on neurodevelopmental effects, which remains central to the Petitioners' claims 7-9.

EPA understands that this conclusion is at odds with its revised risk assessment that it published for comment with the NODA in November 2016. By way of explanation, EPA notes that it has undertaken considerable efforts to assess the available chlorpyrifos data, including the references cited by the Petitioners in support for their claims related to neurodevelopmental effects. Specifically, in Chapter 4 and Appendices 2-4 of the 2014 human health risk assessment, EPA provides a detailed discussion of the strengths and uncertainties associated with

the epidemiology studies. For example, although the studies used US-based exposure profiles in real world situations, EPA noted that the lack of data on the timing of chlorpyrifos applications was a key concern in the exposure assessment. EPA conducted a preliminary review of available literature and research on epidemiology in mothers and children following exposures chlorpyrifos and other OPs, laboratory studies on animal behavior and cognition, AChE inhibition, and mechanisms of action, and took it to the SAP in 2008.

The CCCEH study used concentrations of pesticides (including chlorpyrifos) in umbilical cord blood as a measure of exposure, while two other birth cohorts used urinary biomarkers in the mothers to estimate pesticide exposure. In 2012, the EPA convened another meeting of the FIFRA SAP to review the latest experimental data related to AChE inhibition, cholinergic and non-cholinergic adverse outcomes, including neurodevelopmental studies on behavior and cognition effects. The EPA also performed an in-depth analysis of the available chlorpyrifos biomonitoring data and of the available epidemiologic studies from three major children's health cohort studies in the U.S., including those from the CCCEH, Mt. Sinai, and CHAMACOS. The EPA explored plausible hypotheses on mode of actions/adverse outcome pathways (MOAs/AOPs) leading to neurodevelopmental outcomes seen in the biomonitoring and epidemiology studies.

EPA convened another meeting of the FIFRA SAP in April 2016, which was unique in focus compared to the previous meetings in that EPA explicitly proposed using information directly from the CCCEH published articles for deriving the POD. The 2016 SAP did not support the "direct use" of the cord blood and working memory data for deriving the regulatory endpoint for several reasons, among them, the lack of raw data from the epidemiology study (Ref. 4).

This feedback is consistent with concerns raised in public comments EPA received on the

use of the epidemiology data throughout the course of registration review from the grower community, pesticide registrants, and the U.S. Department of Agriculture. The final FIFRA SAP report provides a detailed account of the concerns associated with the Agency's April 2016 proposed approach to selecting the point of departure (POD) and its use in quantitative risk assessment. Specifically, the SAP report noted that "[t] he majority of the panel stated that using cord concentrations for derivation of the POD could not be justified by any sound scientific evaluation. The Panel was conflicted with respect to the importance of a 2% change in working memory." *Id.* at 19. The Panel went on to note that "the Agency's inability to confidently estimate previous exposure patterns and/or intensity hinders the use of cord blood at delivery as an anchor from which to extrapolate back to a more toxicologically meaningful internal exposure metric." *Id.* at 42. The SAP also noted the insufficient information about timing of chlorpyrifos applications in relation to cord blood concentrations at the time of birth, as well as uncertainties about the prenatal window(s) of exposure linked to reported effects.

EPA acknowledges that the 2012 and 2016 SAPs note effects in the epidemiology and experimental studies below 10% AChE inhibition. In addition, both the 2008 and 2012 SAP commented on the strengths of the CCCEH epidemiologic studies and the value of the information they provide. However, despite these strengths, both the 2008 and 2012 Panels recommended that AChE inhibition remain as the source of data for the PODs. The 2016 SAP expressed significant reservations about the proposed approach to use the cord blood as the source of data for the POD. It noted the incompleteness of the information, including the lack of raw data, reproducibility of analytical blood data, and knowledge about chlorpyrifos application timing relative to pregnancy. EPA has evaluated the SAP's concerns, as well as public comments received on the 2016 updated human health risk assessment echoed a number of the

SAP's concern regarding use of the CCCEH study. Based on the uncertainties identified by the 2016 SAP, the published articles from CCCEH are not complete for deriving a POD. EPA acknowledges this conclusion differs from the position supported in the 2016 revised human health risk assessment, but EPA believes the shortcomings of the data identified raise issues of validity, completeness and reliability under the FFDCA that direct against using the data for risk assessment at this time. As stated in the Denial Order, EPA intends to continue its exploration of the uncertainty around using neurodevelopmental effects to establish a POD as it works to complete registration review, including renewed efforts to obtain the raw data from the epidemiologic studies that are the central to consideration of potential neurodevelopmental effects.

Notably, EPA has made requests to CCCEH, CHAMACOS, and Mt. Sinai to obtain the raw data, and visited Columbia University in an attempt to better understand their study results and what raw data exist. EPA also requested the original CCCEH study protocol to determine whether its specific questions regarding exposure timing could be addressed with the raw data. EPA was informed the CCCEH protocol was not available, and EPA did not receive the raw data from any of those research institutions. Columbia made a public commitment to "share all data gathered," however, to date, CCCEH has not provided EPA with the data, citing subject privacy concerns. In 2018, EPA explored options for blinding the data to eliminate this concern. However, through these conversations, CCCEH indicated there is no effective way to remedy this issue, citing that since the cohort is from a very small geographic area, subject identification would still be possible, and therefore, was still of concern.

In addition, EPA actively sought clarification on the kinds of residential application methods of chlorpyrifos used in New York City (NYC) during the time the CCCEH study was

conducted (1998 – 2000) in order to provide additional context to the results of the CCCEH study conclusions. Through a series of email and telephone conversations with NYC pest control officials in 2016, EPA consistently heard that chlorpyrifos was typically applied as a crack and crevice application between 1998 and 2000. Unfortunately, EPA has no way to verify that this use pattern aligns with the exposures of participants in the CCCEH study and would not be able to corroborate the correlation between crack and crevice application and the observed neurodevelopmental effects.

As indicated, EPA has undertaken considerable efforts to assess the CCCEH study, including submitting EPA's evaluation of the CCCEH study to multiple SAPs. Given that CCCEH has not shared the raw data or the results of their exploratory analyses, EPA cannot validate or confirm the data analysis performed, the degree to which the statistical methods employed were appropriate, or the extent to which (reasonable or minor) changes in assumptions may have changed any final results or conclusions. EPA has been unable to conduct its own evaluation of the study conclusions utilizing the raw data nor has EPA has been able to address the issues identified by the 2016 SAP. While EPA has retained the FQPA 10x safety factor in order to address this potential uncertainty, given the shortcomings to date of the published epidemiology data, EPA does not have sufficiently complete information to currently support using the epidemiology studies as the POD in place of AChE inhibition as the POD.

In conclusion, the epidemiologic studies are central to the Petitioner's claims regarding neurodevelopmental effects, yet the Petitioners and Objectors rely only on summaries in publications to present their case. Petitioners have not presented the raw data from the epidemiology studies for consideration of their claims. EPA has likewise been unable to obtain this critical information, though the FIFRA SAP and commenters have raised many questions

about it. So, EPA has not been able to verify the conclusions of the epidemiology studies due to this lack of raw data. Further, the lack of a clear mechanism of action and the lack of an internationally accepted dosing regimen in the *in vivo* data also preclude EPA from determining the relevance of the limited animal data addressing the potential for neurodevelopmental effects. The Petitioners have therefore failed to meet their initial burden of providing sufficiently valid, complete, and reliable evidence that neurodevelopmental effects may be occuring at levels below EPA's current regulatory standard and no information submitted with the objections addresses this shortcoming of the Petition.

2. *Reconciling FFDCA petitions to revoke and FIFRA Registration Review.* EPA also continues to conclude that denial is appropriate for claims related to matters that are the subject of registration review, specifically for chlorpyrifos, claims related to neurodevelopmental toxicity. In this case, the data deficiencies in the Petition related to neurodevelopmental toxicity that EPA is currently studying in a more up-to-date, thorough and methodical fashion in conjunction with the statutorily prescribed FIFRA re-registration process. In this context, it is particularly appropriate for EPA to take into account the substantive work that it is conducting under FIFRA in reaching its decision on the Petition.

As EPA explained in the Denial Order, to reconcile the FFDCA petition procedures with the FIFRA registration review provisions that require EPA to conduct periodic reviews of all pesticides, EPA must be able to take account of the FIFRA registration review schedule for a pesticide in determining how and when to respond to an FFDCA petition that raises issues that are also the subject of a current registration review. As noted, the Denial Order fully responded to Petitioners' claims that address the substance of EPA's 2006 safety finding, and Petitioners and the other Objectors could have chosen to challenge and litigate that determination through

the petition and judicial review provisions of the FFDCA, had they wished. The objections, however, do not for the most part go to the substance of EPA's 2006 safety finding. Those claims have largely been abandoned and instead the objections now focus only on compelling EPA to resolve on a petitioner-dictated schedule new issues regarding the potential for neurodevelopmental toxicity that are part of an ongoing evaluation in registration review in advance of the statutory deadline (October 1, 2022) provided by Congress in FIFRA section 3(g) for completing that assessment. To that end, Objectors argue that the fact Congress established a 2022 deadline for registration review is no license for EPA to delay its response to an FFDCA petition and that EPA is in fact prohibited from relying on registration review as a basis for determining how to complete other reviews of a pesticide. Specifically, they cite to language in FIFRA section 3(g)(1)(C) that states that "[n]othing in this subsection shall prohibit the Administrator from undertaking any other review of a pesticide under this chapter." Objectors have overlooked the critical language at the end of this passage ("under this chapter") that by its terms only speaks to how EPA should reconcile registration review with other reviews under FIFRA. The language does not address reviews under the FFDCA, much less prohibit EPA from reconciling its responses to FFDCA petitions with the timeframe for registration review under FIFRA. The Objectors also do not point to any language in the FFDCA prohibiting the reconciliation of a response to a petition to revoke tolerances with the registration review schedule for reviewing the pesticide – which includes a determination whether to leave existing tolerances in effect. The 15-year registration review interval reflects Congress's effort to balance the need for EPA to assure that pesticides meet the FFDCA and FIFRA standards, while at the same time recognizing that completing scientific evaluations for over 1000 active ingredients is both time- consuming and resource-intensive. During a registration review, EPA is required to

"assess changes since a pesticide's last [registration] review," including new risk assessment methods, new studies and new data on pesticides. 40 CFR 155.53(a). This is precisely the assessment EPA is in the process of undertaking in the chlorpyrifos registration review with respect to the Petition claims addressing new information on the potential for adverse neurodevelopmental effects. If, as Petitioners and Objectors argue, EPA were required to truncate its ongoing registration review process to make a new FFDCA safety finding every time it received a petition to modify or revoke tolerances, petitioners would effectively have the authority to re-order the Administrator's scheduling of registration review decisions under FIFRA and dictate the extent of inquiry EPA may put to a matter before reaching a resolution. EPA continues to believe that with the passage of FIFRA section 3(g) and the 15-year review cycle created by that provision, Congress directed the Administrator, not FFDCA petitioners, to determine the appropriate timing and process for completing the review of dietary risk within that 15-year review period. EPA therefore concludes that it is also appropriate to deny the objections and the underlying petition to the extent they seek to compel EPA's consideration of neurodevelopmental toxicity issues raised during the course of the current registration review in advance of the schedule provided by Congress under FIFRA section 3(g).

As described previously, EPA has compelling reasons to follow its regulatory process through registration review. Specifically, EPA is working to update a number of assessments that will result in a more complete, accurate assessment of the risks of chlorpyrifos than if EPA were compelled to truncate that review now. The key components of EPA's updates to its analysis are (1) Review of five new laboratory animal studies for consideration in the updated human health risk assessment, and (2) Incorporating refined use information into the 2016 updated drinking water assessment.

With respect to the animal data, in 2018, the California Department of Pesticide Regulation (CDPR) proposed to adopt a regulation designating chlorpyrifos as a toxic air contaminant (TAC) in California. As part of this determination, CDPR developed its "Final Toxic Air Contaminant Evaluation of Chlorpyrifos Risk Characterization of Spray Drift, Dietary, and Aggregate Exposures to Residential Bystanders." The CDPR risk characterization document cites five new laboratory animal studies not previously reviewed by EPA (Gomez-Gimenez et al, 2017, 2018; Silva et al, 2017; Lee et al, 2015; Carr et al, 2017). It is appropriate for EPA to review these five new studies in order to complete EPA's evaluation of potential neurodevelopmental effects. CDPR is using these studies as the main source of information for their new POD for acute oral exposure, so it is prudent for EPA to evaluate the data's quality and whether it provides the strong support for the conclusion that effects on the developing brain may occur below a dose eliciting 10% AChE inhibition that would be used to establish a new POD for the EPA's risk assessment. EPA is conducting its review in accordance with OPP's Guidance for Considering and Using Open Literature Toxicity Studies to Support Human Health Risk Assessment. It has contacted the primary investigators associated with the new animal studies in July-August 2018, and received the raw data associated with one of these studies.

As for EPA's drinking water assessment, the Agency identified certain uses, application rates, and practices described in the current chlorpyrifos labels that are not actually being used in the field and are contributing to an over-estimate of potential drinking water concentrations. EPA has requested additional information from the registrants to confirm the accuracy of these assumptions and anticipates including these updates in the Proposed Interim Decision.

To be clear, EPA remains committed to expediting its registration review determination so that it is completed well in advance of the October 2022 deadline. To that end, EPA

anticipates making available any updates to the human health and drinking water assessments for public availability and comment by summer of 2020. Updates will also include EPA's response to public comments from the previous comment periods. In addition, EPA has been engaged in discussions with the chlorpyrifos registrants that could result in further use limitations affecting the outcome of EPA's assessment. The Proposed Interim Decision incorporating these updated assessments is anticipated for public availability and comment by October 2020. If EPA were compelled to act in advance of these registration review activities, none of these assessments would be available to inform that review. For example, OPP is pursuing the use of surface water monitoring data to confidently estimate pesticide concentrations in surface water that may be sourced by community water systems. A meeting of the FIFRA Scientific Advisory Panel is planned for obtaining expert feedback on tools and methodologies currently in development for using surface water monitoring data quantitatively in drinking water assessments. While the focus of the SAP is not specific to chlorpyrifos, the EPA will consider any recommendations from the SAP that are appropriate for inclusion in the chlorpyrifos drinking water assessment.

B. Objections Asserting that EPA has Found Chlorpyrifos to be Unsafe

The Objectors argue that EPA not only failed to make a safety finding in denying the Petition, but that it has never disavowed previous EPA findings that it could not conclude chlorpyrifos is safe with respect to both the potential for adverse neurodevelopmental effects and harmful drinking water exposures. In particular, the objections point to various statements in EPA risk assessments and in EPA's 2015 proposed tolerance revocation action asserting that EPA is unable to conclude that chlorpyrifos tolerances are safe.

Contrary to these assertions, as noted by Corteva in its response to the objections, EPA has not made any findings that chlorpyrifos tolerances are not safe. In fact, EPA's last final

action with respect to the safety of chlorpyrifos tolerances was its determination in 2006 that chlorpyrifos and the other pesticides in the organophosphate class meet the FFDCA safety standard in connection with FIFRA section 4 reregistration and FFDCA section 408(q) tolerance reassessment. This is the only regulatory finding currently in effect for chlorpyrifos as EPA has taken no final action on the proposed rule it published in 2015 to comply with the Ninth Circuit mandamus order in the *PANNA v. EPA* decision. Proposed rules are just that – proposals; they do not bind federal agencies. Indeed, EPA made clear it was issuing the proposal because of the court order, without having resolved many of the issues critical to EPA's FFDCA determination and without having fully considered comments previously submitted to the Agency (69 FR 69079, 69081-83). Similarly, risk assessments that underly proposed rules are not final agency actions and likewise are not binding.

At this stage, EPA may choose to finalize, modify or withdraw the proposal based on the comments received and EPA's evaluation following its review of the comments. Until such time, EPA's statements in the proposed rule are not binding pronouncements with respect to EPA's decision whether to grant or deny the Petition. See, e.g., *Northwest Coalition for Alternatives to Pesticides v. EPA*, 544 F.3d 1043, 1051 (9th Cir. 2008) ("as long as agencies follow the proper administrative procedures, they have the authority to change their minds before issuing a final order"); *Public Citizen Health Research Grp. v. FDA*, 740 F.2d 21 (D.C. Cir. 1984) ("Neither the substance of the decision to require further study nor the circumstances leading to the decision . . . suffice, however, to permit us to leapfrog back over the Secretary's decision . . . hold the agency to its preliminary decision to promulgate a labeling requirement. In connection with the registration review of chlorpyrifos, which EPA expects to complete in advance of the October 1, 2022 statutory deadline, EPA will make a determination regarding the

safety of chlorpyrifos and will either finalize, modify or withdraw the proposal at that time.

With respect to objections related to drinking water, as explained in Unit II., a party may not raise issues in objections unless they were part of the petition. *Corn Growers v. EPA*, 613 F.3d 266 (D.C. Cir. 2010), cert. denied, 131 S. Ct. 2931 (2011). The Petition did not identify drinking water exposure as a basis for seeking tolerance revocation, and the Objectors cannot therefore raise that concern as a basis for challenging EPA's denial of the Petition. The mere fact that EPA is considering the potential impact of chlorpyrifos exposures in drinking water in the Agency's FIFRA section 3(g) registration review does not somehow provide Petitioners and Objectors with a vehicle for introducing that topic in the objections process on the Petition denial. And the objections phase of the petition process does not provide Petitioners a means to effectively start the petition process over again by raising issues that were not originally raised in the 2007 petition to revoke. Accordingly, EPA denies all objections regarding drinking water exposures. To be clear, however, EPA is continuing its FIFRA section 3(g) registration review and to complete its evaluation of drinking water exposures to chlorpyrifos. EPA will address these issues in its upcoming registration review decision.

C. Objections Asserting that the Denial Order Failed to Respond to Significant Concerns Raised in Comments

The Objectors claim that EPA has committed procedural error in failing to respond to certain comments raised in comments to EPA's 2014 Revised Human Health Risk Assessment and the 2015 proposed revocation. The Objectors appear to assert that in the absence of any comment response document in the record, EPA has violated the requirements of section 553(c) of the Administrative Procedure Act (APA) which requires agencies to give consideration to relevant matter submitted during the comment period on proposed rules. While these objections

correctly recite the requirements of the APA rulemaking provisions, the requirement to respond to comments on proposed rules applies to the "rules adopted" by agencies – i.e., final rules – and EPA has neither finalized nor withdrawn the 2015 proposed revocation rule. Further, the FFDCA does not require EPA to respond to rulemaking comments in issuing petition denial orders under FFDCA section 408(d)(4). In connection with EPA's completion of the FIFRA section 3(g) registration review of chlorpyrifos, EPA will either finalize or withdraw the proposed rule and address significant comments on the proposal at that time. But EPA has no obligation to respond to rulemaking comments in denying the Petition or responding to objections, both of which are adjudicatory actions that are not part of the rulemaking process.

In addition to raising procedural error, Objectors appear to adopt as their own substantive objections some of the comments on the proposed rule and risk assessment. Specifically, they focus on comments asserting that (1) EPA's use of 10% cholinesterase as a regulatory standard is not protective for effects to children's developing brains; (2) EPA inappropriately used Corteva's PBPK model, which is ethically and scientifically deficient, to reduce inter and intra-species safety factors; and (3) EPA has not properly accounted for effects from inhalation of chlorpyrifos from spray drift and volatilization.

The comments adopted by the Objectors regarding effects on the developing brain mirror the claims raised in the Petition regarding the potential for adverse neurodevelopmental effects. Accordingly, EPA restates its response provided in Unit VII.A.1. that the Petition and the objections fail to meet burden of presenting evidence sufficiently valid, complete and reliable to demonstrate that chlorpyrifos results in neurodevelopmental effects that render its tolerances not safe.

With respect to EPA's use of the Corteva PBPK model, these claims, as with claims

respecting drinking water, were not raised in the Petition and cannot be raised for the first time in the objections phase of the petition process. Further, the Objections appear to oppose EPA's use of the PBPK model in conducting the assessment underlying EPA's 2014 and 2016 risk assessments and 2015 proposed tolerance revocation and do not appear to address EPA's Petition denial. This objection therefore does not appear to be relevant to the Denial Order. For these reasons, this objection is also denied.

Regarding the objections related to inhalation risk, Objectors raise three distinct issues from the public comments that relate to EPA's completed inhalation exposure assessment addressing the potential for bystanders to experience cholinesterase inhibition from exposure to spray drift at the time of application and volatilized chlorpyrifos following application. First, the Objectors dispute EPA' s legal authority not to consider in its risk assessment exposures to chlorpyrifos from illegal spraying prohibited by product labeling. Second, the Objectors assert that the Denial Order inappropriately relied on two recent Corteva studies on the effects of chlorpyrifos in its vapor phase to conclude that volatilized chlorpyrifos presents no risk of cholinesterase inhibition. Third, the Objectors assert that documented poisoning incidents demonstrate that the no-spray buffer-zones that EPA approved on product labeling in 2012 are inadequate to address harm from spray drift. Objectors point specifically to a May 2017 poisoning incident in Kern County, California, involving a total of 50 people who were either harmed or put at risk, as evidence for their concern.

In response, EPA believes it is lawful and appropriate for it to consider federally enforceable chlorpyrifos product labeling restrictions in assessing the extent of bystander risk from spray drift under both the FFDCA and FIFRA. Under FIFRA, pesticide labeling use instructions are enforceable limits on the use of the product that serve as the basis for EPA's

evaluation of potential risks. Indeed, in registering pesticides, FIFRA section 3(c)(5) directs EPA to register pesticides when, among other things, a pesticide "will perform its intended function without unreasonable effects on the environment" and "when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment." These directives functionally instruct EPA to consider the intended, widespread and commonly recognized use of a pesticide as set forth on proposed product labeling in determining whether the pesticide will cause unreasonable adverse on the environment. While these provisions do not serve as a bar to EPA considering the impacts from unlawful misuse, unless such misuse is a widespread or commonly recognized practice, it does not provide a basis for regulatory action under FIFRA or a basis for determining that current tolerance levels are unsafe. Rather, misuse is first and foremost a matter for enforcement under FIFRA. It should also be noted that because chlorpyrifos is a restricted use pesticide, applicators must have specific training meant, in part, to assure proper pesticide application. When these restrictions are followed, exposures are significantly limited. To be clear, while drift is minimized when applicators follow label directions, EPA does assume that some residues may settle off-target, and that there may be dermal and incidental oral exposure from contacting residential turf adjacent to treated fields. To address the potential for cholinesterase inhibition from these exposures, EPA assessed the risk from these exposures and establishes appropriate distances between such locations and the site of application. Accordingly, following EPA's assessment of spray drift in 2012, the chlorpyrifos registrants agreed to place additional limitations on use to include use rate reductions and spray drift buffers that are sufficient to eliminate a risk of cholinesterase inhibition from lawful use.

With respect to the objections concerning volatility and the potential for cholinesterase

inhibition, EPA has not changed its position set forth in the Denial Order and does not believe it is disregarding the potential for volatilization exposures. Exposure to low levels of vapor-phase chlorpyrifos following application near treated fields is possible. After the Agency's 2011 preliminary risk assessment, Corteva submitted toxicity data that measured cholinesterase inhibition resulting from acute exposure to vapors of chlorpyrifos and its oxon rather than exposure to aerosols of these compounds as was done for previous assessments. Since inhalation exposure to bystanders will be only to vapor phase chlorpyrifos rather than aerosols due to spray drift restrictions, use of these data to assess inhalation risk of cholinesterase inhibition to bystanders is appropriate. In these vapor-phase toxicity studies, test animals were exposed in atmospheres containing saturation concentrations of chlorpyrifos and its oxon, the maximum potential level of the compounds in air. No cholinesterase inhibition was observed, and the studies were determined to have been conducted properly using saturation concentrations of the compounds and controls appropriate for these types of studies, i.e., animals receiving no pesticide exposure, as further explained in ***"Chlorpyrifos:*** *Reevaluation of the Potential Risks from Volatilization in Consideration of Chlorpyrifos Parent and Oxon Vapor Inhalation Toxicity Studies, W. Britton, W. Irwin, 6/25/14."*

EPA has also done a comprehensive review of chlorpyrifos incidents and found that most were due to accidents and misuse as specified in EPA's most recent final incident review "*Chlorpyrifos: Tier II Incident Report, S. Recore and K. Oo, 7/27/11.*" The agency is aware of the referenced Kern County chlorpyrifos incident that occurred in 2017 in which the pesticide appears to have been applied in a manner in which direct drift onto bystanders occurred, a case of misuse. Spray drift buffers address exposure to bystanders when chlorpyrifos is applied as required by the pesticide label. In addition, it should be noted that EPA's 2000 cancellation of

homeowner products and many indoor and outdoor non-residential uses (e.g., schools and parks where children may be exposed) has led, according to data from 2002-2010, to a 95% decrease in the number of incidents reported in residential areas. In sum, EPA does not believe available incident data suggests that there exists a widespread and commonly recognized practice of misusing chlorpyrifos and EPA therefore believes it is appropriate to use the enforceable label instructions as the basis for evaluating the potential for inhalation exposure from spray drift and volatilization.

VIII. Regulatory Assessment Requirements

As indicated previously, this action announces the Agency's order denying objections filed under FFDCA section 408. 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.

IX. Submission to Congress and the Comptroller General

The Congressional Review Act, 5 U.S.C. 801 *et seq.*, does not apply because this action is not a rule for purposes of 5 U.S.C. 804(3).

X. References

The following is a listing of the documents that are specifically referenced in this document. The docket includes these documents and other information considered by EPA, including documents that are referenced within the documents that are included in the docket, even if the referenced document is not physically located in the docket. For assistance in locating these other documents, please consult the person listed under **FOR FURTHER INFORMATION CONTACT**.

1. The Petition from NRDC and PANNA and EPA's various responses to it are available

in docket number EPA-HQ-OPP-2007-1005 available at *http://www.regulations.gov*.

2. The objections submitted on the Petition Denial are available in docket number EPA-HQ-OPP-2007-1005 available at *http://www.regulations.gov*.

3. For additional information on the organophosphate cumulative risk assessment, see *http://www.epa.gov/pesticides/cumulative/2006-op/op_cra_main.pdf*.

4. FIFRA Scientific Advisory Panel (2016). "Chlorpyrifos: Analysis of Biomonitoring Data". Available at: *https://www.epa.gov/sap/meeting-materials-april-19-21-2016-scientific-advisory-panel*.

5. For additional information on the 2000 chlorpyrifos IRED and 2006 chlorpyrifos RED, see *https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/red_PC-059101_1-Jul-06.pdf*.

6. FIFRA Scientific Advisory Panel (2008). "Scientific Issues Associated with Chlorpyrifos and PON1". Available in docket number EPA-HQ-OPP-2008-0274 available at *http://www.regulations.gov*.

7. EPA, 2012. "Guidance for Considering and Using Open Literature Toxicity Studies to Support Human Health Risk Assessment" as well as it's "Framework for Incorporating Human Epidemiologic & Incident Data in Health Risk Assessment." Available at *https://www.epa.gov/sites/production/files/2015-07/documents/lit-studies.pdf*.

8. EPA, 2016. Record of Correspondence. Available in docket number EPA-HQ-OPP-2015-0653.

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 18, 2019.

Alexandra Dapolito Dunn,

Assistant Administrator, Office of Chemical Safety and Pollution Prevention.