EPA'S EVALUATION AND DETERMINATION OF EPIDEMIOLOGICAL DATA FOR CHLORPYRIFOS

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Among the many legal, regulatory, and policy issues being watched closely by pesticide registrants as the U.S. Environmental Protection Agency's (EPA) long and contentious review of chlorpyrifos registrations continues is the controversy concerning when EPA may appropriately apply a tenfold uncertainty factor pursuant to the Food Quality Protection Act (FQPA 10X). This issue centers around EPA's novel and unprecedented use of epidemiological data and the statutory requirements that govern EPA's determination that sufficient uncertainty exists to warrant applying the FQPA 10X, not only to chlorpyrifos itself, but to all organophosphate (OP) pesticide products. This issue has drawn much attention and concern from pesticide registrants, and from other interested parties. The issues directly affecting chlorpyrifos have played out not only in EPA's registration review process for chlorpyrifos, but also in a court challenge to EPA's decision.

By way of brief background, FQPA establishes a default 10X safety factor for infants and children, but allows EPA to reduce or eliminate this default factor if EPA determines it will be safe for women and children based on "the validity, completeness, and reliability of the available data from studies of the pesticide chemical and pesticide chemical residue," and "the nature of the toxic effect shown to be caused by the pesticide chemical or pesticide chemical residue in such studies." In the past, EPA had repeatedly eliminated the default FQPA safety factor for particular OP pesticides based on extensive data that establish the levels at which OP pesticides inhibit acetylcholinesterase (AChE). In a September 15, 2015, document entitled "Literature Review on Neurodevelopmental Effects & FQPA Safety Factor Determination for the Organophosphate Pesticides" (2015 Literature Review), EPA determined a new FQPA safety factor for all OP pesticides based on several epidemiology studies that EPA asserted show an association between purported neurodevelopmental effects and exposures to chlorpyrifos (an OP pesticide) at levels below the threshold for AChE inhibition. Pesticide registrants criticized the scientific and legal rationale supporting this revised FQPA determination. Among the comments made were that EPA did not identify any potential Mode of Action (MOA) for the purported neurodevelopmental effects of chlorpyrifos at levels that do not inhibit AChE or demonstrate that other OP pesticides would share a similar MOA, and that EPA did not resolve critical questions concerning the absence of replication in similar epidemiology studies, the presence of potential confounding exposures, or the likely role of methodological biases. Moreover, industry stakeholders commented that EPA did not have access to the underlying data for these studies, even though the research in question was partially funded by EPA. At bottom, industry stakeholders were concerned that EPA's use of epidemiological data in making this determination ignored FQPA legal requirements and effectively established an unattainable standard for determining whether there is sufficient uncertainty to warrant retention of the FQPA 10X safety factor.

EPA's use of epidemiological data for the chlorpyrifos risk assessment has been the subject of several Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) meetings, with the most recent of these held after EPA's issuance of the 2015 Literature Review. The SAP's focus in this meeting was on an EPA proposal to use one of the epidemiology studies to establish a quantitative point of departure for the chlorpyrifos risk assessment, rather than on EPA's decision to utilize the 10X uncertainty factor. Nevertheless, the SAP review of the EPA proposal highlighted the unresolved scientific issues raised by EPA's reliance on the epidemiology studies for chlorpyrifos and fueled the concerns of industry stakeholders about the erosion of the FQPA standard governing when

there is sufficient uncertainty to warrant use of the FQPA 10X safety factor. Although the subsequent SAP report criticized EPA's proposal to use a chlorpyrifos epidemiology study to establish a point of departure for risk assessment, during the waning days of the Obama administration, EPA seemed firmly committed to its assessment of the epidemiological data for chlorpyrifos and to its interpretation of the FQPA requirements concerning application of the FQPA 10X.

The arrival of the Trump administration seemed to bring material changes in EPA policy. On March 29, 2017, EPA Administrator Pruitt signed an order denying a September 12, 2007, petition of the Pesticide Action Network North America (PANNA) and the Natural Resources Defense Council (NRDC) requesting that EPA revoke all tolerances and cancel all registrations for chlorpyrifos. This petition and the petitioners' contention that EPA had too long delayed its response have also been the subject of protracted judicial review in the Ninth Circuit Court of Appeals. The most recent case requesting a writ of mandamus was filed on September 10, 2014.

In the order denying the chlorpyrifos decision, Administrator Pruitt made a number of statements that are relevant to EPA's use of epidemiological data for chlorpyrifos risk assessment. With respect to EPA's determination of "whether the potential exists for chlorpyrifos to cause neurodevelopmental effects in children at exposure levels below EPA's existing regulatory standard (10% cholinesterase inhibition)," the order states that "Congress has provided that EPA must complete registration review by October 1, 2022," and that EPA has "concluded that it will not complete the human health portion of the registration review or any associated tolerance revocation of chlorpyrifos without first attempting to come to a clearer scientific resolution" concerning potential neurodevelopmental effects in children. The order further states that the "science addressing neurodevelopmental effects remains unresolved," and "further evaluation of the science during the remaining time for completion of registration review is warranted to achieve greater certainty as to whether the potential exists for adverse neurodevelopmental effects to occur from current human exposures to chlorpyrifos." For these reasons, EPA explains in the order that, given an August 12, 2016, order by the Ninth Circuit that "made clear" that no further extension of the March 31, 2017, deadline for responding to the petition would be granted, EPA decided to deny the petition.

This decision concerning the pending chlorpyrifos petition effectively kicked the can down the road to some extent on the key scientific issue—whether EPA has appropriately evaluated and utilized the epidemiology studies that report an association between exposure to chlorpyrifos and adverse neurological impacts on infants and children. The order language has been debated with regard to whether it also reflects any type of new EPA direction on the FQPA 10X issue. In any event, EPA's decision to deny the petition led to charges by critics of "politics over science," but in responding to the court-ordered deadline of March 31, 2017, EPA declared that it needs more time to resolve difficult science issues, time that would be afforded by the standard registration review process. EPA effectively stated that, if it must make a decision concerning these issues now, there is not an adequate scientific consensus to support regulatory action.

The controversy over EPA's use of epidemiological data and its chlorpyrifos decision generally continues in numerous venues. Petitioners in the Ninth Circuit case on April 5, 2017, filed a motion asking the court to "grant further mandamus relief [for EPA] to act on its findings that chlorpyrifos exposures are unsafe and to establish deadlines for the next steps in the revocation and cancellation processes for chlorpyrifos." A request from Congress to EPA's inspector general (IG) requesting that the IG address questions specifically targeting the rationale, communications, and consideration that Administrator Pruitt took prior to reaching the decision was submitted on April 27, 2017. On

June 5, 2017, an administrative appeal was filed by the attorneys general for California, Maine, Maryland, Massachusetts, New York, Vermont, and Washington that submits legal objections and requests immediate agency action to vacate the March order and revoke the chlorpyrifos tolerances; and a petition for review of the March order was filed in the Ninth Circuit on June 5, 2017.

A significant new development in this ongoing battle occurred on May 25, 2017, when EPA placed in the public dockets for certain OP pesticides an "update" of the September 15, 2015, Literature Review and FQPA determination, along with a response to comments on the original document. These newly disclosed documents were signed by EPA scientists on December 29, 2016. The documents attempt to rebut the various criticisms of EPA's assessment of the epidemiology studies for chlorpyrifos and the original FQPA safety factor determination for OP pesticides, and they reaffirm the policy embodied in the original Literature Review. Because these documents were signed in the last days of the Obama administration, they are likely to be viewed by industry stakeholders as an effort by some at EPA to "lock in" the prior policy concerning OP pesticides before the arrival of the Trump administration.

The legal and policy issues posed by EPA's evaluation of the epidemiological data for chlorpyrifos and by EPA's determination that these data create sufficient uncertainty to warrant retention of the FQPA 10X safety factor for all OP pesticides will be a continued source of controversy, and will be watched with interest by all stakeholders.

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