United States Department of Agriculture

Research, Education, and Economics
Agricultural Research Service

April 30, 2015

Richard Keigwin, Director
Pesticide Re-Evaluation Division (7508P)
Office of Pesticide Programs, Environmental Protection Agency
1200 Pennsylvania Ave., N.W.
Washington, DC 20460-0001

Re: USDA Public Comments on the Chlorpyrifos Registration Review; Revised Human Health Risk Assessment published in the January 14, 2015 Federal Register; EPA docket identification (ID) number EPA-HQ-OPP-2008-0850

Dear Mr. Keigwin:

On behalf of USDA, thank you for the opportunity to comment on EPA's Revised Human Health Risk Assessment for chlorpyrifos published January 14, 2015 in the Federal Register. Chlorpyrifos is an important pest management tool that has been successfully used for over fifty years. USDA appreciates that, in late 2014, EPA further validated the chemical's critical role in U.S. agriculture when chlorpyrifos was listed as one of the alternatives to neonicotinoid seed treatment. (http://www2.epa.gov/sites/production/files/2014-10/documents/benefits_of_neonicotinoid_seed_treatments_to_soybean_production_2.pdf).

However, USDA does have concerns about the risk assessment as it includes potential precedent setting methods for assessing drinking water risk, implementing physiologically-based pharmacokinetic (PBPK) modeling and new methods for deriving the FQPA Safety Factor. The human health assessment could be strengthened by increasing transparency in the discussion of inputs from dietary exposure modeling for the PBPK modeling. It is difficult to identify the use patterns associated with the risk pathways examined. In addition, there is a lack of transparency with regard to the Columbia Study which appears to be the foundation for the FQPA Safety Factor. That study received a critical review by the EPA's Science Advisory Panel in 2012. The criteria for selecting epidemiological studies for use in derivation of safety factors should be provided and reviewed. In this case, without access to the raw data underlying this study it is not possible to fully evaluate the suitability of this study or the degree to which its findings may be generalized for use in a national risk assessment.

USDA's detailed comments are attached. Please let me know if you would like to discuss.

Sincerely,

Sheryl H. Kunickis

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Director

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USDA Comments on Chlorpyrifos Risk Assessment

The EPA risk assessment on chlorpyrifos represents a substantial amount of effort by the Agency. Given that there are over 82 separate files in the docket associated with the risk assessment, the Agency could better improve communication of the results and identification of the likely risk drivers across the various types of assessments and current use patterns. The Guide to Commenters is helpful but falls short of providing an overall organizational structure for the massive amount of information supporting the risk assessment. We greatly appreciate the transparency EPA has shown in providing the number of supporting documents included in the docket. These documents would better contribute to risk communication if there was a "roadmap" for reading them. It would be useful to have a document linking the primary and supporting material in the docket by category type and date. For example, it would be useful to see a chart comparing all of the use patterns by the estimated risk metric from the human health dietary (food only) assessment, drinking water assessment, residential/bystander assessment, and ecological risk assessment. The chart would include the crops and use patterns (i.e., application rates, timing, etc.) evaluated when feasible. For the dietary assessment, the foods determined to be risk drivers would be included in this chart. Even if the risk metric provided is a qualitative categorical summation of the extremely detailed quantitative estimate, this type of chart would provide very useful information to readers, especially agricultural stakeholder and other users of chlorpyrifos. Within each of the assessments, it would be useful to see the assumptions listed in a tabular form as well as the input data used. Another table providing an estimate of the uncertainty associated with assumptions, specific inputs or model structure would be invaluable.

The risk assessment could be further refined. The aggregate assessment finds exposures from food, residential use and drinking water to be above the levels of concern for some vulnerable population groups. It is unclear which foods may be risk drivers as well as unclear which dermal exposure scenarios in combination with food contribute most to the total exposure. Because the drinking water exposure "fits" into the remaining area of the risk cup after accounting for these other exposure sources, there should be some discussion of the sensitivity of the aggregate model to particular input data used in the dietary and residential assessments. If the residential exposure

is the result of a specific set of assumed scenarios, it would be clearer if the Agency provided sensitivity analysis showing how results might differ if other input data from other scenarios were used. The drinking water risk assessment relies on estimated surface water concentrations – this likely overestimates exposure when community drinking water systems provide water as some of the residue or degradation product will likely be removed due to treatment. Assuming treatment of all possible crop acres where chlorpyrifos is registered could be refined, perhaps using data sets such as the California pesticide use data, to include a more representative typical crop treated scenario. With all of the various assessments, providing estimates of uncertainty about the results would provide additional information.

The derivation of the FQPA factor based solely on epidemiological evidence appears to be a novel application. Previously the FQPA safety factor was supported by laboratory tests required under Part 158. Derivation of the FQPA safety factor has evolved from the initial findings based primarily on the completeness of the toxicity database, the type and severity of the effect observed, and the nature and quality of the available exposure data but the use of epidemiological data has not been well discussed. It would be more transparent if the Agency developed a new standard operating procedure for using epidemiological data when deriving a FQPA safety factor and convened an expert panel to review the SOP. It is not possible to obtain the underlying data for the epidemiological study by the Columbia researchers currently relied upon by the agency. Basing the FQPA safety factor on one or even a small number of epidemiological studies raises reproducibility and reliability concerns. The specific characteristics of the study used that make it reliable, reproducible, generalizability to other populations are not well discussed nor is there a robust discussion of potential sources of uncertainty inherent in the study. Standards for acceptance of such epidemiological studies should be defined. We were unable to locate a standard operating procedure applicable to the use of epidemiological studies when setting the FQPA safety factor, although we did find the 2010 Draft Framework for incorporating Human Epidemiologic & Incident Data in Health Risk Assessment. Among the key guidance documents relied upon by the Agency in the table on page 9 of this Draft Framework is the Food Quality Protection Act 10X Safety Factor document. The use of epidemiological data to support the 10X

factor is not discussed in this document. If epidemiological studies are to form the basis of the FQPA factor, a new standard operating is needed.

Unless the risk mitigation actions are to be conducted on a watershed basis, using a watershed or community water system as the geographic scale for the drinking water risk estimation is likely to mischaracterize the risk when considered at a national or regional scale. The Agency asks for comments on this new capability for targeting – further information on the potential use of this information in risk characterization and potentially risk mitigation is needed.

These types of watershed analyses should also include monitoring data or other empirical measurements of chlorpyrifos to provide some evaluation of the ability of the modeling approaches used to simulate actual observed in-stream concentrations. There are many types of uncertainties inherent in watershed simulation. Verification that the modeling approach is reliably able to simulate the behavior of chlorpyrifos concentrations in lotic or lentic environments would increase confidence in the drinking water exposure assessment. Further analysis of monitoring data from finished drinking water samples from community water systems would provide real-world data on actual exposures. More explanation is needed for the Agency's drinking water intake database for identification of vulnerable community water systems. The assumption that a portion of the watershed is treated will influence the estimation of chlorpyrifos concentrations in surface water. This will be difficult to determine in States other than California where pesticide usage is recorded by crop for individual users. Assuming all registered use patterns undergo treatment during the same year or season will overestimate exposure.

EPA Should Reduce the 10X FQPA Safety Factor

USDA encourages EPA to reconsider the retention of the default 10X FQPA safety factor for infants, children, youths, and women of childbearing age, which had been reduced to 1X for most exposure routes in the 2011 Preliminary Human Health Assessment. The primary purpose of the FQPA safety factor is to address inadequacies or gaps in required studies or when important data needed to evaluate risks to children are missing or inadequate ("Determination of the Appropriate FQPA

Safety Factor(s) in Tolerance Assessment," Office of Pesticide Programs, U.S. Environmental Protection Agency, Feb. 28, 2002). USDA believes that no significant data deficiencies exist in this case, and that therefore EPA should not be precluded from reducing the 10X FQPA safety factor.

The points of departure in this assessment are derived from PBPK-PD modeling and are modified by data-derived extrapolation factors (DDEF), as opposed to a traditional approach encompassing a NOAEL and uncertainty factors. EPA's ability to use PBPK-PD modeling and DDEF demonstrates how comparatively data-rich its situation is when addressing chlorpyrifos. As a result of the many years of thorough study and evaluation of chlorpyrifos, it is inappropriate to use the default 10X FQPA safety factor which is intended for assessments with significant data deficiencies.

The purpose of the FQPA safety factor is to account for uncertainties present in the relationship between an adverse outcome observed in research studies (usually quantified in a point of departure) and a *corresponding* acceptable human exposure level (such as a population adjusted dose). In this assessment, EPA is evaluating two separate adverse outcomes: 10 % inhibition of RBC AChE and the neurodevelopmental effects potentially detected by the Columbia Study. The 10X FQPA safety factor is ostensibly *justified* due to uncertainty associated with the neurodevelopmental effects, but it is then *applied* to the point of departure based on 10 % inhibition of RBC AChE. This point of departure is based on extensive data and research, and does not contain any of the uncertainties that would usually require an FQPA safety factor greater than 1X.

If EPA could substantiate the connection between exposure to chlorpyrifos and the neurodevelopmental effects observed in the Columbia Study and could calculate a point of departure for these adverse outcomes, it might be appropriate to apply uncertainty and safety factors to this new neurodevelopmental point of departure. However, the limitations of the epidemiologic studies, which do not provide a clear understanding of exposure, dose-response, or mode of action/adverse outcome pathway, do not allow such a point of departure to be

calculated. These same, limited epidemiologic studies should not be used to justify the addition of an FQPA safety factor to the much more robust 10 % inhibition of RBC AChE point of departure.

Epidemiological Issues

USDA agrees with the concern raised by some SAP members in 2012 regarding the potential neurodevelopmental effect of chlorpyrifos based on the Columbia cohort. Exposure to other chemicals other than chlorpyrifos may have influenced the outcome. The Panel suggested that, given the short half-life of chlorpyrifos, a longitudinal study with frequent measurements throughout pregnancy would "fill many of the data gaps." A well-designed study would overcome "inadequate sample size" limitations.

USDA urges that the data be made available to the broader toxicology community for quality review given that the SAP "expresses concern over the Agency's focus on a 10% AChE (acetyl cholinesterase) activity reduction." The Panel worried that "there is no proposed mechanism whereby a 10% AChE activity reduction would be responsible for a cognitive defect or developmental delay in their offspring."

http://www.epa.gov/scipoly/sap/meetings/2012/april/041012minutes.pdf,

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"Although in agreement with the Agency that chlorpyrifos could have played a role in the neurodevelopmental outcomes observed in the Columbia cohort, some panel members expressed concern about associating the observed deficits in neurodevelopmental outcomes in children with a single chemical. This is because the studies entail a multichemical exposure spanning a multi-year period that encompasses an important period of sequential developmental processes necessary for brain maturation. Thus, panel members caution that it is very difficult to attribute the independent physiological effects to a single chemical in this type of multi-chemical exposure

scenario. An additional concern raised by the Panel is the modest sample sizes of the studies. They deem inadequate sample size as one of the most important limitations of these studies."

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"The Panel notes that it is important to realize that the short half-life of chlorpyrifos and its metabolites in the body calls into question any "spot data" that might be used. Large cross-sectional studies may capture some exposure but they do not put these exposures into context. Longitudinal investigations with frequent samplings are more likely to provide data that are more useful. Thus, the Panel recommends that a longitudinal study with measurement throughout the pregnancy (rather than a few samples in the last trimester) would fill many of the data gaps that currently exist for this group. Such a study is needed given the potential for neurodevelopmental effects on the fetus as well as the metabolic differences in pregnant women versus the workers from the 1984 study."

"Lastly, the Panel expresses concern over the Agency's focus on a 10% AChE activity reduction. They point out that to their knowledge there is no proposed mechanism whereby a 10% AChE activity reduction in pregnant women would be responsible for a cognitive defect or developmental delay in their offspring."

Occupational Risk Assessment

USDA notes that the use of a 10X safety factor employed in the chlorpyrifos risk assessment as a result of the Columbia University cohort was incorporated into the occupational assessment for chlorpyrifos. USDA considers that the application of a default FQPA10X safety factor for women of child-bearing age for workers is beyond the scope of the requirements of the Food Quality Protection Act. During the Registration Review effort, EPA had appropriately adhered to the FQPA requirements by combining exposures from only dietary, residential, and drinking water sources.

In keeping with the recommendation of the 2012 SAP, USDA urges that EPA call-in data from the registrant for improving the endpoints of the chlorpyrifos occupational risk assessment. PBPK

modeling might be used to determine an appropriate intraspecies uncertainty factor specific for chlorpyrifos for women in pregnancy.

http://www.epa.gov/pesticides/regulating/laws/fqpa/fqpa_implementation.htm
" FQPA requires EPA to consider all "aggregate risk" from exposure to a pesticide from multiple sources when assessing tolerances."

"EPA has developed sound scientific procedures for evaluating aggregate exposures to pesticides. These new and improved procedures have enabled EPA to conduct risk assessments that combine exposures from dietary, residential, and drinking water sources, and to ensure that exposure to pesticides in food are safe in light of the aggregate exposure."

Critical need for chlorpyrifos

Chlorpyrifos is a broad-spectrum control material that has been a part of growers' IPM programs for about 50 years to control a wide array of primary and secondary pests in over 75 cropping systems. The impacts to these cropping systems if chlorpyrifos was eliminated or severely restricted would be immediate and deeply experienced, in terms of efficacy of pest management programs, increased costs to growers switching to more expensive, more frequently applied and less effective alternatives, and disruption to current and historical IPM programs across these cropping systems. In some systems a lack of effective alternatives targeting control of primary pests, such as root maggot in sugar beets, presents serious concern of economic damage if the pest is left uncontrolled.

Crop uses: Major Crops: Soybean, corn (field, sweet and seed), cotton, wheat, sorghum, sugar beet, sunflower, tobacco, and almond.

Minor Crop Uses (chlorpyrifos use in minor crops is applied predominantly with the use of ground application technologies (ground booms and airblast), with some aerial applications made in walnut): apples, grape, stonefruit (5 crops), pears, alfalfa, fig, strawberry, cole crops (18 crops), legume vegetables (over 3 dozen),

cucumber, ginseng, citrus (15 crops), cranberry, mint, onion, peanuts, sunflower, sweet potatoes, walnuts, filberts, pecans, asparagus, brussel sprouts, cranberries, broccoli, and cauliflower.

Non-crop uses: Golf courses, turf (sod), green houses, Christmas trees, non-structural wood treatments such as utility poles and fence posts, ant bait stations, fire ant control and mosquitoes, clover for seed, and ornamental trees (nursery).

In addition to its efficacious broad-spectrum control, growers have a historical knowledge of how chlorpyrifos fits into a season-long control program to manage an array of pests. For example, use of chlorpyrifos in tree fruit and tree nut crops is timed to target control of pest insects with minimum harm to beneficial natural enemies of mites, aphids and scale insects, thereby maximizing control of these secondary pests through conservation biocontrol. Many of the alternatives to chlorpyrifos, primarily pyrethroid insecticides, are lethal to beneficial natural enemies, thereby requiring additional spray applications to control secondary pests.

Chlorpyrifos is also an important tool for growers in addressing consumer and regulatory demands for zero tolerance for insect infested fruit at harvest. Alternatives to chlorpyrifos present an array of challenges to producers, including meeting Maximum Residue Limits (MRL) for sale of food and fiber to export markets and management of invasive pest species, such as the brown marmorated stinkbug.

Chlorpyrifos currently has many use restrictions to mitigate risk in a number of cropping systems to workers and the environment. Use for in-season application in grapes is not allowed (no application to fruit or foliage), is limited to one dormant/delayed application in stone and pome fruit (a post-bloom application to the lower four feet of apple tree trunks to protect against tree-boring insects), has a 24-hour use restriction in conjunction with flood irrigation to avoid contamination of tail waters, and an array of Pre-Harvest Intervals (21 day PHI in peanut, 60 days in onion, 90 days in mint and 125 day PHI in sweet potato), to manage residue on food and protect

workers. Use is currently restricted to one application per year in apple (either pre-bloom dormant or post-bloom tree trunk), cranberry, legume vegetables (except soybean), onion, peanut (pre-plant), pear (post-harvest), mint, strawberry, sweet potato, tobacco, almond (no application on almonds in the following counties in California: Butte, Colusa, Glenn, Solano, Sutter, Tehama, Yolo, and Yuba) walnut, nectarine, and peach.