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Office of Pesticide Programs (OPP)
Regulatory Public Docket (7502P)
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington DC 20460-0001

Re: Human Health Risk Assessments. Revisions to Chlorpyrifos Registration Review.
Docket Number: EPA-HQ-OPP-2008-0850

Dear Sir/Madam,

We are submitting comments on the U.S. Environmental Protection Agency's (EPA) most recent revisions to the human health risk assessment for chlorpyrifos. Beyond Pesticides has submitted several comments to the agency in regard to chlorpyrifos' continued registration. These comments reiterate calls in previous comments to revoke the registration of chlorpyrifos and its food tolerances, given the serious toxicological issues associated with chlorpyrifos use and exposures, and its failure to meet the standards set forth in Section 3(c)(5)(C) of the *Federal Insecticide Fungicide and Rodenticide Act* (FIFRA). Continued use poses "unreasonable adverse effects on the environment."

Chlorpyrifos is a cholinesterase inhibitor that binds irreversibly to the active site of an essential enzyme for normal nerve impulse transmission, acetylcholine esterase (AchE), inactivating the enzyme. The scientific evidence of neurotoxic dangers associated with chlorpyrifos exposure is extensive and consistent. Epidemiological data also points to subpopulations that are disproportionately affected by chlorpyrifos exposures. Low-income African-American and Latino families, including farmworker families, continue to suffer the most, and this disproportionate impact creates an environmental justice issue that the agency must not continue to ignore. In its assessments, EPA has relied on the PBPK-PD model to update its human health risk assessment. However, while models are useful, they should be used as supplemental tools and not substitute for sound laboratory and biomonitoring data.

Last year, groups sued EPA (Pesticide Action Network North America et al. v. U.S. Environmental Protection Agency, case number 14-72794) to compel the agency to fully respond to a 2007 petition after a lengthy seven-year delay. The groups are asking the court to find that EPA "unreasonably delayed fulfilling its legal obligations" and that the agency respond to the 2007 petition by issuing a final decision. Beyond Pesticides supports calls for the agency to respond the legal challenges regarding continued chlorpyrifos use, and again urges the agency to remove the toxic chemical from the market,

especially in light of alternatives currently available. At the end of this registration review for chlorpyrifos, the agency must deny its registration eligibility.

Limitations of the PBPK-PD model

Physiologically-based pharmacokinetic and pharmacodynamic models (PBPK-PD) have a useful place in the risk assessment process. The PBPK-PD model incorporates physiologic processes to describe relationships between the dose to which an organism is exposed and the biologically effective concentration that acts at the target tissue(s), taking into account the organism's weight, age sex, metabolic rates and other parameters.[1] These models can also shed light on biological mechanisms and the development of a particular endpoint, as well as interspecies extrapolations. However, like most models, there are several inherent limitations that should prevent a dependency on model outputs.

The PBPK-PD model requires sufficient and accurate experimental data to construct and validate the model. Unfortunately, data gaps and insufficient scientific data continue to plague the agency's assessment of many pesticide substances. Additionally, if the input data and assumptions used to build the model are flawed, then the model output will be flawed. For instance, assumptions about metabolic kinetics may be oversimplified and not representative of what really occurs in the body depending on age, weight, or gender of the species in question. As such, the PBPK-PD model, while useful as a supplemental tool in the risk assessment process, may never be able to duplicate the complexity of an organism's biological kinetics and dynamics, and thus must not dominate EPA's risk assessment process. EPA should be extremely cautious with its intention to reduce certain uncertainty factors based on the PBPK-PD model.

Instead, EPA must focus on improving the scientific integrity and evaluation of human and epidemiological data in its risk assessments, and work to eliminate data gaps from its registration process.

FQPA 10X Safety Factor Retention

In the 2011 assessment, EPA proposed to reduce the *Food Quality Protection Act* (FQPA) safety factor for certain exposures. This safety factor is an additional "margin of safety" put in place to protect vulnerable populations, especially children, from pesticide exposures. Beyond Pesticides and others in comments challenged EPA's reduction of the safety factor, given that the human health risk, especially to children, is associated with significant neurodevelopmental effects. In response to this, recent neurotoxicity data, and feedback from a 2012 Scientific Advisory Panel that found chlorpyrifos exposures during certain developmental periods produced significant and long-term effects, EPA now states that it will retain the FQPA 10X safety factor for "infants, children, youths, and women of childbearing age for all exposure scenarios."[2]

[1] Sullivan, J and Krieger, G. (Eds.). (2001). Clinical Environmental Health and Toxic Exposures. Second Edition. Lippincott Williams and Wilkins 2001.

[2] USEPA. 2014. Chlorpyrifos: Updated Occupational and Residential Exposures Assessment for Registration Review. Office of Chemical Safety and Pollution Prevention. Washington DC.

The fact remains that a reduction in the FQPA safety factor for a highly toxic pesticide like chlorpyrifos should never have been considered. Given the wealth of laboratory and epidemiological data on the neurotoxicity of chlorpyrifos, removing this safety factor puts the most vulnerable at extreme risk.

Existing Epidemiological Evidence of Chlorpyrifos' Neurotoxic Potential Calls for Registration Revocation

Evidence of the neurotoxic dangers associated with chlorpyrifos' exposure are well-known, extensive and consistent. Studies have documented that exposure to low levels of chlorpyrifos during pregnancy can impair learning, change brain function, and alter thyroid levels of offspring into adulthood, especially females.[3,4,5,6] In the preliminary human health assessment, EPA identified recent epidemiological study with mothers and their children for review.[7] This updated human health assessment has reviewed the data identified, and EPA now agrees that chlorpyrifos did play a role in the neurological outcomes reported by the study. The study in question, conducted by researchers at the Mailman School of Public Health at Columbia University, measured chlorpyrifos in umbilical cord blood and conducted intelligence tests for children of these mothers at age 7 years. The study was part of a series of ongoing prospective cohort studies in inner-city minority populations, linking exposure to chlorpyrifos to early childhood developmental delays. One study from this research group, published in the *American Journal of Public Health,* compared motor and mental development to levels of exposure to the pesticide at birth in 266 children born between 1998 and 2002 living in low-income neighborhoods of the South Bronx and northern Manhattan in New York City. The study found that concentrations of chlorpyrifos in umbilical cord blood correspond to a decrease in the psychomotor development and a decrease in the mental development in 3 year olds.[8] A follow-up study in 2012 finds that children with high exposure levels of chlorpyrifos have changes to the brain, including enlargement of superior temporal, posterior middle temporal, and inferior postcentral gyri bilaterally, and enlarged superior frontal gyrus, gyrus rectus, cuneus, and precuneus along the mesial wall of the right hemisphere.[9] For children with lower exposures, a significant exposure/ IQ interaction is observed due to chlorpyrfos' disruption of normal IQ associations.

Additional research by Rauh et al. finds that children exposed to high levels of chlorpyrifos had mental development delays, attention problems, attention-deficit/hyperactivity disorder problems, and

[3] Haviland et al. 2009. Long-term sex selective hormonal and behavior alterations in mice exposed to low doses of chlorpyrifos in utero. *Reproduc. Tox*. 29(1):74-9.
[4]Abou-Donia MB, et al. 2006. In utero exposure to nicotine and chlorpyrifos alone, and in combination produces persistent sensorimotor deficits and Purkinje neuron loss in the cerebellum of adult offspring rats. *Arch Toxicol.*;80(9):620-31.
[5] Abdel-Rahman A, et al. 2003. Increased expression of glial fibrillary acidic protein in cerebellum and hippocampus: differential effects on neonatal brain regional acetylcholinesterase following maternal exposure to combined chlorpyrifos and nicotine. *J Toxicol Environ Health A*.;66(21):2047-66.
[6] Icenogle LM, et al. 2004. Behavioral alterations in adolescent and adult rats caused by a brief subtoxic exposure to chlorpyrifos during neurulation. *Neurotoxicol Teratol*;26(1):95-101.
[7] USEPA. 2011. Chlorpyrifos: Preliminary Human Health Assessment for Registration Review. Office of Chemical Safety and Pollution Prevention. Washington DC.
[8] Lovasi, GS, et al. 2011. Chlorpyrifos Exposure and Urban Residential Environment Characteristics as Determinants of Early Childhood Neurodevelopment. *Am J Public Health;*101(1):63-70.
[9] Rauh VA, Perera FP, Horton MK, et al. 2012. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. *Proc Natl Acad Sci U S A*. 109(20):7871-6.

pervasive developmental disorder problems at three years of age.[10,11] The results of these cohort studies have consistently found that depressed cognitive development, birth weights and other neurodevelopmental endpoints are adversely impacted by chlorpyrifos and other pesticidal exposures.[12]

One study from the University of California, Berkeley, examining families in the intensive agricultural region of Salinas Valley, California, found that IQ levels for children with the most organophosphate (OP) exposure were a full seven IQ points lower than those with the lowest exposure levels. The Berkeley team also found that every tenfold increase in measures of OPs detected during a mother's pregnancy corresponded to a 5.5 point drop in overall IQ scores in the seven-year-olds.[13] Researchers from Mount Sinai School of Medicine also found that prenatal exposure to organophosphates is negatively associated with cognitive development, particularly perceptual reasoning, with evidence of effects beginning at 12 months and continuing through early childhood.[14] Additionally, research from the University of California, Davis, Childhood Autism Risks from Genetics and the Environment (CHARGE) study finds that pregnant women who live within a mile of agricultural fields treated with insecticides are more likely to have their child develop autism.[15] For women who lived less than one mile from crops sprayed with OP insecticides during their pregnancy, researchers found the likelihood of their child being diagnosed with autism increased 60%. Women in the second trimester living near fields treated with chlorpyrifos are 3.3 times more likely to have their children diagnosed with autism.

Fortunately, as a result of EPA's review of the Columbia University study, the agency has stated it will retain the 10X FQPA safety factor for infants, children, youths, and women of childbearing age, as noted above. However, these studies call for a much broader precautionary measure and restriction of this pesticide. Protection of these vulnerable populations will only be achieved by a complete ban of the chlorpyrifos.

Farmworkers and their Families Still at Risk

Previous chlorpyrifos assessments found that certain occupational exposures are of concern, even with all feasible personal protective equipment (PPE) or engineering controls. EPA has been aware that more PPEs will not significantly reduce exposure risks, yet the agency went forward with recommending the use of PPEs. This updated assessment also finds that certain occupational handler exposure scenarios pose risks to workers. According to the agency, of the 285 scenarios assessed, 126 exposure scenarios remain a concern, in spite of the adoption of personal protective equipment (PPE) or application measures. The agency also identified 27 exposure scenarios that are risks of concern, which the agency

[10] Rauh VA. 2006. Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. *Pediatrics*;118(6):e1845-59.
[11] Rauh V, Arunajadai S, Horton M, Perera F, Hoepner L, Barr DB, et al. 2011. Seven-Year Neurodevelopmental Scores and Prenatal Exposure to Chlorpyrifos, a Common Agricultural Pesticide. *Environ Health Perspect* 119:1196-1201.
[12] Perera FP, et al. 2005. A summary of recent findings on birth outcomes and developmental effects of prenatal ETS, PAH, and pesticide exposures. *Neurotoxicology*;26(4):573-87.
[13] Bouchard MF, Chevrier J, Harley KG, Kogut K, Vedar M, Calderon N, et al. 2011. Prenatal Exposure to Organophosphate Pesticides and IQ in 7-Year-Old Children. *Environ Health Perspect*. 119:1189-1195.
[14] Engel, S. et al. 2011. Prenatal Exposure to Organophosphates, Paraoxonase 1, and Cognitive Development in Childhood. *Environ Health Perspect.* 119:1182-1188.
[15] Shelton, J, Geraghty, EM, Tancredi, DJ, et al. 2014. Neurodevelopmental Disorders and Prenatal Residential Proximity to Agricultural Pesticides: The CHARGE Study. *Environ Health Perspect*. 122:1103–1109.

believes can be mitigated with additional PPEs. However, mitigation using PPEs will not reduce exposure risks.

Recently, EPA held for public comment the draft revisions to the worker protection standards (WPS). The WPS is an important measure to help protect farmworkers from chlorpyrifos and other pesticides, and must be a robust set of standards that account for the inherent dangers of drift that come with pesticide use. Several commenters, including Beyond Pesticides, highlighted some recommendations to the proposed rule. These include establishing broader drift and volatilization protections, and improving safeguards and technologies for worker PPEs. But, even if there were to be significant improvements to PPE design and construction, workers will face dangers from unintended exposures resulting from the inevitable pesticide migration off treated sites.

Farmworker communities tend to live adjacent to target fields, and within the buffer zones of many agricultural fields. Farmworker studies routinely show high exposure risks and disease from pesticide drift in these communities.[16,17,18] While occupational assessments address worker exposures, they do not address exposures occurring in and outside the home of these worker communities, which also house vulnerable children. Indoor residues of chlorpyrifos have been detected in relatively high concentrations.[19] One study looking at migrant farmworker housing reports multiple detections of pesticides in the urine of the workers, with chlorpyrifos detected in 44 percent of the community sample.[20] Incidentally, in this study none of the participants were pesticide applicators, but were involved in harvesting. The study finds that exposures can continue within the housing community, via pathways that are not accounted for in the risk assessment process, e.g., inhalation and dermal exposures from lingering residues on contaminated clothing and shoes stored within the home. A recent incident reported by the Centers for Disease Control and Prevention (CDC) details the poisoning of farmworkers from pesticide drift from an adjacent field.[21] Here, pesticide residues were found on not only the workers' clothing, but also on the portable toilets used by the workers demonstrating that workers can be exposed directly and indirectly from drifting pesticides, when PPEs are not in use.

Despite federal regulations to reduce pesticide exposure (e.g., PPEs) among farmworkers, research conducted in farmworker communities show that such regulations are only partially enforced.[22] High levels of pesticides, including chlorpyrifos, continue to be detected among farmworker communities across the country as evidence that PPEs and other controls do not go far enough to protect these

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[16] Das R, Steege A, Baron S, et al. 2001. Pesticide-related illness among migrant farm workers in the United States. *Int J Occup Environ Health*. 7(4):303-12.

[17] Reeves M, Schafer KS. 2003. Greater risks, fewer rights: U.S. farmworkers and pesticides. *Int J Occup Environ Health*. 9(1):30-9.

[18] CDC. 2006. Worker illness related to ground application of pesticide--Kern County, California, 2005. *MMWR Morb Mortal Wkly Rep*. 55(17):486-8.

[19] Harnly ME, Bradman A, Nishioka M, et al. 2009. Pesticides in dust from homes in an agricultural area. *Environ Sci Technol*. 43(23):8767-74.

[20] Raymer, JH, Studabaker, W, et al. 2014. Pesticide Exposures to Migrant Farmworkers in Eastern NC: Detection of metabolites in farmworker urine associated with housing violations and camp characteristics. *Am J Ind Med.* 57(3): 323–337.

[21] Calvert, G, Rodriguez, L at al. 2015. Worker Illness Related to Newly Marketed Pesticides — Douglas County, Washington, 2014. *Morbidity and Mortality Weekly Report (MMWR).* 64(02);42-44.

[22] Arcury, T. and Quandt, S. (eds). Latino Farmworkers in the Eastern United States. Chapter 5. Pesticide Exposure Among Farmworkers and Their Families in the Eastern United States: Matters of Social and Environmental Justice. DOI: 10.1007/978-0-387-88347-2_5. Springer Science +Business Media . LLC 2009.

vulnerable populations, given the impact pesticide drift has on these communities. This is a social and environmental justice issue that must quickly be addressed by the agency. EPA's assessments continue to show that chlorpyrifos uses cannot be adequately mitigated by PPEs and thus these uses should be revoked.

Volatilization is a Critical Component of Chlorpyrifos Assessment

As a result of new data submitted by the registrant, Dow AgroSciences, EPA has changed how it "considers the hazard to chlorpyrifos and chlorpyrifos oxon vapor."[23] According to the agency, the 2013 preliminary assessment of the potential risks from volatilization -which found that offsite levels of chlorpyrifos and chlorpyrifos oxon may exceed target concentrations established for lung cholinesterase inhibition, was revised in 2014 to reflect new industry calculations. The 2013 document reported that about 30% of applied chlorpyrifos is emitted from treated sites within the first 24 hours, with peak emissions during the warmest parts of the day, and that volatilization of chlorpyrifos from these treated areas may result in bystander exposure to *vapor phase* chlorpyrifos and chlorpyrifos oxon.[24]

Now, Dow's animal studies are reporting that no toxicity occurs even at high concentrations of chlorpyrifos vapor after six hours of exposure. The 2014 document, "Chlorpyrifos: Reevaluation of the Potential Risks from Volatilization in Consideration of Chlorpyrifos parent and Oxon Vapor Inhalation Toxicity Studies,"[25] explains that the 2013 evaluation used aerosolized chlorpyrifos inhalation data, in lieu of vapor, since vapor data was unavailable. Dow's studies submit new information on vapor exposure. Accordingly the studies report no statistically significant inhibition of acetylcholinesterase (AChE) activity. Based on these studies, EPA asserts there is "no risk potential" from volatilization exposure to chlorpyrifos or chlorpyrifos oxon. Specifically, the agency now notes that, "If there is no risk due to exposure to chlorpyrifos or chlorpyrifos oxon, only a qualitative risk assessment was completed for volatilization,"[26] and states that there is no need to perform quantitative risk estimates for off-field exposures.

While this new data on vapor vs. aerosolized exposure is important in understanding the nuances of pesticide exposure pathways and inhalation exposure, the agency must obtain more information to develop a robust database, preferably with independent and peer-reviewed studies on the issue, and not rely solely on two studies submitted by the registrant. If studies do not currently exist in the scientific literature, EPA must support and encourage research on the subject matter. Additionally, Dow's studies were short-term acute studies and did not measure exposures beyond six hours. This is critical since farmworkers and others living adjacent to treated fields will undoubtedly have greater than six hour continuous exposures to chlorpyrifos vapor. Given that chlorpyrifos has been detected in indoor

[23] USEPA. 2014. Chlorpyrifos: Reevaluation of the Potential Risks from Volatilization in Consideration of Chlorpyrifos Parent and Oxon Vapor Inhalation Toxicity Studies. Office of Chemical Safety and Pollution Prevention. Washington DC.
[24] USEPA. 2013. Chlorpyrifos; Preliminary Evaluation of the Potential Risks from Volatilization. Office of Chemical Safety and Pollution Prevention. Washington DC.
[25] Ref 23.
[26] USEPA. 2014. Chlorpyrifos: Updated Occupational and Residential Exposures Assessment for Registration Review. Office of Chemical Safety and Pollution Prevention. Washington DC.

air, even in childcare centers,[27] indicating unaccounted for chronic exposures, the agency must not forgo a thorough assessment of the risks from chlorpyrifos inhalation exposure, given the history of underestimating real-world exposures. Additionally, EPA must not roll back the 'limited' mitigation measures (buffer zones, reduced application rates, etc) laid out in the 2012 and 2013 assessments, based on unsubstantiated industry data showing 'no risks' from chlorpyrifos inhalation.

Ultimately, under the *Federal Insecticide Fungicide and Rodenticide Act* (FIFRA), the agency has a mandate to ensure that all pesticides are registered and that any registered pesticide presents "no unreasonable adverse effects."[28] "Unreasonable adverse effects" are defined in part as "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide. . ."[29] Pesticides with specially recognized high toxicity, like chlorpyrifos, that volatilize and migrate off site must not be allowed to put the public, farmworker communities, or the environment at risk.

Drinking Water Contamination Further Underscores a Need for a Chlorpyrifos Ban

A screening level drinking water assessment found that the chlorpyrifos oxon -transformed from the parent during chlorination in drinking water treatment, poses a threat to drinking water. The agency, in this updated assessment, finds that "even with only one application, several chlorpyrifos uses may exceed the DWLOC [drinking water level of comparison] at rates lower than maximum labeled rates,"[30] indicating that chlorpyrifos has the potential to pose risks to watersheds used for drinking water.

Even though little environmental data exists for chlorpyrifos oxon, it can persist through water treatment and thus remains in drinking water for at least 72 hours.[31] According to EPA's assessment, "watershed vulnerability is expected to be greatest for smaller watersheds with high percent cropped areas. Smaller community water systems are generally more vulnerable due to short distribution times and the reliance of chlorination to treat source surface water as well as limited access to other treatment methods such as granular activated carbon."[32]

This updated information should indicate to the agency that continued chlorpyrifos use has more environmental cost than benefit. Given that the agency notes that "drinking water treatment processes, with the exception of activated carbon, have been shown to have little impact on removal of pesticide residues,"[33] and many municipal water treatment plants, with limited resources, are faced with the daunting task of protecting their communities from pesticide exposures, chlorpyrifos registration should be revoked.

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[27] Morgan, M. K., Wilson, N. K., and Chuang, J. C. 2014. Exposures of 129 Preschool Children to Organochlorines, Organophosphates, Pyrethroids, and Acid Herbicides at Their Homes and Daycares in North Carolina. *International Journal of Environmental Research and Public Health*, *11*(4), 3743–3764. doi:10.3390/ijerph110403743.

[28] 7 U.S.C. § 136a.

[29] 7 U.S.C. § 136 (bb).

[30] USEPA. 2014. Chlorpyrifos: Updated Drinking Water Assessment for Registration Review. Office of Chemical Safety and Pollution Prevention. Washington DC.

[31] Kamel A, et al. 2009. Oxidation of selected organophosphate pesticides during chlorination of simulated drinking water. *Water Res*; 43(2):522-34.

[32] Ref 30.

[33] Ibid.

Conclusion

The agency's updated human health risk assessment continues to illustrate that there are serious exposure risks associated with continued chlorpyrifos use that can only be mitigated with a complete revocation of chlorpyrifos registration. As mentioned in previous comments to the agency, Beyond Pesticides is concerned about EPA's apparent focus on risk reduction strategies to come up with "acceptable," yet unnecessary, rates of illness across the population. EPA continues to ignore the dangers to farmworkers, farm families, especially vulnerable children,[34] and others living near agricultural areas.[35] Chlorpyrifos and its transformation product are water contaminants, endangering drinking water supplies and communities that rely on those supplies. Human health data continue to show that exposures result in developmental delays, low birth weights, and other serious health effects.[36]

The fact remains that chlorpyrifos is an old organophosphate pesticide that is highly toxic and has no place in modern agriculture. With the number of alternatives available, the agency should be working to phase this chemical out of production and use, and not engineering additional mitigation measures to justify continued use. Given the serious risks involved, the agency must act to eliminate this public health threat and revoke chlorpyrifos' registration.

Respectfully,

Nichelle Harriott
Science and Regulatory Director

[34] Beamer, PI, et al. 2009 Farmworker children's residential non-dietary exposure estimates from micro-level activity time series. *Environ Int* ;35(8):1202-9.

[35] Harnly, ME, et al. 2009. Pesticides in dust from homes in an agricultural area. *Environ Sci Technol*;43(23):8767-74.

[36] Venerosi, A et al. 2010. Gestational exposure to the organophosphate chlorpyrifos alters social-emotional behaviour and impairs responsiveness to the serotonin transporter inhibitor fluvoxamine in mice *Psychopharmacology*. 2010 Jan;208(1):99-107.