Farmworker and Conservation Comments on Chlorpyrifos Issues Paper: Evaluation of Biomonitoring Data from Epidemiology Studies

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Comments to the FIFRA Scientific Advisory Panel on the EPA Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies

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INTRODUCTION

Thank you for the opportunity to comment on the important topic of how biomonitoring data will be used in Environmental Protection Agency's ("EPA's") assessment of the pesticide chlorpyrifos. The following comments are being submitted on behalf of Natural Resources Defense Council, Farmworker Justice, Earthjustice, Pesticide Action Network, United Farm Workers, California Rural Legal Assistance Foundation, and Pineros y Campesinos Unidos del Noroeste. These groups have no direct or indirect financial or fiduciary interest in the manufacture or sale of any chemical that would be the subject of the deliberations of this Panel.

These comments begin by first describing the context in which this Scientific Advisory Panel ("SAP") review is occurring; specifically, EPA has proposed revoking all food tolerances for chlorpyrifos based on unsafe drinking water exposures. Second, the human health risk assessment underlying that proposal, however, is based on acute poisoning risks, rather than neurodevelopmental harm to children that EPA has determined has occurred at far lower doses. Extensive peer-reviewed scientific studies document and EPA has found that serious neurodevelopmental harm is associated with chlorpyrifos exposure and that harm is permanent and irreversible. To be protective, EPA has appropriately determined that it must either develop a point of departure based on the neurodevelopmental harms or employ additional safety factors to guard against such harm. The Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies proposes the former corrective approach for peer review by the SAP. Third, these comments endorse EPA's approach not only as being necessary, but also as rigorous and in keeping with EPA policies and underlying legal requirements. Finally, incorporating the proposed point of departure into the human health risk assessment reveals alarmingly dangerous exposures to chlorpyrifos in food, in drinking water, and from occupational exposures. The results underscore the untenable and illegal health risks from chlorpyrifos and the urgent need to revoke all tolerances and cancel all registrations of chlorpyrifos.

I. THE CONTEXT IN WHICH THIS SCIENTIFIC ADVISORY PANEL REVIEW ARISES.

This SAP review builds on prior SAP reviews and on a series of EPA findings and its October 2015 proposal to revoke all chlorpyrifos tolerances because children and others are being exposed to unsafe levels of chlorpyrifos and its oxon in drinking water. These EPA reviews were spurred by a 2007 petition filed by Natural Resources Defense Council and Pesticide Action Network urging EPA to revoke all chlorpyrifos tolerances based, in large part, on neurodevelopmental harm to children documented in epidemiology studies, including the study conducted by the Columbia Center for Children's Environmental Health ("CCCEH").

After obtaining SAP advice on the use of epidemiology studies, EPA used a systematic review process to complete transparent and comprehensive literature reviews for the 2014 chlorpyrifos revised human health risk assessment ("RHHRA")[1] and the 2015 review for all organophosphate (OP) pesticides[2]. In the

[1]US EPA, 2014. Chlorpyrifos: Revised Human Health Risk Assessment for Registration Review. Available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0195.

RHHRA, EPA accurately finds that prenatal exposures result in adverse neurodevelopmental effects, including loss of working memory, attention problems, developmental disorders in early childhood, and intelligence decrements in school age children who were exposed prenatally.[3] Moreover, "[s]ince the 2012 FIFRA SAP, epidemiologists from the three US cohorts have continued to publish papers on the adverse effects in children up to ages 7–11 suggesting the lack of reversibility of the outcomes; these findings have heightened the agency's concern."[4]

Heeding the 2012 SAP's advice, EPA reconstructed levels of chlorpyrifos to which the mothers were exposed. EPA determined that the neurodevelopmental effects occurred at exposures that were associated with negligible cholinesterase inhibition. In other words, the harmful effects to children occurred at doses lower than those that would cause 10% cholinesterase inhibition, which was EPA's risk assessment and regulatory endpoint for OPs.

Based on these findings, EPA retained a Food Quality Protection Act ("FQPA") 10X safety factor due to gaps in the toxicological database regarding adverse neurodevelopmental effects to children. EPA then used the 10% cholinesterase inhibition endpoint, along with the retained 10X FQPA safety factor in its RHHRA. The risk assessment found that most label uses of chlorpyrifos result in drinking water contamination levels that exceed EPA's levels of concern for infants and children, as well as many dozens of risks of concern to workers from both handling chlorpyrifos and entering treated fields.

While EPA was previously soliciting advice from the SAP and conducting numerous chlorpyrifos assessments, some of the undersigned – Natural Resources Defense Council, Pesticide Action Network, and Earthjustice – had asked the courts to direct EPA to respond to the 2007 petition to revoke all chlorpyrifos tolerances. In August 2015, the Ninth Circuit Court of Appeals found that EPA's nearly nine year delay in responding to the 2007 petition "is egregious" and set an October 31, 2015 deadline "to end this cycle of incomplete responses, missed deadlines, and unreasonable delay."[5] The court concluded that in view of EPA's representation that "chlorpyrifos poses such a significant threat to water supplies that a nationwide ban on the pesticide may be justified,. . .we have little difficulty concluding it should be compelled to act quickly to resolve the administrative petition."[6]

By the court-ordered October 31, 2015 deadline, EPA proposed to revoke all chlorpyrifos tolerances. As a result of the drinking water contamination levels documented in the RHHRA, EPA concluded that it "cannot make a safety finding based on drinking water exposures." [7] In the absence of such a safety finding, the FQPA prohibits maintaining tolerances that would allow chlorpyrifos use and residues on food. The court has ordered EPA to finalize the revocation process by the end of the year.

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[2]EPA OPP, Literature Review on Neurodevelopmental Effects & FQPA Safety Factor Determination for the Organophosphate Pesticides (Sept. 15, 2015), at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2010-0119-0023.

[3] RHHRA at 42-43.

[4]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 76

[5] *In re Pesticide Action Network of North America v. EPA*, 798 F.3d 809, 811 813 (9th Cir. 2015).

[6] *Id*. at 814.

[7] Proposed Revocation of Chlorpyrifos Tolerances, 80 Fed. Reg. 69.080, 69,082-83, 69.085, 69,106 (Nov. 6, 2015).

II. EPA HAS APPROPRIATELY DECIDED THAT IT MUST ESTABLISH AN END POINT OR SAFETY FACTORS THAT GUARD AGAINST NEURODEVELOPMENTAL HARM TO CHILDREN FROM *IN UTERO* EXPOSURES.

We submitted comments on both the RHHRA and the proposed revocation concurring that all tolerances must be revoked, but also highlighting a critical flaw in EPA's human health risk assessment. As our comments discussed at length, significant adverse outcomes on children's neurodevelopment were seen at chlorpyrifos exposure levels far below those required to cause 10% red blood cell acetylcholinesterase inhibition (RBC AChE inhibition).[8] Yet EPA continued to use 10% AChE inhibition as the basis for the point of departure ("PoD") in its 2014 Chorpyrifos Revised Human Health Risk Assessment. Continuing to use 10% AChE inhibition as the point of departure in the face of EPA's findings that damage to children's brains occurs at far lower doses fails to protect children from neurodevelopmental harm.

EPA is now proposing to correct this flaw. In its chlorpyrifos issue paper, it reiterates its finding that ". . . the internal blood concentrations required to achieve 10% RBC AChE inhibition are substantially higher than those reported by CCCEH and associated with neurodevelopmental outcomes suggesting that the RBC AChE inhibition PoDs are not sufficiently health protective."[9] EPA recognizes that continuing to use 10% AChE inhibition would be under-protective and would likely make EPA unable to support an affirmative FQPA safety finding. EPA appropriately concludes that it has two options to ensure that its risk assessments guard against neurodevelopmental harm:

(1) "The agency could consider continuing to use the AChE PoDs, but additional safety factors beyond the FQPA Safety Factor 10X would be needed to have sufficient confidence to conclude that there is a reasonable certainty of no harm under the FQPA. However, the agency would still need to quantify such additional factors—and the analysis to quantify them would again require the agency to make quantitative use of the CCCEH cord blood data with the same uncertainties described above.
(2) Although either approach would be possible, the agency has elected to propose to use the cord blood directly as the PoD as the simpler, more understandable approach."[10]

We agree, as we discussed in our two sets of comments to the Agency. [11] Our analysis also indicated that additional safety factors, totaling at least 1000X but whose exact magnitude would be calculated from

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[8]Earthjustice, *et al.,* Farmworker and Conservation Comments on Chlorpyrifos Revised Human Health Risk Assessment (April 30, 2015) at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0848

Earthjustice, *et al.,* Comments on EPA Proposal To Revoke Chlorpyrifos Tolerances EPA-HQ-OPP-2015-0653 (January 5, 2016) at https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2015-0653-0390

[9]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 77

[10]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pp. 39-40

the CCCEH data, would be needed to ensure that PoDs based on AChE inhibition are sufficiently protective. But the critical effect for risk assessment is neurodevelopmental outcomes in children because these represent the most sensitive endpoints, not 10% AChE inhibition. Hence, the neurodevelopmental outcomes are the appropriate endpoint for EPA to use for quantitative risk assessment and we agree with the agency's proposal to use the Columbia Center for Children's Environmental Health (CCCEH) data directly in order to calculate the PoD. **(Charge question 5a)**

The 2014 Revised Human Health Risk Assessment[12], and the 2015 Literature Review for OP Pesticides[13], supplemented by the biomonitoring issue paper[14], reviewed all critical aspects of the CCCEH study and found that the study design, biomarkers measured, and the methods used for measuring outcomes and statistical analysis are strong and valid.

In order to use the CCCEH data to calculate the PoD, the agency has used a PBPK model to characterize the dose estimates in the studies and conduct additional dose-response analyses, as recommended by the 2012 SAP.[15]

III. EPA'S USE OF CORD BLOOD DATA TO DEVELOP A POINT OF DEPARTURE IS THOROUGH, RIGOROUS, AND IN KEEPING WITH AGENCY POLICIES.

A. EPA's PBPK model allows characterization of the CCCEH data with the confidence needed to support their use in quantitative risk assessment.

We commend the agency for undertaking the comprehensive, strong and transparent analysis presented in this Issue Paper. EPA used appropriate methodologies and assumptions to calculate the new Point of Departure (PoD) based on a neurodevelopmental outcome and then estimated exposures to women, infants and workers. EPA followed the guidelines for use of epidemiological data in risk

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[11]Earthjustice, et al., Farmworker and Conservation Comments on Chlorpyrifos Revised Human Health Risk Assessment (April 30, 2015) at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0848

Earthjustice, et al., Comments on EPA Proposal To Revoke Chlorpyrifos Tolerances EPA-HQ-OPP-2015-0653 (January 5, 2016) at https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2015-0653-0390

[12]US EPA, 2014. Chlorpyrifos: Revised Human Health Risk Assessment for Registration Review. Available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0195.

[13]EPA OPP, Literature Review on Neurodevelopmental Effects & FQPA Safety Factor Determination for the Organophosphate Pesticides (Sept. 15, 2015), at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2010-0119-0023.

[14]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pp. 11-14

[15]FIFRA SAP Meeting Minutes: A Set of Scientific Issues Being Considered by the EPA Regarding Chlorpyrifos Health Effects (April 2012) at 74 "It is further suggested that the Agency focus on the data of chlorpyrifos levels in the cord blood samples as the base to develop the POD for chronic exposures to chlorpyrifos based on a PBPK/PD model."

assessment, as well as the precedent established by methylmercury, with its use of this strong epidemiological data for quantitative risk assessment. [16]

Importantly, the agency provides all the code needed to run the PBPK simulations, the full output of the PBPK simulations, as well as a clear description of the assumptions used. This type of transparency is critical for stakeholders to be able to evaluate and comment on the strengths and weaknesses of the methodology.
EPA's decision not to use the updated DAS pregnancy model for their new analysis is appropriate since the predictive capacity of the updated DAS model cannot be evaluated.[17] Additionally, the California Department of Pesticide Regulation documented a number of uncertainties and limitations of the DAS model which further call into question the accuracy of the model.[18]

EPA concludes that they can reliably estimate blood levels of chlorpyrifos for females of childbearing age and that the blood levels of the mother are a reasonable surrogate for the fetus (pg. 17)[19] We agree with this conclusion as multiple analyses show that maternal and cord blood levels are highly correlated. **(Charge Question 1a)**

In order to better characterize exposure sources for the CCCEH cohort, EPA conducted a pharmacokinetic analysis and also evaluated drinking water, food and residential exposures for the cohort.[20] The 2012 SAP indicated that further exposure and dose-response characterization using a PBPK model was needed in order to use the CCCEH data to derive a PoD[21]. This is exactly what the agency has done here and the results validate the use of the CCCEH data and the PBPK model for quantitative risk assessment.

Overall, we agree with the agency's conclusions that "Taken together, this exposure characterization analysis suggests that the CCCEH values are plausible and reasonable based on the agency's analysis and likely driven by residential exposure…the agency's exposure characterization analysis compared to the CCCEH data in Figure 1 support the conclusion that the reported biomonitoring data reflect the likely

[16] EPA OPP, Draft Framework for Incorporating Human Epidemiologic & Incident Data in Health Risk Assessment (Jan. 7, 2010) http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0851-0004

[17] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 16

[18] California Department of Pesticide Regulation. Chlorpyrifos Risk Characterization Document. (December 31, 2015) at pp. 121-123. Available at www.cdpr.ca.gov/docs/risk/rcd/chlorpyrifos_draft.pdf

[19] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016)

[20] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pp. 17-38

[21] FIFRA SAP Meeting Minutes: A Set of Scientific Issues Being Considered by the EPA Regarding Chlorpyrifos Health Effects (April 2012) at 50

exposure patterns of chlorpyrifos across the time period of 1998–2004 and thus provide confidence in their use in risk assessment."[22] **(Charge question 4)**

B. The agency performs a rigorous analysis to derive the PoD for neurodevelopmental outcomes.

The agency's use of a Benchmark Dose (BMD) approach to derive the PoD is consistent with the data indicating that the association of chlorpyrifos exposures with working memory effects is continuous with no threshold. EPA has also appropriately applied its standard policy of using the lower limit (BMDL) in deriving the PoD. **(Charge question 5b)**

The agency's analysis finds that the PoD is 2% reduction in working memory which corresponds to an internal dose BMDL of 2.16 pg/ g.[23] We note that an association with reduction in working memory of less than 2% (*i.e.,* 1%) is supported by the CCCEH data and that such a reduction is likely still an adverse effect; however this uncertainty associated with the selection of the 2% reduction is addressed by the retention of the 10X FQPA safety factor as described in more detail below. **(Charge question 5c)**

Note that we can't compare this new PoD directly to the old PoD from the 2014 RHHRA. This is because the new PoD is an internal dose corresponding to a 2% reduction in working, while the old PoD is the external exposure needed to cause 10% AChE inhibition (the old PoD was 78 ug/ kg/ day for adult females).

However, EPA does use the PBPK model to estimate the internal exposures that would result from external exposures at the old PoD.[24] These can be compared to the new PoD:

For females 13-49 years old with food exposure at 78 ug/ kg /day (the old PoD):

Daily blood level peak= 7572 pg/ g (*This is 3500X higher than new PoD of 2.16 pg/g*)
Lowest blood level over 21 day exposure simulation= 100 pg/ g (*This is 46X higher than new PoD*)

This comparison is one more piece of evidence indicating that the PoD based on AChE inhibition is not protective for the neurodevelopmental effects; exposure at the old PoD results in internal levels of chlorpyrifos orders of magnitude greater those that cause a reduction in working memory.

C. EPA Appropriately Retained Safety Factors to Reflect Uncertainty.

EPA conducted a thorough analysis of uncertainties and selected appropriate safety factors to account for the remaining uncertainties.

[22] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 38 and pg. 77

[23] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 42

[24] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 39 and Appendix I, pg 100

First, EPA appropriately used the default 10X intra-species uncertainty factor to account for both pharmacodynamic and pharmacokinetic intra-species variability. This is consistent with the methyl mercury risk assessment where there were similar key uncertainties. Specifically, with respect to pharmacodynamics, the critical windows of susceptibility, exposure timing, and generalizability from the CCCEH cohort are unknown, so EPA cannot calculate a data-derived factor and retains the default (3X). For pharmacokinetics, since a pregnancy PBPK model is not available, EPA cannot calculate a data-derived factor and retains the default (3X). **(Charge question 6a)**

Second, we agree that the evidence supports retaining the 10X FQPA safety factor. The FQPA instructs EPA "to take into account potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children." Extensive data from laboratory animals shows that the post-natal period represents a susceptible life stage with regards to chlorpyrifos exposures and adverse neurological effects. However, the CCCEH data and most other epidemiology studies investigated prenatal exposures only and thus there is remaining uncertainty regarding postnatal exposures. Further, because CCCEH is one modest size cohort, uncertainty also remains as to whether the dose-response relationship derived from these data is representative for the U.S. population.

In addition, as mentioned above, there is uncertainty associated with the selection of a 2% reduction in working memory as the outcome on which to base the PoD, as a 1% reduction may still constitute an adverse effect.

To account for uncertainties regarding post-natal exposure, dose-response, and the selection of 2% working memory reduction as the critical outcome, it is necessary to retain the FQPA 10X factor. **(Charge question 6b-c)**

EPA must revoke all chlorpyrifos tolerances and cancel all registrations because food, drinking water and occupational exposures are extremely unsafe. **(Charge Question 7)** Given that the EPA's previous 10% AChE inhibition endpoint results in much higher internal exposure than the point of departure derived using cord blood, it should come as no surprise that exposures from current uses far exceed safe levels, often orders of magnitude more than the drinking water risks found in EPA's RHHRA. These findings underscore the untenable risks to children and workers from chlorpyrifos and the need to revoke all tolerances and cancel all uses as soon as possible.
Applying the PoD and uncertainty factors above, EPA finds that the Reference Dose (RfD) for assessing food and water exposures is 0.022 pg/g and the Margin of Exposure (MOE) for other exposure assessments is 100.[25]

A. Food exposures are unsafe.

EPA used the PBPK model to estimate the internal chlorpyrifos levels that would result from food exposure in women of child-bearing age. EPA used its standard methodology to calculate food exposures. The internal levels resulting from food exposure are compared to the RfD in Table 1.

[25]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 50

Table 1. *Comparison of EPA's food exposure estimates and corresponding chlorpyrifos blood levels with the RfD. Exceedances of the RfD are highlighted in red. Food exposure and blood level data from EPA Table 8.*[26]

Percentile of Exposure	**Exposure from Calendex**	**Max Blood Levels of CPFOS (pg/g)** from Food Runs at Various Percentiles of Exposure from Calendex	% exceedance of RfD = 0.022 pg/ g	**10-hour Blood Levels Post Exposure** Values of CPFOS (pg/g) from Food Runs at Various Percentiles of Exposure from Calendex	% exceedance of RfD = 0.022 pg/ g	**24-hour Blood Levels Post Exposure** Values of CPFOS (pg/g) from Food Runs at Various Percentiles of Exposure from Calendex	% exceedance of RfD = 0.022 pg/ g
10	0.003 µg/kg/day	0.29	1318%	0.060	273%	0.021	95%
30	0.005 µg/kg/day	0.48	2182%	0.099	450%	0.034	155%
50	0.007 µg/kg/day	0.67	3045%	0.139	632%	0.048	218%
70	0.009 µg/kg/day	0.86	3909%	0.179	814%	0.062	282%
90	0.014 µg/kg/day	1.33	6045%	0.278	1264%	0.096	436%
95	0.018 µg/kg/day	1.71	7773%	0.358	1627%	0.124	564%
97.5	0.023 µg/kg/day	2.19	9955%	0.457	2077%	0.158	718%
99	0.029 µg/kg/day	2.76	12545%	0.576	2618%	0.200	909%
99.5	0.037 µg/kg/day	3.52	16000%	0.735	3341%	0.255	1159%
99.9	0.075 µg/kg/day	7.14	32455%	1.490	6773%	0.517	2350%

Chlorpyrifos exposures from food exceed the RfD for basically all percentiles of exposure at all time periods considered. Exceedances range from 155% at 24 hours post exposure in the low percentile of exposures to 32,000% for the maximum chlorpyrifos blood levels in the highest percentile of exposure. These large and consistent exceedances across the board demonstrate that for pregnant women, current levels of exposure from food are unsafe and the chlorpyrifos tolerances must be revoked.

[26]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 55

B. Drinking water exposures are unsafe.

EPA focused on chlorpyrifos in drinking water, as opposed to the chlorpyrifos-oxon, as the relationship between exposures to the oxon and neurodevelopmental outcomes is unknown. EPA evaluated two scenarios: (1) estimated drinking water concentrations (EDWC) generated using standard models and methodology for a low-end application scenario (bulb onion using 1 lb of active ingredient per acre per year); and (2) drinking water concentrations estimated from monitoring data. EPA then used the PBPK model to estimate the internal chlorpyrifos levels that would result from drinking water exposures in women of child-bearing age and infants.

These are reasonable approaches to consider low-end exposure estimates. The internal levels resulting from drinking water exposures are compared to the RfD in Table 2.

Table 2. *Comparison of EPA's chlorpyrifos blood level estimates occurring from drinking water exposures with the RfD. Exceedances of the RfD are highlighted in red. Blood level data from EPA Figures 12, 14 and Table 10.*[27]

Population	**Model Estimated (EDWC) Chlorpyrifos Blood Concentrations**	% exceedance of RfD = 0.022 pg/ g	**Measured (Monitoring Data) Maximum Chlorpyrifos Blood Concentrations**	% exceedance of RfD = 0.022 pg/ g
Infants: Formula Fed (with water)	Max: 21.6 pg/g Lowest for 120 day simulation: 5 pg/ g	98182% 22727%	6.24 pg/g	28364%
Females of Childbearing Age (13–49 years old)	Max: 6.99 pg/g Lowest for 120 day simulation: 1 pg/ g	31773% 4545%	1.97 pg/g	8955%

The RfD is exceeded for all scenarios considered for both infants and women of child-bearing age. Further, for the blood levels based on the drinking water model, chlorpyrifos concentrations in blood remain significantly above the RfD for the entire 120 day simulation. These values are conservative because the modeled scenario is for low end use—EPA expects that other uses would result in higher water concentrations and higher blood levels.[28]

These results show that pregnant women and infants are exposed to extremely unsafe levels of chlorpyrifos in drinking water from food uses and therefore all tolerances must be revoked.

[27] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pp. 64, 66, and 67

[28] EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pg. 67

Moreover, drinking water contamination is not limited to food uses of chlorpyrifos. For example, EPA estimated drinking water concentrations resulting from use scenarios on cotton, turf, right-of-ways, and other non-food uses in its 2014 Updated Drinking Water Assessment for Registration Review and found drinking water contamination.[29] This analysis supports cancelling all registrations due to runoff to surface water and drinking water contamination.

C. Occupational exposures are unsafe.

EPA used the PBPK model to estimate the internal chlorpyrifos levels that would result from low-end exposure scenarios for handlers who are women of child-bearing age. EPA used its standard methodology to calculate handler exposures. The internal levels in the handler exposure scenarios are compared to the MOE in Table 3.

Table 3*. Comparison of EPA's chlorpyrifos blood level estimates occurring from handler exposures with the MOE. MOEs of concern are highlighted in red (an MOE less than 100 is of concern). Blood level data from EPA Tables 11 and 12.*[30]

Worker Activity	**Use Site**	**Maximum Venous Blood Chlorpyrifos (pg/g)**	Comparison to MOE = 100	**24-hour Venous Blood Chlorpyrifos (pg/g)**	Comparison to MOE = 100	**10 hous After the Last Peak on Day -12 Blood Chlorpyrifos (pg/g)**	Comparison to MOE = 100
EC	Corn (pre-plant)	413	5.23E-03	6.6	3.27E-01	34.4	6.28E-02
	Cole Crops	329	6.57E-03	5.3	4.08E-01	27.4	7.88E-02
Dry Flowable in WSP	Cole Crops	404	5.35E-03	8	2.70E-01	38.4	5.63E-02
Spray (all starting forms)	Corn (pre-plant)	243	8.89E-03	3.8	5.68E-01	20	1.08E-01
	Cole Crops	194	1.11E-02	3	7.20E-01	16	1.35E-01
EC	Beans, peas	954	2.26E-03	12.4	1.74E-01	71.1	3.04E-02
EC	Corn	214	1.01E-02	2.8	7.71E-01	16	1.35E-01

An MOE of less than 100 poses a risk of concern. None of the MOEs from this analysis comes close to 100, and many reveal risks that an order of magnitude greater than acceptable risk levels. Indeed, MOEs

[29]EPA, Office of Chemical Safety and Pollution Prevention, Chlorpyrifos: Updated Drinking Water Assessment for Registration Review (Dec. 23, 2014)

[30]EPA's Office of Pesticide Programs, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies (March 11, 2016) at pp. 74 and 75

are of concern for all scenarios and time periods evaluated.[31] EPA used handler scenarios that have low occupational exposure potential and yet found these extremely high risks to workers. Worker scenarios with higher exposures would subject workers to even greater risks, resulting in even lower MOEs.

This analysis confirms that for pregnant workers, current levels of exposure are extremely unsafe. The risks of concern extend beyond food uses of chlorpyrifos. For example, EPA estimated occupational exposures resulting from use scenarios on nursery plants, turf grass, Christmas trees and other non-food uses in their 2014 Updated Occupational and Residential Exposure Assessment for Registration Review.[32] To protect workers and children, all chlorpyrifos tolerances must be revoked and registrations cancelled.

We strongly support the agency's proposal to move forward with revoking all chlorpyrifos tolerances; as the agency notes such an action would likely mean the end of chlorpyrifos use on food crops, and in processed foods. Furthermore, the analysis presented in this biomonitoring issue paper indicates that the agency should cancel all chlorpyrifos registrations, even those not associated with food uses, because such uses still could result in drinking water contamination exceeding levels of concern and present serious occupational risks.

CONCLUSION

EPA has performed a robust analysis which reveals risks of concern for women of child-bearing age and children from food, drinking water and occupational exposures. The agency should move forward expeditiously to finalize its proposal to revoke all food tolerances. In addition, because chlorpyrifos poses such extreme and untenable risks to children and workers, EPA should immediately initiate proceedings to cancel all chlorpyrifos registrations.

Thank you for the opportunity to provide comments. Please do not hesitate to contact us if we can be of further assistance.

[31] EPA assumes that exposures stop at the end of an 8-hour workday even though workers lack shower and laundry facilities to ensure that exposures in fact stop, as we pointed out in our comments on the RHHRA at 68-69.

[32] EPA, Office of Chemical Safety and Pollution Prevention, Chlorpyrifos: Updated Occupational and Residential Exposure Assessment for Registration Review (Dec. 29, 2014)