

**Responses to Technical Public Comments on the  
August 2017 Draft Evaluation of Chlorpyrifos as a Toxic Air Contaminant**

Department of Pesticide Regulation

COMMENT		RESPONSE*
<b>Policy-Directed Comments</b>		
1	The Department of Pesticide Regulation (DPR) should allow for a period of time for review and comment on mitigation measures before implementation.	Any mitigation measures DPR is considering for chlorpyrifos are beyond the scope of the risk assessment.
2	The risk assessment does not protect farmworkers	The risk assessment is being developed as part of the Toxic Air Contaminant (TAC) process. This process focuses on ambient air contamination by pesticides. The focus is on residents and bystanders (who may also be farmworkers) and may be exposed to pesticides in ambient air. DPR uses other authority to protect pesticide handlers, pesticide applicators and other farmworkers. DPR is not ignoring occupational risk. For example, farmworkers in fields near chlorpyrifos applications are considered bystanders and are addressed in the risk assessment. Additionally, DPR's process to evaluate and mitigate bystander exposures may also address applicator and other handler exposures. For example, DPR may implement additional restrictions on methods to apply chlorpyrifos and these may reduce handler exposures. If they do not, DPR can follow up with a more comprehensive evaluation and mitigation of handler exposures. In the meantime, DPR is addressing bystander exposures at this time.
3	DPR should revoke the State registration of chlorpyrifos.	The comment is beyond the scope of the risk assessment.
4	Under its authority to regulate pesticides, DPR is also directed to consider the benefit of a pesticide.	DPR's authority specifically requires DPR to consider public health protection when making regulatory decisions. However, Federal law requires the United States Environmental Protection Agency to consider the benefit of a pesticide when registering a pesticide.
5	In its current form, the Draft Evaluation grossly underestimates the risk experienced by communities.	This comment does not specify the reasons of why the risk assessment is underestimating risk. Therefore, the comment cannot be specifically addressed.
6	The Draft Evaluation must be significantly revised to adequately assess, and eliminate significant adverse health impacts as required by California Food and Agriculture Code (FAC) Section 14024.	DPR agrees to the obligation to eliminate significant adverse health impacts as required by Section 14024.
7	The Draft Evaluation must be significantly revised to ensure that pesticides registered for use in California are not detrimental to public and health and safety under FAC Sections 12825 and 13129.	DPR agrees to the obligation to ensure that pesticides registered for use in California are not detrimental to public health and safety under Sections 12825 and 13129.

\* Note: All DPR documents referred to in the responses are available at [www.cdpr.ca.gov/docs/whs/active\\_ingredient/chlorpyrifos.htm](http://www.cdpr.ca.gov/docs/whs/active_ingredient/chlorpyrifos.htm)

<b>Exposure Assessment-related Comments</b>		
1	The scenarios appear to over-estimate risk through the scenarios chosen (e.g., sparse, young, dormant applications) versus typical use when trees are full-leaf/full canopy. In addition, several of the narratives included within the spray drift residue exposure estimates appear to be an inaccurate characterization of likely 1-2 year old human exposure. The reliance on the US EPA residential SOP weighs all uses so that they are based on behavior of 1-2 year olds, regardless of likelihood, which is inappropriately conservative	This risk assessment characterized the reasonable worst case exposure scenarios associated with applications allowed by the current labels. This use includes dormant sprays on apples. For more responses on this issue in general, see DPR's response to Dow AgroSciences LLC comments in the memo dated August 15, 2017 (responses 1, 2, 20, and 25).
2	Dormant applications use a specific formulation to reduce drift, and are prohibited in much of the Sacramento Valley- it wasn't clear that this was considered.	The AgDRIFT model empirical equations were developed base on Spray Drift Task Force field data collected in California during dormant spray season. Thus, the modeling reflects Sacramento Valley dormant spray conditions.
3	Some modeled application rates were higher than actual rates used in almonds.	This risk assessment addresses the potential risk associated with all legal applications of chlorpyrifos. The maximum application rates for each application method are the highest legal rates. This means some of the application rates may be higher than the maximum application rate allowed for almonds.
4	Tree nuts applications are 3 times per season. It should be noted that use a maximum use rates would allow for one dormant, and potentially two foliar sprays applications (p.89). The statement that, "exposure to CPF due to off-site product movement is considered to be a series of short-term exposures," should be further clarified with a specific number of modeled, estimated exposures.	The spray drift modeling represents a single dormant spray application. The purpose of analyzing aerial and airblast application frequencies was to evaluate, in addition to the short-term exposure, the need for addressing spray drift exposure from longer terms (i.e., intermediate-term and/or long-term). As described in the draft risk assessment, chlorpyrifos exposure due to off-site product movement is considered to be a series of short-term exposures.
5	The scenarios used to characterize exposure of adults and children are not necessarily appropriate.	HHA is confident in the exposure scenarios chosen to appropriately characterize exposure of adults and children. The scenarios chosen represent reasonable worst case application scenarios in California.
6	Real-world monitoring data should be used to confirm modeling and residue estimates.	The California Pesticide Use Reporting (PUR) database reports on a 1-square mile resolution which is too coarse to compare to a single orchard application. Monitoring results from the DPR Air Monitoring Network represent ambient air concentrations which are regional in nature. This risk assessment estimates risks associated with a single orchard application in the local context.

7	Modeled nozzles should reflect actual required use. In an effort to reduce drift, CDPR should initiate a review of any of the data on ways to reduce spray drift from airblast sprayers.	This risk assessment focuses on reasonable worst case use scenarios consistent with legally allowed use of chlorpyrifos in California. Consideration of drift reduction technology, however, is most appropriately conducted during the mitigation phase.
8	DPR uses a spray drift model used for predicting offsite accumulation to estimate air concentrations for potential inhalation by bystanders. However, the model used has not been validated for the prediction of air concentrations.	The content of this comment are addressed in DPR's response to Dow AgroSciences LLC comments in the memo dated August 15, 2017 (see responses 10 and 25).
9	To appropriately justify the use of exposures to combined media, the agency should distinguish between exposure scenarios of agricultural applications and those of anticipated high exposures from treated turf via dermal contact and inhalation.	The residential bystander scenarios chosen represent the reasonable worst case legal agricultural application scenarios in California. The potential residential bystander dermal exposure is assumed to take place on turf that receives spray drift residue associated with a legal agricultural application nearby a home. The potential inhalation exposure occurs in the same setting during the legal application.
10	Risk from full aggregate exposure is not assessed for exposures from air blast or ground-boom applications. The margins of exposure (MOEs) are only assessed for drift-related exposures and dietary, drinking water, and dust exposures are not included.	Only dust exposure is not directly included in the aggregated MOEs. All other exposures are included. Exposure to contaminated dust is addressed in DPR's response to comments from the Office of Environmental Health Hazard Assessment (OEHHA) in a memo dated August 15, 2017. See page 3.
11	Risk from aggregate exposure is not assessed for women of childbearing age despite being the most vulnerable population for neurodevelopmental effects.	On the contrary, the August 2017 draft risk assessment evaluated aggregate exposures from food and drinking water, and spray drift exposures from inhalation and deposition (i.e., dermal contact) for children and women of childbearing age. The aggregate exposures for children included additional exposures that are only expected for a young child such as mouthing activities object-to-mouth, hand-to-mouth, and incidental ingestion (see pp. 102 and 126 in the August 2017 draft evaluation).
12	The draft risk assessment does not aggregate dust exposure with the other routes of exposure in the Risk Appraisal. Dust collection studies in Kern and Tulare Counties where use is higher may more accurately represent statewide exposure levels. In addition, workers may take-home exposures, and both they and their families may be subject to both acute and chronic excess exposures after work ends.	House dust exposure will be included in evaluating the aggregate risk associated with chlorpyrifos exposure during the next revision of the risk assessment.
13	Air monitoring in California has repeatedly detected chlorpyrifos in air at considerable distances from	The contents of this comment are addressed in DPR's response to comments from OEHHA in a memo dated August 15, 2017. See page 37.

	<p>application sites. Chlorpyrifos may have a propensity to move off-site and potential for long-range transport in the atmosphere. In addition, to properly account for volatilization of chlorpyrifos vapor and its contribution to aggregate exposure, at a minimum DPR should supplement its air monitoring results with results from other vapor-based monitoring studies in Lindsay and Shafter (California).</p>	
14	<p>DPR fails to account for real-world exposure conditions and durations in assuming that the exposure interval is no more frequent than once every 10 days and that inhalation exposure will occur for 1 hr per day. This disregards the real-world scenarios of exposure to chlorpyrifos volatilizing for a number of days from a field and the location of residences and schools close to multiple fields which are not necessarily treated on the same days. DPR may consider longer durations, such as 2-hr or 3-hr TWA air concentrations at various distances from the site of application to see if these changes would impact inhalation exposure.</p>	<p>With regards to volatilization, the contents of this comment are addressed in DPR's response to comments from OEHHA in a memo dated August 15, 2017. See page 37. The appropriateness of the 1-hr per day exposure for short-term (1 day) exposure assessment, see the October 2, 2017 DPR memorandum "Evaluation and options for interim mitigation measures to reduce acute chlorpyrifos exposure to bystanders." Briefly, it may seem that a longer term air concentration would be more appropriate to characterize a ground boom or orchard airblast application. However, due to the nature of atmospheric mixing and the variability of wind direction over time, the 1 hr averaging time estimate will yield a higher air concentration. Thus, the 1-hr scenario is the worst case short-term inhalation exposure. Aerial applications of even large applications are completed within about 1 hr. Wind direction can be assumed to be reasonably constant in a single direction for 1 hr. If all other factors including position of the bystander relative to the application are held constant, any averaging time longer than 1 hr will effectively be lower than the 1 hr concentration because longer averaging times result in the concentrated plume being more fully dispersed.</p>
15	<p>DPR's assessment ignores risks to farmworkers.</p>	<p>See responses to comment #2.</p>
16	<p>Farmworkers are directly impacted by both accidents and improper use.</p>	<p>Exposure scenarios are reasonable worst case for legal California usage developed as described in Barry (2017). Also, the nature of addressing illegal exposures such as improper use is addressed in DPR's response to comments from OEHHA in a memo dated August 15, 2017 (page 32) Briefly, direct exposures (via inhalation or dermal contact) are prohibited by the product labels. The California Code of Regulation § 6614 also makes any direct exposure to human a violation that may result in legal actions by the county or the State. DPR's risk assessments only address legal application scenarios. Therefore, the direct pathways suggested in this comment are not included in risk assessment.</p>
17	<p>DPR noted that vapor was not evaluated and cited a new toxicological study submitted to US EPA that showed saturated air concentration of chlorpyrifos did</p>	<p>Using the modified Grain method (Lyman, 1985) as recommended by US EPA (2007), the vapor pressure of chlorpyrifos at 115 °F (i.e., 46 °C) was estimated as <math>3 \times 10^{-4}</math> mmHg. This estimated vapor pressure is a factor ~14 higher than that at room temperature (i.e., 2.1 x</p>

	not result in more than 10% RBC acetylcholinesterase inhibition. DPR should consider how high ambient temperature (> 115°F) affects the saturated air concentration of chlorpyrifos and inhalation exposure.	<p><math>10^{-5}</math> mmHg at 78 °F or 25 °C). Based on this observation, more chlorpyrifos would be expected to enter into the gas-phase with increasing ambient temperature. However, due to transport through various diffusive (e.g., advection) and non-diffusive processes (e.g., photo-oxidation) in the atmosphere, saturated vapor pressure (i.e., air concentration) of chlorpyrifos would not be achievable in an open field. Also, the photooxidation rate of chlorpyrifos in the air is rapid (i.e., half-life = 1.4 hours at 25°C) (Munoz et al., 2014) and increases with increasing temperature (i.e., shorter half-life at a higher temperature) (Atkinson, 2007). Hence, inhalation exposure to chlorpyrifos based on the saturated air concentration would exaggerate the health risk associated. An alternative approach will be explored to address the temperature effect on inhalation exposure to chlorpyrifos during the next revision of the risk assessment.</p> <p><i>References:</i>  Atkinson, R. 2007. Gas-phase tropospheric chemistry of organic compounds: a review. Atmospheric Environment 41:200-240.  Lyman, W. J. 1985. Estimation of physical properties. In Environmental exposure from chemicals, edited by W. B. Neely, and G. E. Blau. Boca Raton, Fla.: CRC Press.  Munoz, A., Rodenas, M., Borrás, E., Vazquez, M., and Vera, T. 2014. The gas-phase degradation of chlorpyrifos and chlorpyrifos-oxon towards OH radical under atmospheric conditions. Chemosphere 111:522-528.  US EPA 2007. Science Advisory Board (SAB) Review of the Estimation Programs Interface Suite (EPI Suite™).</p>
18	In the most recent mitigation efforts, DPR deemed chlorpyrifos a Restricted Use Material, a move that significantly limits use and provides additional precautions to protect human health through additional setbacks and use approval from county agricultural commissioners. These practices if observed in the scenarios outlined in this draft evaluation would prove to provide protection of human health above and beyond what is required.	Exposure scenarios are reasonable worst case for legal California usage developed as described in Barry (2017). The restricted use designation controls who may use chlorpyrifos and introduces some additional mitigation measures. However, the restricted use designation may not fully mitigate bystander exposures under reasonable worst case legal use scenarios. The draft risk assessment presents those scenarios.
19	The risks of indoor chlorpyrifos exposures to pregnant women and children where biodegradation does not occur as readily is not addressed.	The risk assessment evaluates risks due to acute exposure. Therefore, biodegradation has not been used as a factor to reduce potential exposure. That is, DPR assumes that all chlorpyrifos that may be present is bioavailable and none has decomposed to other compounds. For an assessment of risk from specific indoor exposures, please see Section IV.A.2.d. Exposure from House Dust (p. 101) in the August 2017 draft risk assessment.
20	Risk from full aggregate exposure is not assessed for exposure from air blast or ground boom applications,	Table 56 on page 131 in the August 2017 draft risk assessment shows aggregate risk, including dietary and drinking water for ground boom due to spray drift. Table 58 on page

	but only for drift related exposures.	134 in the August 2017 draft risk assessment shows aggregate risk, including dietary and drinking water for orchard airblast due to spray drift. Dust exposure is not included in these aggregate risk estimates. Please see response to comment #12 above for a discussion on dust exposure incorporation into the aggregate risk estimates.
21	Risk from aggregate exposure for women of childbearing age despite being the most vulnerable population for neurodevelopmental effects. A full accounting of the aggregate exposure which include dietary and drinking water, and dust is not included.	With respect to dietary and drinking water exposures, please see the response to comment# 20. Section IV.A.2.d “Exposure from House Dust” in the draft risk assessment addressed issue on chlorpyrifos exposure via house dust. Because the origin of chlorpyrifos on the dust particles could not be determined, the draft risk assessment made no distinction of dusts from “take-home” or “track-in” etc. In other words, the draft risk assessment considered house dust derived from all sources including “track-in.” House dust exposure will be used for evaluating the aggregate risk associated with chlorpyrifos exposure during the next revision of the risk assessment.
22	There have been several recent incidents involving chlorpyrifos drift after field applications that have put nearby workers and communities at risk. Recent air monitoring data reveal that chlorpyrifos residues are more than 18 times higher than federal levels of concern.	From the comment submitted, it is unclear which federal level of concern is being referenced. It would be inappropriate to presume either the level of concern or the exposure period the commenter is referencing. None of the measured chlorpyrifos concentrations listed in the 2017 DPR air monitoring report exceeded any of the established DPR screening levels.
23	DPR assumes that chlorpyrifos use equates with exposure.	The exposure assessment does not associate proximity to application sites or data from the Pesticide Use Reporting database. A summary of findings of a study was included in the human epidemiology section of the risk assessment in which the authors estimated the association between pesticide application data and adverse health outcomes (see pg. 57 in August 2017 draft). The concluding statement in the study summary was from the authors of the study, and should not be interpreted as concurrence of findings by DPR.
<b>Toxicology-related Comments</b>		
1	DPR used inappropriate exposure estimate based predominantly on a scenario where a child is downwind at the edge of a field and exposed to a chlorpyrifos application every day for 21 consecutive days.	The draft risk assessment did not perform the described “inhalation and dermal exposure calculations for 1 – 1.5 hours every day for 21 days in a row.” The 21 days exposure scenario was employed by the U.S. EPA for deriving route-specific PoD values in the Agency’s 2014 risk assessment of chlorpyrifos.
2	The draft evaluation does not provide an analysis of how the 10x uncertainty factor will be protective of neurodevelopmental effects. There is no evidence for the sufficiency of this uncertainty factor, other than results from the zebrafish assay.	As discussed in several sections of the draft RCD, DPR recognizes the uncertainties associated with the use of a default factor of 10 to account for potentially more sensitive neurodevelopmental effects than AChE inhibition, the critical endpoint used to characterize the risk from CPF exposure. Effects on cognition, motor control and social behavior have been consistently reported in the CPF epidemiology and animal toxicology studies, and are carefully reviewed in the DPR revised risk assessment. However, please note that these studies were not sufficient to derive critical points of departure for

		<p>neurodevelopmental effects due to uncertainties associated with dose-response characteristics and exposure duration. Moreover, most animal studies were conducted with doses that also produced AChE inhibition at some time during the exposure. The revised draft does include evidence for CPF-induced behavioral effects in young rats that may occur at doses up to 10-fold lower than the threshold established for RBC AChE inhibition, though as noted, precise quantification was not possible.</p>
3	<p>DPR relies on the Columbia study to determine hypothetical risks and to make regulatory decisions, and did so without defining criteria for incorporating epidemiology data into risk assessments. Results from epidemiology studies were used to justify applying an additional safety factor of 10x for neurodevelopment effects, when this approach is not shared by EFSA or Australia in their most recent risk assessments.</p>	<p>For clarification, DPR did not use the Columbia Center for Children’s Environmental Health study to establish the point of departure (the regulatory target). The points of departure proposed in the DPR August 2017 draft are based on cholinesterase inhibition similar to those found in the 2014 US EPA revised Human Health Risk Assessment. As explained in DPR’s response to comment received from Dow AgroSciences LLC on the December 2015 draft, the Columbia Cohort study does not provide dose-response data for quantitative risk assessment. Likewise, DPR did not set a regulatory target based on data from the Columbia Cohort, but rather developed targets based on physiological-based pharmacokinetic-pharmacodynamic modeling that estimated the inhibition of red blood cell cholinesterase activity in humans from exposure via different routes. However, DPR has an obligation to review all data concerning any potential human health effects from exposure to chlorpyrifos as part of the department’s completeness and transparency of the risk assessment process. Therefore, DPR did its due diligence to critically review all ongoing epidemiological studies that are investigating associations between potential gestational environmental exposures and health outcomes in offspring later in life.</p> <p>DPR has not developed formalized criteria for incorporating epidemiological data into quantitative risk assessments. However, US EPA developed a framework in 2016 to incorporate epidemiology into pesticide risk assessment which was reviewed by the FIFRA Scientific Advisory Panel (SAP). US EPA is beginning to implement systematic review procedures consistent with the Integrated Risk Information System and the National Toxicology Program. As those processes evolve, DPR will consider how to best incorporate epidemiological data into our risk analyses. Until then, epidemiological data may be considered in the weight of evidence, but not to establish points of departure.</p> <p>Based on the review of the entire CPF database, DPR concluded that the available epidemiology and animal toxicology studies were not sufficient to derive critical point of departure for neurodevelopmental effects. Consequently, DPR used a default factor of 10 to account for the potentially more sensitive neurodevelopmental effects than AChE inhibition. Uncertainties associated with dose-response characteristics and exposure duration in these studies are found in the DPR draft risk assessment.</p>

4	<p>DPR’s draft evaluation dismisses the US EPA finalized 2016 Risk Assessment. In addition, DPR does not explain why it chose not to use the revised US EPA steady-state inhalation POD of 0.00021 mg/m<sup>3</sup> for residential/bystander, but rather retained the POD from the 2014 draft HHRA.</p>	<p>As discussed throughout the draft risk assessment, DPR is aware of the uncertainties associated with the use of AChE inhibition as the critical effect for assessing the risk from CPF exposures when potentially more sensitive neurodevelopmental effects have been reported in epidemiology and animal toxicology studies. However, at this time DPR chose not to use the PoDs estimated in the Nov 2016 US EPA revised risk assessment. These PoDs were derived using physiologically-based pharmacokinetic modeling to predict time weighted average (TWA) blood concentrations of CPF for the women in the Columbia cohort. DPR carefully reviewed this novel approach and concluded that these PoDs carry substantial uncertainty due to the unknown exposure levels, duration of exposure, and critical windows of susceptibility, especially in utero. Because of these uncertainties, DPR has continued to rely on the 2014 US EPA risk assessment that established critical PoDs based on 10% RBC AChE inhibition and to further reduce these values by a factor of 10 to account for the possibility of neurodevelopmental effects. DPR is in close contact with US EPA as they continue to finalize their risk assessment ahead of the 2022 reregistration deadline, and we look forward to the results of any future external scientific review on the 2016 US EPA revised risk assessment.</p>
5	<p>DPR’s risk assessment does not address combined or cumulative impacts of multiple agricultural chemicals, including other organophosphates with similar mechanisms of action.</p>	<p>Assessing and mitigating cumulative risk from multiple pesticides is both technically and legally challenging. Although DPR does not routinely assess the risk from exposure to multiple chemicals, it commonly includes the identical breakdown products of significant toxicological concerns in a single-chemical risk assessment. For example, in the previous ambient air risk assessment of methyl parathion the exposure to the metabolite methyl paraoxon was accounted for using the toxicity equivalence factor approach. This approach involves the comparison between the toxicity of methyl parathion and methyl paraoxon based on available data (i.e., reported LD50 values and the inhibition of plasma and brain ChE activities).</p> <p>Addressing cumulative risk within the current legal framework is also challenging because State law and regulations are designed for individual pesticides. For example, DPR’s regulations include an exposure threshold to determine if a pesticide is a toxic air contaminant. If exposure to individual pesticides does not meet the threshold, but the combined exposure to multiple pesticides does, it is not legally clear which if any of the pesticides should be designated as toxic air contaminants.</p> <p>With the 2006 publication of a framework for OP Cumulative Risk Assessment, US EPA initiated “group review” for organophosphates in 2008. This group review is “simultaneously reviewing related pesticides in groups” (see <a href="https://www.epa.gov/pesticide-reevaluation/groups-pesticides-registration-review">https://www.epa.gov/pesticide-reevaluation/groups-pesticides-registration-review.</a>)</p>



		<p>According to US EPA, the agency’s approach to simultaneous review is an internal process designed to increase program efficiencies and optimize internal resources, and to allow EPA to consider similar technical or regulatory issues in a chemical class. However, US EPA, like DPR, does not publish human health risk assessments for groups of active ingredients. But, rather, because each active ingredient needs to be regulated individually, human health risk assessments will be conducted on individual chemicals.</p>
6	<p>DPR’s assessment of dietary and drinking water residues does not include detections of illegal residues.</p>	<p>US EPA sets the legal limit (tolerance) for the amount of pesticide residues allowed in food. Over the years, DPR’s residue monitoring program has detected illegal chlorpyrifos residues on various commodities, most or all of which were imported. Neither DPR nor US EPA assesses the health implications of illegal residues on agricultural commodities in their dietary exposure assessments, which are restricted to analyzing the health implications of legal residues. However, DPR’s Enforcement Branch enforces US EPA tolerances under the California Pesticide Residue Monitoring Program, which collects domestic and imported produce samples throughout the channels of trade, including wholesale and retail outlets, distribution centers, and farmers markets. These samples are analyzed for pesticide residues at laboratories run by the State of California’s Department of Food and Agriculture. When a pesticide residue is determined to be illegal by virtue of (a) its occurrence on a commodity for which there is no established tolerance; or (b) its level exceeding the established tolerance, DPR’s Human Health Assessment Branch (HHA) conducts a special dietary exposure assessment to determine if an acute health risk exists from consumption of that lot. The results are then communicated to the Enforcement Branch, which has the authority to remove affected produce from channels of trade.</p> <p>To estimate the CPF exposure in drinking water, HHA conducted refined, probabilistic analyses using the entire range of residues measured by DPR’s Environmental Monitoring Branch in surface and ground water in CA. [Note: Drinking water residues cannot be considered to be “illegal” because US EPA does not establish tolerances in this medium. For some pesticides, the allowable level of chemical in the water is established through Maximum Contaminant Levels (MCLs), although there is no MCP for chlorpyrifos.]</p>
7	<p>In the calculation of margins of exposure (MOE), DPR applied an uncertainty factor (UF) of 10 to account for intraspecies variability. However, an UF of 30 may be more appropriate because of differences in physiology (ex: oral absorption efficiency may vary up to 3x from person to person), genetics, and life stage (such as hormonal and physiological changes associated with pregnancy).</p>	<p>The draft RCD has extensive discussions with respect to the default intra-human variability factor of 10. Additional considerations pertaining to the influence of genetics and life stage were provided in the response to comments from the Office of Environmental Health Hazard Assessment dated August 18, 2017.</p>

8	<p>The PON1 gene has the ability to hydrolyse and detoxify organophosphorus compounds. Low PON1 activity found in children may increase their susceptibility to organophosphates. As a result, some babies have been found to be 25-50 times more vulnerable to the neurotoxic effects of organophosphates.</p>	<p>While differences in PON1 activity may partially account for differences in sensitivity to OPs, the range of sensitivity in human populations depends on more than just the activity of this enzyme alone. Other factors impacting the activity of the enzyme include the substrate specificity and binding efficiencies, the rate of oxon formation via phase I metabolism, competing pathways for the removal of the parent compound, metabolic interactions with endogenous compounds, and therapeutic drugs that compete for CYPs, as well as certain lifestyle or environmental factors. All of the factors that may contribute to OP sensitivity are not known nor have their quantitative contribution to sensitivity been elucidated. But based on current knowledge, we propose that a default intraspecies variability factor of 10 will adequately protect human populations. For further discussion on the PON1 status, please see DPR response to comments from the Office of Environmental Health Hazard Assessment dated August 18, 2017 (pp. 23-24).</p>
9	<p>“Steady state” effects of 21-30 days do not equate with chronic and recurrent exposures experiences in agricultural communities.</p>	<p>Please note that the current risk assessment addresses only acute exposure estimates. As resources allow, DPR may address subchronic and chronic exposures in the future.</p>