

No.	Comment/Response	Commenter
1	<p>DPR should cancel the registration of pesticide products containing the active ingredient chlorpyrifos.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	A1-A3815; B1-B45; 4, 8, 9; T1-T5, T7, T9-T12, T14, T15, T17
2	<p>DPR should suspend the registration of pesticide products containing the active ingredient chlorpyrifos.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to FAC section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	B34, B41-45; 1, 2, 5, 6; T7, T12, T13, T15
3	<p>Support listing chlorpyrifos as a toxic air contaminant.</p> <p><i>DPR agrees.</i></p>	B34, B37-38, B40-45; 1, 2, 3, 5; T12, T14, T15
4	<p>Chlorpyrifos should be restricted or have further restrictions.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to FAC section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	4, 8
5	<p>Create rich, biodynamically viable soil and use companion planting and beneficial bacterial and insect controls instead. So many wasted resources converted into deadly toxins on land and in water and air. Intelligent use and distribution of these can reverse increasing levels of toxicity and reduce carbon emissions.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to FAC section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	B14
6	<p>There are enough pesticides on the market that the removal of this extremely harmful pesticide should be allowed.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to FAC section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	B27
7	<p>DPR has the authority to halt exposures immediately by suspending use in California (FAC sections 12825 and 12826) while formal assessment of control options are considered.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to FAC section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	6

8	<p>Dow AgroScience believes DPR's Final Evaluation misinterprets key toxicological points and the exposure assessment lacks refinement. The Final Evaluation therefore significantly over-estimates potential exposure and risk. Refinements discussed in these and previous comments demonstrate acceptable levels of risk and Margins of Exposure with current use patterns, and therefore chlorpyrifos does not meet the criteria for listing as a toxic air contaminant. Further refinements the Final Evaluation can and should be made prior to a final decision on DPR's proposal to add chlorpyrifos to the Toxic Air Contaminants List and before developing any further risk mitigations.</p> <p><i>See response to comments 10, 12, 13, and 14.</i></p>	10
9	<p>DPR should review and consider the previous Dow AgroScience comments submitted to DPR and the Scientific Review Panel (SRP).</p> <p><i>DPR considered and responded to Dow AgroScience's comments on the draft August 2017 and December 2015 draft risk assessment.</i></p>	10
10	<p>Cholinesterase inhibition remains a conservative regulatory endpoint protective of all other toxicities including possible neurodevelopmental effects.</p> <p>There is strong, consistent, and compelling evidence spanning more than 50 years of experimental study in animals that acetylcholinesterase inhibition is a sensitive endpoint that is protective of all other toxicities including neurobehavioral, neuropharmacologic, and morphologic alterations.</p> <p><i>Chlorpyrifos meets the criteria of a Toxic Air Contaminant designation whether the cholinesterase inhibition endpoint or the developmental neurotoxicity endpoint is used.</i></p> <p><i>As described in detail in the August 2018 Final Evaluation of Chlorpyrifos as a Toxic Air Contaminant, DPR reviewed recent in vivo animal studies reporting developmental toxicity in rodents at doses causing minimal or no brain acetylcholinesterase inhibition. Our understanding is that these studies were not included in the 2016 U.S. Environmental Protection Agency (U.S. EPA) revised human health assessment for chlorpyrifos. With the exception of Lee et al. (2015), the Australian Pesticides and Veterinary Medicines Authority (APVMA) 2017 Supplementary Toxicology Report did not include the in vivo studies DPR and the TAC SRP evaluated. The 2014 European Food Safety Authority (EFSA) document did not list primary literature sources. However, because of the date of publication, it is unlikely that these in vivo studies were included in EFSA's review since they were conducted after EFSA rendered its decision.</i></p>	10

As stated in the August 2018 final TAC evaluation, the in vivo studies DPR and the Scientific Review Panel reviewed consisted of four studies in rats and one study in mice. Exposure was by the oral route (three by gavage, two through the diet). Two studies employed both gestational and lactational exposure through the dams (a total of 35 doses, 14 consecutive daily doses during pregnancy and 21 doses during lactation). Two studies employed direct pup exposure for either one or seven days starting at post-natal day 10.

Neurodevelopmental responses in offspring were tested either in young pups (post-natal day 21-25) or in adults (60-90 days). Three studies reported increased motor or total activity, two studies showed altered anxiety levels (decreased or increased), and one study detected impaired spatial learning. The lowest-observed-effect levels (LOELs) for the observed neurodevelopmental effects were 0.1-0.5 mg/kg/day. In four of the studies, the LOEL was the lowest tested dose. Applying an uncertainty factor of 10 to those LOELs would result in an estimated no effect level (ENEL) for developmental neurotoxicity of 0.01-0.05 mg/kg/day. One study included a no-observed-effect level (NOEL) dose based on increased anxiety and motor activity in rats that were exposed in utero with chlorpyrifos for 6 days (Silva et al., 2017). Only one study concurrently measured acetylcholinesterase activity, setting the LOEL for brain acetylcholinesterase inhibition at 1.0 mg/kg/day (Carr et al., 2017). These new findings indicate that the developing nervous system is sensitive to low doses of chlorpyrifos that are not expected to inhibit brain or red blood cell acetylcholinesterase activities.

Based on the five studies, the collective LOEL for neurodevelopmental effects including in cognition, motor control, and behavior in rats and mice, is 0.1 mg/kg/day. A NOEL of 0.01 mg/kg/day was established by Silva et al., (2017) based on increased anxiety and motor activity in rat pups. This NOEL is supported by the ENELs of 0.05- 0.01 mg/kg/day estimated from the developmental neurotoxicity LOELs of 0.5-0.1 by applying a 10 fold uncertainty factor. The exposure duration in the five published studies varied from 1 to 35 days. Therefore, the NOEL of 0.01 mg/kg/day could be applicable to acute and repeated exposures to chlorpyrifos in infants, children, and females of childbearing age.

As a reminder, DPR did not use the epidemiological studies to establish a point of departure for neurodevelopmental effects, as a quantitative exposure-effect relationship could not be established from the available human data.

The Scientific Review Panel approved DPR's August 2018 Final Evaluation of Chlorpyrifos as a Toxic Air Contaminant, concluding unanimously that the report is based on sound scientific knowledge and represents a balanced assessment of current scientific understanding. The panel also concluded unanimously that

	<i>chlorpyrifos should be listed as a toxic air contaminant and that developmental neurotoxicity is the appropriate regulatory endpoint.</i>	
11	<p>Cholinesterase inhibition remains a conservative regulatory endpoint protective of all other toxicities including possible neurodevelopmental effects.</p> <p>Evaluation of animal studies does not support an allegation of adverse effects below the current regulatory endpoint of Red Blood Cell Cholinesterase Inhibition (RBC ChEI).</p> <p><i>Please see response for comment no. 10.</i></p>	10
12	<p>Cholinesterase inhibition remains a conservative regulatory endpoint protective of all other toxicities including possible neurodevelopmental effects.</p> <p>Claims of a mode-of-action for effects below the current regulatory endpoint (RBC ChEI) are speculative at best, and no biological plausibility then exists for associating exposure to chlorpyrifos to neurodevelopmental outcomes below RBC ChEI.</p> <p><i>Human neurodevelopment is multifactorial. Recent findings indicate a growing association between chlorpyrifos exposures during gestation and impacts on human growth and development, even though an adverse outcome pathway for chlorpyrifos neurotoxicity has not yet been elucidated. There may be multiple pathways or covariates independent of acetylcholinesterase inhibition at play, such as PON1-mediated oxidative stress (Harley et al., 2011). In addition, there is evidence that in vitro neuronal growth is impacted by the active metabolite, chlorpyrifos-oxon at concentrations below those that inhibit acetylcholinesterase (reviewed in Eaton et al., 2008). There are challenges in incorporating epidemiological results into quantitative risk assessment because of limited exposure data and inconsistencies across studies in dose and effect. However, a lack of a clear mechanism of action does not negate results from numerous observational studies. It is important to consider potential associations documented in epidemiological studies as important mechanistic investigations continue. The final TAC evaluation reflects the most current and available in vivo animal and epidemiological evidence. DPR and the SRP evaluation of these data provide the current possible sensitivity of the developing nervous system to low doses of chlorpyrifos.</i></p>	10
13	<p>The DPR Final Evaluation included potential non-occupational bystander (adults and children) exposure from spray drift aerosols following the agricultural use of chlorpyrifos, as a component of aggregate exposure. The bystander and aggregate exposure assessment includes factors resulting in overestimation, i.e., exaggeration of estimates for adults and children. Refinements to the predicted exposures are necessary to support credible, science-based evaluation and related decision-making.</p>	10

	<p>The bystander exposure scenario is defined as episodic (single day) bystander (adults and 1-2 year old children) inhalation exposure for 1 hour (in addition to dermal and incidental oral) from aerosol drift associated with aerial, airblast and groundboom agricultural applications. As acknowledged by DPR, in their Draft Evaluation, based on the inhalation Point of Departure (POD) currently being proposed based cholinesterase inhibition, assumes that a spray drift bystander inhalation exposure event occurs every day for 21 consecutive days. This is inconsistent with label instructions and agricultural practices. The inhalation POD should be adjusted to reflect actual application intervals.</p> <p><i>DPR’s December 2017 draft evaluation 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-day exposure scenario was employed by U.S. EPA for deriving route-specific points of departure in the Agency’s 2014 human health risk assessment of chlorpyrifos. The same steady-state assessment was not included by DPR in its final, SRP reviewed, TAC evaluation of chlorpyrifos because the critical endpoint was changed from acetylcholinesterase inhibition (with points of departure derived from the PBPK-PD model) to developmental neurotoxicity (with points of departure derived from in vivo animal studies).</i></p>	
14	<p>In the DPR aggregate assessment, the assumed bystander spray drift-related aerosol inhalation exposures contributed up to 95 percent to the total aggregate exposure from these screening-level modeling estimates. This finding contradicts biological monitoring data which indicate that the primary source of exposure is diet alone, not spray drift (or drinking water). Thus, further scrutiny and evaluation of the bystander exposure scenario is needed to better understand sources of uncertainty and bias. The theoretical worst-case bystander exposure scenario is a young child, standing only a few feet from the field during the entire time of an application each day for 21 days. Without this over-estimation of bystander inhalation risk, current buffer zones are shown to continue to protect public and environmental health.</p> <p><i>DPR did not use an aggregate exposure methodology for the final 2018 TAC evaluation of chlorpyrifos. Rather, individual margins of exposure were derived from each individual exposure route. Please refer to Section V, Risk Characterization, starting on page 78 of the 2018 final evaluation document for the evaluation of spray drift and dietary exposure using a developmental neurotoxicity point of departure.</i></p>	10
15	<p>The spray drift and bystander exposure model used by DPR was developed and validated for deposition on surfaces, not for predicting air concentrations of inhalable (< 100 µm aerodynamic diameter) aerosols and vapors for inhalation exposure estimates. Drift of inhalable aerosol-size particles and potential inhalation exposure is far more complex, and the model has not been validated for this use. DPR assumes the bystander is exposed to drift with 100 percent of the spray being of an inhalable (< 100 µm aerodynamic diameter) aerosol particle size and does not recognize that only a fraction of the total aerosol mass will be within an aerosol size</p>	10

	<p>range that can be inhaled and potentially deposited in the respiratory tract. Appropriate adjustment for inhalable (< 100 microns) and/or respirable (< 10 micron) particles sizes would demonstrate significantly lower Margins of Exposure, i.e., reasonable certainty of no harm.</p> <p><i>DPR specifically requested the SRP to comment on the question of whether the assessment overestimates the inhalable fraction of chlorpyrifos, and they recommended assuming 100 percent of the aerosols are inhalable.</i></p>	
16	<p>There are multiple factors contributing to the unrealistic, remote probability of this scenario occurring and indicate the need for further refinement. No label use allows for an application that occurs every day for 21 days. A field application is a discrete, defined event and potential bystander exposure through inhalation would be limited at worst to a short duration, such as 1 hour or less, but as mentioned above, the assessment done by DPR creates an exposure estimate as if a child is at edge of field for 21 days. Any exposures through other routes, such as dietary that might occur on those days would be much less than assumed in the DPR approach (i.e., dietary exposures occur at the 99.9th percentile predicted level every day). Maximum label use rates, rather than typical use rates are assumed. The child in the bystander scenario is always considered to be downwind of the application, thus receiving the maximum possible exposure. Every day the child is also assumed to be engaged not only in activities which result in high contact with surfaces that receive the hypothetical drift, but also ones that maintain an elevated breathing rate. Even if this was true for one application, it is unrealistic to assume it happens every day for 21 consecutive days. Using actual product use information via the California Pesticide Use Reporting (PUR) system, and thereby taking into account the probability of just some of the aspects of the exposure scenario occurring, such as actual application rates and their frequency of occurrence over time in selected geographic areas, along with the fraction of inhalable or respirable particles, provides important refinement to AgDrift modeling. Further, refinement to other exposure factors could be considered such as being downwind of an application, living next to an agricultural field. These would provide important improvements to bystander exposure and absorbed dose estimates. The probabilities associated with bystander exposure magnitude and frequency are also important considerations for regulatory decision-making.</p> <p><i>See response to comment no. 13.</i></p>	10
17	<p>The fact that a large percentage of any potential drift would be vapor and not aerosol is important since research confirms that inhalation of chlorpyrifos in its vapor state, even at the highest amount that can be established in the air, would not present a risk above the current regulatory endpoint of red blood cell cholinesterase inhibition. This significantly over-estimates exposure and risk.</p> <p><i>See response to comment no 15.</i></p>	10

18	<p>The product use rates evaluated are not all supported by product labeling. Maximum rates allowed for ground broadcast application is 4 lb ai/acre, with the great majority of uses at 1 to 2 lb ai/acre. In addition, some buffer zone distances that were evaluated for bystander risk are not allowed under current labeling.</p> <p><i>All risk assessments including the chlorpyrifos TAC evaluation are designed to address the potential risks associated with current legal uses per the label. The maximum application rates for chlorpyrifos that were used to estimate exposures for each application method are the highest legally allowed rates. For potential residential bystander dermal exposure, we assumed that the exposure occurs on turf that receives spray drift residue associated with a legal agricultural application adjacent to a home. The potential inhalation exposure occurs in the same setting during the legal application. In the end, the residential bystander scenarios chosen represent the reasonable worst case legal agricultural application scenarios in California.</i></p>	10
19	<p>Aerial applicators routinely make practical operational decisions to mitigate spray drift by selecting appropriate nozzles, modifying airspeed, adjusting application volumes, adjusting for wind conditions, and optimizing equipment settings. With proper parameterization, these can be well-reflected with modelling and offer more rigor to the assessment.</p> <p><i>See response to comment no. 18.</i></p>	10
20	<p>The use of the existing chlorpyrifos PBPK-PD model provides a validated, robust methodology for determining route-specific, and total absorbed dose. DPR has used this model for Point of Departure derivation. The model can also be used to determine more accurate estimates of absorbed dose as a function of time post-exposure. This would be a refinement to methods currently being used.</p> <p><i>In the December 2017 Draft Evaluation of Chlorpyrifos as a Toxic Air Contaminant, the critical NOELs for evaluating oral, dermal, and inhalation exposure to chlorpyrifos from diet and spray drift were toxicological points of departure based on red blood cell acetylcholinesterase inhibition. DPR used the points of departure from the U.S. EPA 2014 Revised Human Health Risk Assessment as a starting point for both the December 2017 and August 2017 draft evaluations. These points of departure were PBPK-PD model-derived human equivalent doses based on 10 percent inhibition red blood cell acetylcholinesterase activity after an acute (single day, 24 hr) or steady-state (21 days) chlorpyrifos exposure in humans. However, when the critical endpoint was revised from acetylcholinesterase inhibition to developmental neurotoxicity, the final points of departure were based on five in vivo animal experiments from which a NOEL of 0.01 mg/kg/day was derived.</i></p>	10

21	<p>Multiple years of air sampling in California show chlorpyrifos detections are infrequent and at levels below any significant health risk.</p> <p><i>The highest detection of chlorpyrifos from DPR’s Air Monitoring Network meets the criteria for listing as a TAC. Moreover, the results from DPR’s Air Monitoring Network are not representative of exposure that can occur adjacent to an application. The Network is designed to estimate seasonal and long-term exposures to regional use of multiple pesticides, by evaluating the concentration of pesticides in ambient air. The Network is not designed to provide data on worst-case acute exposures to chlorpyrifos, which is the type of data normally evaluated when performing a human health risk assessment.</i></p>	10
22	<p>We are concerned that DPR has ignored evidence that real-world air samplings show current restrictions and grower management practices for applications are effective. Actual air sampling in California over several years shows chlorpyrifos detections are rare. DPR’s Air Monitoring Network has over the last 7-year period been focused in high pesticide use areas, yet detections for Chlorpyrifos are infrequent and when detected, most of those detections were trace levels at or above the limit of detection, but below a quantifiable limit. And in each year of the monitoring program, detections were well below the Department’s acute, subchronic, and chronic screening levels. These results clearly demonstrate that current mitigation practices are effective and additional mitigations are not needed. Considering the success of current practices, we ask that if DPR moves forward with listing chlorpyrifos as a TAC, it not add additional mitigations that would add unnecessary costs to growers.</p> <p><i>See response to comment no. 21.</i></p>	11
23	<p>We respectfully urge DPR to reconsider its decision to list chlorpyrifos as a TAC.</p> <p><i>DPR acknowledges the comment but disagrees.</i></p>	12
24	<p>Our growers take pride in the ability to produce a crop in the safest and most responsible manner. It is because of this stewardship that chlorpyrifos detection through the department’s own Air Monitoring Network that detections have been rare and infrequent. We ask that the department take this matter into consideration as well as further refining bystander exposure estimates to reflect real-world application, label rates and current mitigation measures.</p> <p><i>See response to comment no. 21.</i></p>	13, 14

25	<p>We feel that that the listing of chlorpyrifos as a Toxic Air Contaminant with additional mitigation measures is founded upon unrealistic and over-estimating scenarios, and ignores the precautionary measures currently observed by the industry including compliance of the product's Restricted Use Material status.</p> <p><i>DPR's risk assessment indicates that DPR's current recommended permit conditions do not completely mitigate exposure to chlorpyrifos. Also, see response to comment no. 21.</i></p>	13, 14
26	<p>If additional restrictions were to be imposed, we ask that DPR consider the damage that would be done to the integrated pest management system in place today.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	13, 14
27	<p>DPR should allow exemptions to their proposed mitigation techniques, including allowing use of chlorpyrifos for certain critical needs or under special circumstances.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	15, 16
28	<p>DPR should consider certain circumstances and pest management difficulties where chlorpyrifos can be used due to necessity.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	16
29	<p>Based on the results of the SRP's findings, did DPR determine or take into account which chlorpyrifos formulation type could pose or present more of a potential hazard? Eliminating one formulation could be a simple mitigation solution.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	16

30	<p>I cannot express enough my grave concerns at the thought of DPR creating further regulations proposing acreage restrictions for application.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	16
31	<p>We feel that the science used to come up with the decision to list chlorpyrifos as a toxic air contaminant does have its issues, namely that the expectations of its use are unrealistic.</p> <p><i>See response to comment no. 13.</i></p>	T18
32	<p>We ask that DPR keep an open mind when it comes to the mitigation process for chlorpyrifos, especially for citrus.</p> <p><i>The purpose of the proposed action is to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code (FAC) section 14023(a). These comments are outside of the scope of the proposed regulation.</i></p>	T18