****DRAFT FOR DISCUSSION****

Findings of the Scientific Review Panel on the Proposed Identification of Chlorpyrifos as a Toxic Air Contaminant as adopted at the Panel's July 30, 2018 Meeting

The Scientific Review Panel on Toxic Air Contaminants (Panel) reviewed the draft document "**Evaluation of Chlorpyrifos as a Toxic Air Contaminant**," prepared by the Department of Pesticide Regulation (DPR) along with findings prepared by the Office of Environmental Health Hazard Assessment (OEHHA) that propose to identify chlorpyrifos as a toxic air contaminant.

In addition, the Panel reviewed DPR's responses to the comments in the OEHHA document, as well as public comments received during DPR's public comment process and DPR's responses to those comments, and public comments submitted to the Panel during its review.

The Panel received a briefing on the initial DPR draft report in a meeting on December 13, 2017, and a full presentation by DPR staff in its January 23, 2018 meeting. The Panel subsequently reviewed revised reports in meetings on March 2, 2018 and June 12, 2018. At its January 23, 2018 meeting and in subsequent meetings, in addition to hearing presentations from DPR and OEHHA staff, the Panel provided recommendations to DPR, most notably that the primary health endpoint should be developmental neurotoxicity (DNT).

As part of its statutory responsibility, the Panel prepared the following findings based on its review of the chlorpyrifos risk characterization, which are submitted to the DPR Director.

The materials as noted above convincingly demonstrate that:

(1) Chlorpyrifos is a widely used insecticide in California.

(2) Chlorpyrifos exposure is associated with developmental neurotoxicity that has been documented in human epidemiology studies and in laboratory animal studies. Developmental neurotoxicity has been demonstrated to occur at levels substantially below those that cause 10% acetylcholinesterase (AChE) inhibition, an endpoint that was used in previous assessments of Chlorpyrifos toxicity.

(3) Based on a full review of all currently available science, developmental neurotoxicity is the appropriate regulatory endpoint for Chlorpyrifos to protect health.

(4) Its physical and chemical properties and the manner in which it is applied are such that its environmental fate includes release into the environment as an airborne contaminant.

(5) Such airborne release may occur through its routine use.

(6) Illnesses that may have been caused by exposures to Chlorpyrifos have been documented in DPR's Pesticide Illness Surveillance Program and evidence is sufficient to indicate that exposures related to the use of the application of this compound to crops are a matter of health concern.

(7) Chlorpyrifos is an organophosphate insecticide that inhibits the enzyme acetylcholinesterase which is critical for neurological functions.

(8) Although intake of Chlorpyrifos via food and water make significant contributions to the total body burden of Chlorpyrifos, this compound meets the criterion for designation as a toxic air contaminant even if one limits consideration to the combined inhalation and dermal exposure.

(9) The estimated bystander exposures to Chlorpyrifos are at levels that cause concern about the associated health risks. DPR regulations state that if the air concentrations of a pesticide are not ten-fold below the reference concentration (RfC) that is considered protective of human health, the pesticide meets the criteria to be listed as a toxic air contaminant (i.e., exposures should be less than 10% of the RfC). A margin of exposure (MOE) approach leads to this conclusion with respect to Chlorpyrifos when one considers developmental neurotoxicity as the key endpoint. However, the same conclusion is reached when one evaluates AChE inhibition, with an appropriate safety factor to account for neurotoxicity effects that occur at levels substantially below the 10% AChE inhibition level used in previous assessments of Chlorpyrifos.

The Panel commends DPR for a comprehensive and coherent review of the available literature and the synthesis which lead to a risk assessment that is firmly based on the available scientific information to date. The Panel notes that the science on organophosphate pesticide exposures is developing and expanding and that the final revision of the document brings the assessments up to the current state of the science.

DPR conducted a comprehensive review of recently available animal studies and focused on the evidence of neurodevelopmental toxicity at low dose levels. Critical Points of Departure (PoDs) were established from animal studies reporting effects at dose levels that were approximately 10-fold lower than those that inhibit red blood cell AChE. A target MOE of 100 was selected to be protective of human health for the neurodevelopmental endpoint and is comprised of 10x for interspecies sensitivity and 10x for intraspecies variability. With this approach, there is no need for an additional uncertainty factor for neurodevelopmental effects. The risk of exposures to inhalation and spray drift is exacerbated also by consumption of food and drinking water in this approach.

The database for developmental neurotoxicity is growing, and as new data become available DPR can further refine this assessment.

The critical NOELs and the reference concentrations are summarized in the table below, which was excerpted from the Final Report.

In conclusion, DPR evaluated the strengths and uncertainties associated with the use of the available database for deriving critical endpoints for Chlorpyrifos. DPR provided objective approaches for setting regulatory values that are designed to protect sensitive subpopulations from exposure to Chlorpyrifos. Following the recommendation of the Panel, DPR thoroughly evaluated and identified developmental neurotoxicity as the critical endpoint for the Chlorpyrifos risk assessment.

As required by law, the Panel has reviewed the scientific data on which the report is based, the scientific procedures and methods used to support the data, and the conclusions and assessments on which the report is based. The Panel concludes that the report, with the revisions specified by the Panel, is based on sound scientific knowledge, and represents a balanced assessment of our current scientific understanding.

Based on this comprehensive and thorough evaluation of the toxicity database on Chlorpyrifos, the Panel concludes that Chlorpyrifos should be listed as a toxic air contaminant and recommends that the DPR Director initiate regulatory steps to list Chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code section 14023.

Table 23. Critical NOELs for Developmental Neurotoxicity used for the Risk Characterization of Chlorpyrifos

Route	PoD[a]	RfD[b] or RfC
Uncertainty Factors (UF)		**10 inter 10 intra 1 DNT**
Acute Oral [mg/kg/day] Infants Children 1-2 Children 6-12 Females 13-49	0.01	0.0001
Acute Dermal [mg/kg/day]# Infants Children 1-2 Children 6-12 Females 13-49	0.104	0.001
Acute Inhalation [mg/m^3]# Infants Children 1-2 Children 6-12 Females 13-49	 0.405 0.459 0.624 0.862	 0.004 0.005 0.006 0.009

[a] PoD - Point of Departure (PoD): The critical acute oral PoD for CPF is a NOEL (No-Observed Effect Level) for developmental neurotoxicity in animals based on changes in cognition, motor control and behavior in rats and mice (Lee et al, 2015, Silva et al, 2017, Carr et al, 2017, Gómez-Giménez, 2017, 2018).

[b] RfD - Reference Dose (RfD) or Reference Concentration (RfC): RfD and RfC are derived by dividing the appropriate PoD by the product of all uncertainty factors (UF).

Route to route extrapolation:

Dermal: Route specific dermal PoD: oral PoD in animals (mg/kg/day) / dermal absorption in human (9.6% ; Thongsinthusak, 1991).

Inhalation: Route specific inhalation PoD: oral dose mg/kg/day / [Breathing Rate (BR) m3/hr/Body Weight (BW) kg]; Oral PoD=0.01 mg/kg/day; Infants BR=0.188 m3/h BW= 7.6 kg; Children 1-2 yrs BR=0.283 m3/h BW=13 kg; Children 6-12 yrs BR= 0.417 m3/h, BW=26 kg; Females 13-49 yrs BR=0.833 m3/h, BW 71.8 kg (derived from Andrews and Patterson (2000) assuming 24-hr breathing rates of 0.59, 0.52, 0.38 and 0.28 m3/kg/24 hr for infants, children 1-2 yr, children 6-12 yr and females 13-49 yr, respectively.) [See Appendix 4.]