UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: September 21, 2020

SUBJECT: Chlorpyrifos: Third Revised Human Health Risk Assessment for Registration Review.

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Decision No.: 559846	**Registration No.:** NA
Petition No.: NA	**Regulatory Action:** Registration Review
Risk Assessment Type: Single Chemical Aggregate	**Case No.:** NA
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As part of Registration Review, the Pesticide Re-evaluation Division (PRD) of the Office of Pesticide Programs (OPP) has requested that Health Effects Division (HED) evaluate the hazard and exposure data and conduct dietary (food and drinking water), residential, aggregate, and occupational exposure assessments to estimate the risk to human health that will result from the currently registered uses of pesticides. This memorandum serves as HED's draft human health risk assessment (DRA) for chlorpyrifos to support Registration Review.

The most recent human health risk assessment for chlorpyrifos was completed in 2016 (W. Britton *et al*, D436317, 11/03/2016). The following revisions have been included in the current risk assessment:

- The toxicological points of departure (PODs) are derived from 10% red blood cell (RBC) acetyl cholinesterase (AChE) inhibition using a physiologically-based pharmacokinetic-pharmacodynamic (PBPK-PD) model, as reported in the 2014 revised chlorpyrifos Human Health Risk Assessment (HHRA) (2014 (D. Drew *et al.*, D424485, 12/29/2014);
- Because the science addressing neurodevelopmental effects remains unresolved, the dietary, residential, aggregate, and non-occupational risk assessments have been conducted both with retention of the 10X Food Quality Protection Act (FQPA) safety factor (SF) and without retention of the 10X FQPA SF (*i.e.*, FQPA SF reduced to 1X). Similarly, the occupational risk assessments have been conducted both with and without retention of a 10X Database Uncertainty Factor (UF_{DB}).

As part of an international effort, the EPA's Office of Research and Development (ORD) has been developing a battery of new approach methodologies (NAMs)[1] for evaluating developmental neurotoxicity (DNT). The suite of *in vitro* assays developed by ORD evaluates the majority, but not all, of the critical processes of neurodevelopment. The ORD assays will be presented, using the organophosphates (OPs) as a case study, to the Federal Insecticide, Fungicide, and Rodenticide (FIFRA) Scientific Advisory Panel (SAP) in September 2020.[2] Additional assays that evaluate processes not covered by the ORD assays are currently under development by researchers funded by the Europen Food Safey Authority (EFSA). Once data are available from these additional assays, any OP data may be considered in combination with the results of the ORD assays in the future as part of an overall weight of evidence evaluation of the DNT potential for individual OPs, including chlorpyrifos.

[1] The term NAM has been adopted as a broadly descriptive reference to any non-animal technology, methodology, approach, or combination thereof that can be used to provide information on chemical hazard and risk assessment.
[2] https://www.epa.gov/sap/use-new-approach-methodologies-nams-derive-extrapolation-factors-and-evaluate-developmental

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1.0 Executive Summary

This document presents the third revision to the human health risk assessment for the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Registration Review of the organophosphate (OP) insecticide chlorpyrifos.

Background
A preliminary human health risk assessment (HHRA) for chlorpyrifos was completed on June 30, 2011 (D. Drew *et al.*, D388070, 06/30/2011) as part of the FIFRA Section 3(g) Registration Review program. A revised HHRA was completed in 2014 (D. Drew *et al.*, D424485, 12/29/2014) to address comments received on the preliminary HHRA and to incorporate new information and new approaches that became available since the June 2011 risk assessment. Most notably, the 2014 revised HHRA incorporated the following: (1) a physiologically-based pharmacokinetic-pharmacodynamic (PBPK-PD) model for deriving toxicological points of departure (PODs) based on 10% red blood cell (RBC) acetyl cholinesterase (AChE) inhibition; and (2) evidence on neurodevelopmental effects in fetuses and children resulting from chlorpyrifos exposure as reported in epidemiological studies, particularly the results from the Columbia Center for Children's Environmental Health (CCCEH) study on pregnant women which reported an association between fetal cord blood levels of chlorpyrifos and neurodevelopmental outcomes. The 2014 HHRA retained the 10X Food Quality Protection Act (FQPA) Safety Factor (SF) because of the uncertainties around doses that may cause neurodevelopmental effects.

Based on the aggregate risks identified in 2014 (D. Drew *et al.*, D424485, 12/29/2014), a proposed rule (PR) for revoking all tolerances of chlorpyrifos was published in the Federal Register on November 6, 2015 (80 FR 69079). At that time, the EPA had not completed a refined drinking water assessment or an additional analysis of the hazard of chlorpyrifos that was suggested by several commenters to the EPA's 2014 revised HHRA. Those commenters raised the concern that the use of 10% RBC AChE inhibition for deriving PODs for chlorpyrifos may not provide a sufficiently health protective human health risk assessment given the potential for neurodevelopmental outcomes. Accordingly, following the issuance of the proposed rule, the EPA conducted additional hazard analyses using data on chlorpyrifos levels in fetal cord blood (reported by the CCCEH study investigators) as the source for PODs for the 2016 risk assessment (W. Britton *et al.*, D436317, 11/03/2016). In the 2016 assessment, the 10X FQPA SF was retained.

In the current risk assessment, EPA is utilizing the same endpoint and points of departure as those used in the 2014 HHRA (i.e., the PBPK-PD model has been used to estimate exposure levels resulting in 10% RBC AChE inhibition following acute (single day, 24 hours) and steady state (21-day) exposures for a variety of exposure scenarios for chlorpyrifos and/or chlorpyrifos oxon). Despite several years of study, the science addressing neurodevelopmental effects remains unresolved. Therefore, the dietary, residential, aggregate, and non-occupational risk assessments have been conducted both with retention of the 10X FQPA SF and without retention of the 10X FQPA SF (*i.e.*, FQPA SF reduced to 1X). Similarly, the occupational risk assessments have been conducted both with and without retention of a 10X Database Uncertainty Factor (UF_{DB}).

This 2020 human health risk assessment substantially relies on the previous documents developed for chlorpyrifos, along with an updated animal toxicity literature review, and an updated drinking water assessment. Those primary documents include the following:

- D. Drew *et al.,* Chlorpyrifos: Revised Human Health Risk Assessment for Registration Review, December 29, 2014, D424485;
- U.S. Environmental Protection Agency, Literature Review on Neurodevelopment Effects & FQPA Safety Factor Determination for the Organophosphate Pesticides, September 15, 2015, D331251;
- R. Bohaty, Updated Chlorpyrifos Refined Drinking Water Assessment for Registration Review, September 15, 2020, D459269.
- R. Bohaty, Evaluating the Impact of Removal of the 10x FQPA Safety Factor on Chlorpyrifos, September 15, 2020, D459270.
- U.S. Environmental Protection Agency, Chlorpyrifos Issue Paper: Evaluation of Biomonitoring Data from Epidemiology Studies, March 11, 2016 and supporting analyses presented to the FIFRA Scientific Advisory Panel's (SAP) meeting on April 19-21, 2016, (EPA-HQ-OPP-2016-0062).
- W. Britton *et al*., Chlorpyrifos: Revised Human Health Risk Assessment for Registration Review, November 3, 2016, D436317.
- E. Méndez, Chlorpyrifos: Review of 5 Open Literature Studies Investigating Potential Developmental Neurotoxicity Following Early Lifestage Exposure, June 1, 2020, D457378.

Hazard Characterization

The hazard characterization for chlorpyrifos and its oxon is based on adverse health effects in animals and humans related to two different endpoints - AChE inhibition and potential for neurodevelopmental effects. A weight-of-the-evidence (WOE) analysis on the potential for neurodevelopmental effects following chlorpyrifos exposure has been completed using OPP's *Framework for Incorporating Human Epidemiologic & Incident Data in Health Risk Assessment* (USEPA, 2010; FIFRA SAP 2010). The Agency is using a robust PBPK-PD model to estimate human PODs for chlorpyrifos and/or its oxon for multiple exposure pathways (e.g., food, water, occupational, non-occupational, and residential) and using the PBPK-PD model to replace default inter- and intra-species factors for risk assessment.

The key issues considered in the WOE are 1) whether chlorpyrifos causes long-term effects from prenatal and/or early lifestage exposure and 2) whether adverse effects can be attributed to doses lower than those which elicit 10% inhibition of RBC AChE. Evidence from 1) the experimental toxicology studies evaluating adverse outcomes such as behavior and cognitive function; 2) mechanistic data on possible modes of action/ adverse outcome pathways (MOAs/AOPs); and 3) epidemiologic and biomonitoring studies, must be considered in making these determinations.

Despite several years of study, the science addressing neurodevelopmental effects remains unresolved. Therefore, the dietary, residential, aggregate, and non-occupational risk assessments have been conducted both with and without retention of the 10X FQPA safety factor; the occupational risk assessments have been conducted both with and without retention of a 10X UF_{DB}.

EPA has applied the Data-Derived Extrapolation Factor (DDEF) guidance (USEPA, 2014), in its use of the PBPK-PD model; the human model replaces the use of default intra-species uncertainty factor for some populations. The PBPK-PD model simulates human RBC AChE inhibition from exposures via oral, dermal, and inhalation routes and thus obviates the need for a default inter-species uncertainty factor to convert an animal POD to a human POD. In addition, the PBPK-PD model incorporates inter-individual variation in response to chlorpyrifos to estimate a distribution of administered doses that could have resulted in 10% RBC AChE inhibition in humans. The DDEF for intra-species extrapolation can then be estimated as the ratio between the mean dose and a dose at the tail of the distribution representing sensitive individuals. For this risk assessment, the 99th percentile of the distribution is being used to account for variation of sensitivity; the intra-species DDEF is 4X for chlorpyrifos and 5X for the oxon for all groups except women who are pregnant or may become pregnant for whom the 10X intra-species factor was retained (Dow, 2014b). While the current PBPK-PD model accounts for age-related growth from infancy to adulthood by using polynomial equations to describe tissue volumes and blood flows as a function of age, this model does not include any descriptions on physiological, anatomical and biochemical changes associated with pregnancy. Due to the uncertainty in extrapolating the current model predictions among women of childbearing age, the Agency is applying the standard 10X intra-species extrapolation factor for women of childbearing age.

In addition to DDEF, the PBPK-PD model has been used to estimate exposure levels resulting in 10% RBC AChE inhibition following acute (single day, 24 hours) and steady state (21-day) exposures for a variety of exposure scenarios for chlorpyrifos and/or chlorpyrifos oxon. For OPs, repeated exposures generally result in more AChE inhibition at a given administered dose compared to acute studies. Moreover, AChE inhibition in repeated dosing guideline toxicology studies with OPs show a consistent pattern of inhibition reaching steady state at or around 2-3 weeks of exposure in adult laboratory animals (U.S. EPA, 2002). This pattern observed with repeated dosing is a result of the amount of inhibition coming to equilibrium (or steady state) with the production of new enzyme. As such, AChE studies of 2-3 weeks generally show the same degree of inhibition with those of longer duration (*i.e.*, up to 2 years of exposure), so the model simulates a 21-day exposure as a steady-state condition.

Separate PODs have been calculated for dietary (food, drinking water), residential, non-occupational, and occupational exposures by varying inputs on exposure routes (dermal, oral, inhalation), exposure duration and frequency (such as 2 hours per day), and populations exposed based on body weights at different life stages (such as infants or adults).

Use Profile

Chlorpyrifos is a broad-spectrum, chlorinated OP insecticide. Registered use sites include a large variety of food crops and non-food use settings. Public health uses include aerial and ground-based fogger adulticide treatments to control mosquitoes. There is a wide range of registered formulations, application rates, and application methods. Registered labels generally require that handlers use normal work clothing (i.e., long sleeved shirt and pants, shoes and socks) and coveralls, chemical resistant gloves, and dust/mist respirators. Also, some products are marketed in engineering controls such as water-soluble packets. The restricted entry intervals (REIs) on the registered chlorpyrifos labels range from 24 hours to 5 days. The pre-harvest intervals (PHIs) range from 0 days (Christmas trees) to 365 days (ginseng).

Dietary Risk Assessment
The acute and steady state dietary (food only) exposure analyses are highly refined. The majority of food residues used were based upon U.S. Department of Agriculture's (USDA's) Pesticide Data Program (PDP) monitoring data. Percent crop treated information and food processing factors were included, where available. All commodities with U.S. tolerances for residues of chlorpyrifos are included in the assessment.

Acute dietary (food only) risk estimates are all <100 % of the acute population adjusted dose for food ($aPAD_{food}$) at the 99.9^{th} percentile of exposure and are not of concern. With the 10X FQPA SF retained, the population with the highest risk estimate is females (13-49 years old) at 3.2 % $aPAD_{food}$. With the FQPA SF reduced to 1X, the acute dietary risk estimates are <1% of the $aPAD_{food}$ for all populations.

Steady state dietary (food only) risk estimates are all <100 % of the steady state PAD for food ($ssPAD_{food}$) at the 99.9^{th} percentile of exposure and are not of concern. With the 10X FQPA SF retained, the population with the highest risk estimate is children (1-2 years old) at 9.7 % $ssPAD_{food}$. With the FQPA SF reduced to 1X, the steady state dietary risk estimates are <1% of the $ssPAD_{food}$ for all populations.

The total dietary exposure to chlorpyrifos is through both food and drinking water. The acute and steady state dietary exposure analyses discussed above only include food and do not include drinking water; the drinking water exposure and risk assessment is discussed in the aggregate exposure/risk characterization portion of this document (Section 7).

Residential (Non-occupational) Risk Assessment
Based upon review of all chlorpyrifos registered uses, only the registered roach bait products may be applied by a homeowner in a residential setting. Residential handler exposure from applying roach bait products has not been quantitatively assessed because these exposures are considered negligible. Residential post-application exposures can occur for adults and children golfing on chlorpyrifos-treated golf course turf and from contacting treated turf following a mosquitocide application. The residential post-application assessment considered and incorporated all relevant populations and chemical-specific turf transferable residue (TTR) data. The residential post-application risk assessment results incorporate PODs derived from 10% RBC AChE inhibition using the PBPK-PD model and assuming both that the FQPA SF is retained at 10X and reduced to 1X.

There are no residential post-application risk estimates of concern for adults or children from chlorpyrifos use on golf course turf or as a mosquitocide on the day of application assuming either the FQPA SF is retained at 10X or reduced to 1X.

Non-Occupational Spray Drift Exposure and Risk Assessment
An updated quantitative non-occupational spray drift (from treatment of agricultural fields) assessment was conducted to assess the potential for residential bystander (who live on, work in,

or frequent areas adjacent to chlorpyrifos-treated agricultural fields) exposures. The potential risks from spray drift and the impact of potential risk reduction measures were assessed in a July 2012[3] memorandum. To increase protection for children and other bystanders, chlorpyrifos technical registrants voluntarily agreed to lower application rates and adopt other spray drift mitigation measures such as buffer zones.[4] The spray drift risk assessment results incorporate PODs derived from 10% RBC AChE inhibition using the PBPK-PD model and assuming both that the FQPA SF is retained at 10X and reduced to 1X. There are no risk estimates of concern incorporating the agreed-upon buffer distances[5] and droplet sizes/nozzle types by the EPA and the technical registrants in 2012 if the FQPA SF FQPA SF is retained at 10X or reduced to 1X.

Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Assessment
In January 2013, a preliminary assessment of the potential risks from chlorpyrifos volatilization was conducted.[6] However, this assessment was revised in June 2014[7] following submission of two high-quality vapor phase nose-only inhalation toxicity studies for chlorpyrifos and chlorpyrifos oxon[8]. The studies were conducted to address the uncertainty surrounding exposure to aerosol versus vapor phase chlorpyrifos. At the saturation concentration there was no statistically significant inhibition of AChE activity in RBC, plasma, lung, or brain at any time after the six-hour exposure period in either study. Under actual field conditions, exposures are likely to be much lower to vapor phase chlorpyrifos and its oxon as discussed in the January 2013 preliminary volatilization assessment. Because these studies demonstrated that no toxicity occurred even at the saturation concentration, which is the highest physically achievable concentration, there are no anticipated risks of concern from exposure through volatilization of either chlorpyrifos or chlorpyrifos oxon.

Aggregate Risk Assessment
The Agency has considered aggregate exposures and risks from combined food, drinking water, and residential exposures to chlorpyrifos and chlorpyrifos oxon. The acute aggregate assessment includes only food and drinking water. The steady state aggregate assessment includes exposures from food, drinking water, and residential uses. Exposure to the parent compound chlorpyrifos is

[3] J. Dawson, W. Britton, R. Bohaty, N. Mallampalli, and A. Grube. Chlorpyrifos: Evaluation of the Potential Risks from Spray Drift and the Impact of Potential Risk Reduction Measures. 7/13/12. U.S. EPA Office of Chemical Safety and Pollution Prevention. D399483, D399485.
[4] R. Keigwin. Spray Drift Mitigation Decision for Chlorpyrifos (059101). 7/2012. U.S. EPA Office of Chemical Safety and Pollution Prevention. EPA-HQ-OPP-2008-0850-0103.
[5] The 2012 agreement between EPA and the technical registrants (R. Keigwin, 2012) indicates that buffer distances of 80 feet are required for coarse or very coarse droplets and buffer distances of 100 feet are required for medium droplets for aerial applications for application rates $\geq$ 2.3 lb ai/A. In addition, the 2012 agreement requires buffer distances of $\geq$ 25 feet and medium to coarse drops for airblast applications at rates >3.76 lb ai/A.
[6] R. Bohaty, C. Peck, A. Lowit, W. Britton, N. Mallampalli, A. Grube. Chlorpyrifos: Preliminary Evaluation of the Potential Risks from Volatilization. 1/31/13. U.S. EPA Office of Chemical Safety and Pollution Prevention. D399484, D400781.
[7] W. Britton. W. Irwin. J. Dawson. A. Lowit. E. Mendez. Chlorpyrifos: Reevaluation of the Potential Risks from Volatilization in Consideration of Chlorpyrifos Parent and Oxon Vapor Inhalation Toxicity Studies. 6/25/2014. U.S. EPA Office of Chemical Safety and Pollution Prevention. D417105.
[8] W. Irwin. Review of Nose-Only Inhalation of Chlorpyrifos Vapor: Limited Toxicokinetics and Determination of Time-Dependent Effects on Plasma, Red Blood Cell, Brain and Lung Cholinesterase Activity in Femal CD(SD): Crl Rats. U.S. EPA Office of Chemical Safety and Pollution Prevention. 6/25/14. D411959. TXR# 0056694. EPA MRID# 49119501.

expected for food and residential uses. Exposure to either chlorpyrifos or chlorpyrifos oxon may be expected from drinking water sources. The drinking water assessment assumed 100% conversion of chlorpyrifos to the more toxic chlorpyrifos oxon (the predominant chlorpyrifos transformation product formed during drinking water treatment (*e.g.*, chlorination)).

For acute and steady state aggregate assessments, EPA has used a drinking water level of comparison (DWLOC) approach to calculate the amount of exposure available in the total "risk cup" for chlorpyrifos in drinking water after accounting for any chlorpyrifos exposures from food and residential uses. This DWLOC can be compared to the estimated drinking water concentrations (EDWCs) of chlorpyrifos oxon to determine if there is an aggregate risk of concern. The EDWCs are presented in the Environmental Fate and Effects Division's (EFED) updated drinking water assessment (DWA) (see R. Bohaty, 09/15/2020, D459269 and 09/15/2020, D459270).

The acute aggregate assessment includes only food and drinking water. Acute DWLOCs were calculated for infants, children, youths, and adult females. With the 10X FQPA SF retained, the lowest acute DWLOC calculated was for infants (<1 year old) at 23 ppb. With the FQPA SF reduced to 1X, the lowest acute DWLOC calculated was for infants (<1 year old) at 230 ppb.

The steady state aggregate assessment includes dietary exposures from food and drinking water and dermal exposures from residential uses (dermal exposures represent the highest residential exposures). Steady state DWLOCs were calculated for infants, children, youths, and adult females. With the 10X FQPA SF retained, the lowest steady state DWLOC calculated was for infants (<1 year old) at 4.0 ppb. With the FQPA SF reduced to 1X, the lowest steady state DWLOC calculated was for infants (<1 year old) at 43 ppb.

Occupational Handler Risk Assessment

In this assessment for the non-seed treatment scenarios, a total of 288 steady state occupational handler exposure scenarios were assessed. Using the PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming a 10X database uncertainty factor has been retained (LOC = 100), 119 scenarios are of concern with label-specified personal protective equipment (PPE; baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs < 100). Risks of concern for 45 additional exposure scenarios could potentially be mitigated if engineering controls are used. If the 10X database uncertainty factor is reduced to 1X (LOC = 10), 19 scenarios are of concern with label-specified PPE (baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs < 10). Risks of concern for 15 additional scenarios could potentially be mitigated if engineering controls are used.

For the seed treatment scenarios, a total of 93 steady state scenarios were assessed. These scenarios are assessed using default amount handled assumptions for short-term and intermediate exposure durations. These assumptions are appropriate for the steady state exposures. Assuming the 10X database uncertainty factor has been retained (LOC = 100), 12 short-term exposure and 10 intermediate-term scenarios are of concern with label-specified PPE (baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs < 100). Assuming the 10X database uncertainty factor has been reduced to 1X (LOC = 10), there are no short- or intermediate-term risk estimates of concern with label-specified PPE (baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs > 10).

Occupational Post-Application Risk Assessment
Steady state occupational post-application exposures and risks were assessed for any crops where hand labor is anticipated following applications of chlorpyrifos. The assessment was completed using seven chlorpyrifos dislodgeable foliar residue (DFR) studies. Chlorpyrifos parent compound is the residue of concern for occupational post-application exposures that occur outdoors; however, it may be possible that the formation of chlorpyrifos oxon is greater and its degradation slower in greenhouses when compared to the outdoor environment. Occupational post-application assessments were performed for: 1) exposures to the parent compound chlorpyrifos in outdoor environments (uses other than greenhouse), 2) exposures to the parent chlorpyrifos (only) in greenhouses and 3) exposures to both the parent and chlorpyrifos oxon in greenhouses.

Current labels require a Restricted Entry Interval (REI) of 24 hours for most crops and activities, but in some cases such as tree fruit, REIs are up to 5 days after application. All post-application worker risks have been updated in the current assessment to incorporate PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the database uncertainty factor has been either retained at 10X and reduced to 1X. Using the PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the UF_{DB} of 10X has been retained, the majority of the post-applications scenarios are not of concern 1 day after application (REI = 24 hours). However, for some activities such as irrigation, hand harvesting, scouting, and thinning result in risks of concern up to as many as 10 days following application for the non-microencapsulated formulations and > 35 days for the microencapsulated formulation.
Using the PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the UF_{DB} has been reduced to 1X, the majority of the post-application risk estimates are not of concern 1 day after application (REI = 24 hours).

Due to uncertainty regarding the formation of chlorpyrifos oxon in greenhouses, HED also estimated risks for reentry into treated greenhouses (all 4 formulations) for the parent chlorpyrifos plus chlorpyrifos oxon using a total toxic residue approach. The total toxic residue approach[9] estimates the chlorpyrifos oxon equivalent residues by 1) assuming a specific fraction of the measured chlorpyrifos dislodgeable foliar residues are available as the oxon and 2) factoring in the relative potency of chlorpyrifos oxon with use of a TAF of 18. It was conservatively assumed that 5% (0.05) of the total chlorpyrifos present as DFR in greenhouses is available for worker contact during post-application activities. When the total toxic residue approach is used and with the PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming a 10X UF_{DB} has been retained, MOEs are not of concern 0 to 6 days after treatment for non-microencapsulated formulations. For the microencapsulated formulation, MOEs are not of concern 3 to > 35 days after treatment (the completion of the monitoring period), depending on the exposure activity considered.

When the total toxic residue approach is used and with the PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the 10X UF_{DB} has been reduced to 1X, there

[9] Total DFR ($\mu g/cm^2$) = [Chlorpyrifos DFR ($\mu g/cm^2$) * TAF] + [Chlorpyrifos DFR ($\mu g/cm^2$)]

are no risk estimates of concern with the current labeled REI (24 hours), except for the microencapsulated formulation. For the microencapsulated formulation, MOEs are of concern 0 to > 35 days after treatment (the completion of the monitoring period), depending on the exposure activity considered.

2.0 Risk Assessment Conclusions

Despite several years of study, the science addressing neurodevelopmental effects remains unresolved. Therefore, the dietary, residential, aggregate, and non-occupational risk assessments have been conducted both with retention of the 10X FQPA SF and without retention of the 10X FQPA SF (*i.e.*, FQPA SF reduced to 1X). Similarly, the occupational risk assessments have been conducted both with and without retention of a 10X Database Uncertainty Factor (UF_{DB}). There are no acute or steady state dietary (food only) risks of concern with or without the retention of the 10X FQPA SF. There are no residential post-application risk estimates of concern for adults or children with or without the 10X FQPA SF. The aggregate risks are variable and can be determined by comparison of the calculated DWLOCs presented herein with the EDWCs presented in EFED's DWA. Many occupational handler scenarios are of concern with the retention of a 10X $UF_{DB.}$ With the 10X UF_{DB} removed, there are still some handler scenarios of concern. For occupational post-application exposures, even with the 10X UF_{DB} removed, some scenarios are of concern one day after application.

2.1 Data Deficiencies

<u>*Toxicology*</u>
None.

<u>*Residue Chemistry*</u>

860.1500:
Separate magnitude of the residue studies for lemons are needed after application of Lorsban 4E and 75% WDG formulations in order to reevaluate the existing tolerance for chlorpyrifos for the citrus fruit crop group.

Magnitude of the residue studies are needed to establish a tolerance for residues of chlorpyrifos on wheat hay.

860.1520:
Processing studies are needed for soybean meal, hulls and refined oil.

<u>*Occupational/Residential*</u>

No new data requirements have been identified for chlorpyrifos; however, in the 2011 preliminary HHRA, additional studies to address the uncertainties regarding the formation and degradation of chlorpyrifos oxon in greenhouses were recommended. To date, those data have not been submitted. In the absence of the recommended data, and to account for the potential for oxon to form in greenhouses, EPA has used a conservative total toxic residue approach for parent chlorpyrifos plus the chlorpyrifos oxon.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

The methods in the Pesticide Analytical Manual (PAM) Volume II are adequate to analyze the residue of concern for tolerance enforcement purposes, chlorpyrifos only. The limit of detection of these methods is adequate to cover the lowest tolerance level included in the 40 CFR 180.342 for detection of chlorpyrifos only, 0.01 ppm. In addition, chlorpyrifos is completely recovered using FDA multiresidue protocols D and E (nonfatty matrices) and partially recovered using multiresidue method protocol E (fatty matrices).

2.2.2 Recommended & Established Tolerances

According to HED's *Guidance on Tolerance Expressions* (S. Knizner, 05/27/2009), the tolerance expression for chlorpyrifos in the 40 CFR§180.342 should read as follows:

> "(a) General. (1) Tolerances are established for residues of chlorpyrifos, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only chlorpyrifos (*O,O* -diethyl *O* -(3,5,6-trichloro-2-pyridyl) phosphorothioate."

The current tolerance expression reads "Tolerances are established for residues of the pesticide chlorpyrifos *per se* (*O,O*-diethyl-*O*-(3,5,6-trichloro-2-pyridyl) phosphorothioate) in or on the following food commodities."

Based on residue data, HED is recommending tolerances for chlorpyrifos on the following: cotton, gin byproducts (15 ppm); grain, aspirated fractions (30 ppm); corn, field, milled byproducts (0.1 ppm); and wheat, milled byproducts (1.5 ppm). These recommendations, along with recommendations for revisions to current tolerances based on the Organization for Economic Cooperation and Development (OECD) rounding class practice, commodity definition revisions, crop group conversions/revisions, and harmonizition with Codex, are presented in Tables 2.2.2.1 and 2.2.2.2.

Table 2.2.2.1. Summary of Tolerance Revisions for Chlorpyrifos (40 CFR §180.342(a)).[1]

Commodity/ **Correct Commodity Definition**	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Alfalfa, forage	3.0	3	Corrected values to be consistent with OECD Rounding Class Practice.
Grain, aspirated fractions	--	22	Recommended tolerance based on submitted residue data.
Beet, sugar, dried pulp	5.0	5	Corrected values to be consistent with OECD Rounding Class Practice.
Beet, sugar, roots	1.0	1	Corrected values to be consistent with

Table 2.2.2.1. Summary of Tolerance Revisions for Chlorpyrifos (40 CFR §180.342(a)).[1]			
Commodity/ **Correct Commodity Definition**	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
			OECD Rounding Class Practice.
Beet, sugar, leaves [2]	--	8	Commodity definition revision. Corrected values to be consistent with OECD Rounding Class Practice.
Beet, sugar, tops	8.0	remove	
Brassica, leafy greens, subgroup 4-16B	--	1	Crop group conversion/revision.[3,4]
Cherry, sweet	1.0	1	Corrected values to be consistent with OECD Rounding Class Practice.
Cherry, tart	1.0	1	Corrected values to be consistent with OECD Rounding Class Practice.
Fruit, citrus, group 10-10, dried pulp	--	5	Crop group conversion/revision. Corrected values to be consistent with OECD Rounding Class Practice.
Citrus, dried pulp	5.0	remove	
Fruit, citrus, group 10-10, oil	--	20	Crop group conversion/revision.
Citrus, oil	20	remove	
Corn, field, forage	8.0	8	Corrected values to be consistent with OECD Rounding Class Practice.
Corn, field, stover	8.0	8	Corrected values to be consistent with OECD Rounding Class Practice.
Corn, milled byproducts	--	0.1	Recommended tolerance based on submitted residue data.
Corn, sweet, forage	8.0	8	Corrected values to be consistent with OECD Rounding Class Practice.
Corn, sweet, stover	8.0	8	Corrected values to be consistent with OECD Rounding Class Practice.
Cotton, gin byproducts	--	15	Recommended tolerance based on submitted residue data.
Cotton, undelinted seed	0.2	0.3	Harmonization with Codex.
Cranberry	1.0	1	Corrected values to be consistent with OECD Rounding Class Practice.
Fruit, citrus, group 10-10	--	1	Crop group conversion/revision. Corrected values to be consistent with OECD Rounding Class Practice.
Fruit, citrus, group 10	1.0	remove	
Kohlrabi	--	1	Crop group conversion/revision.[3,4]
Kiwifruit, fuzzy	--	2	Commodity definition revision. Corrected values to be consistent with OECD Rounding Class Practice.
Kiwifruit	2.0	remove	
Milk	--	0.01	Commodity definition revision.
Milk, fat	--	0.25	
Milk, fat (Reflecting 0.01 ppm in whole milk)	0.25	remove	
Pepper, bell	--	1	Commodity definition revision. Corrected values to be consistent with OECD Rounding Class Practice.
Pepper, nonbell	--	1	
Pepper	1.0	remove	
Peppermint, fresh leaves	--	0.8	Commodity definition revision.
Peppermint, tops	0.8	remove	
Peppermint, oil	8.0	8	Corrected values to be consistent with OECD Rounding Class Practice.
Radish, roots	--	2	Commodity definition revision. Corrected values to be consistent with OECD Rounding Class Practice
Radish	2.0	remove	

Table 2.2.2.1. Summary of Tolerance Revisions for Chlorpyrifos (40 CFR §180.342(a)).[1]			
Commodity/ **Correct Commodity Definition**	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Rutabaga, roots	--	0.5	Commodity definition revision.
Rutabaga	0.5	remove	
Spearmint, fresh leaves	--	0.8	Commodity definition revision.
Spearmint, tops	0.8	remove	
Spearmint, oil	8.0	8	Corrected values to be consistent with OECD Rounding Class Practice.
Sorghum, grain, stover	2.0	2	Corrected values to be consistent with OECD Rounding Class Practice.
Strawberry	0.2	0.3	Harmonization with Codex.
Sweet potato, tuber	--	0.05	Commodity definition revision.
Sweet potato, roots	0.05	remove	
Turnip, roots	1.0	1	Corrected values to be consistent with OECD Rounding Class Practice.
Turnip, leaves	--	0.3	Commodity definition revision.
Turnip, tops	0.3	remove	
Vegetable, brassica, head and stem, group 5-16	--	1	Crop group conversion/revision.[3] Corrected values to be consistent with OECD Rounding Class Practice.
Vegetable, brassica, leafy, group 5	1.0	remove	
Wheat, forage	3.0	3	Corrected values to be consistent with OECD Rounding Class Practice.
Wheat, milled byproducts	--	1.5	Recommended tolerance based on submitted residue data.
Wheat, straw	6.0	6	Corrected values to be consistent with OECD Rounding Class Practice.

[1] This table only includes recommended revisions to established tolerances and recommended establishment of new tolerances. For a complete list of all established tolerances see the International Residue Level Summary (IRLS) in Appendix 4.
[2] Sugar beet leaves/tops are no longer considered a significant livestock feed item. Commodity/tolerance may be removed.
[3] The recommended conversion of existing tolerance in/on **Vegetable, brassica, leafy, group 5** is to the following: **Vegetable, brassica, head and stem, group 5-16; Brassica, leafy greens, subgroup 4-16B;** and **Kohlrabi** (**"**Crop Group Conversion Plan for Existing Tolerances as a Result of Creation of New Crop Groups under Phase IV (4-16, 5-16, and 22)" dated 11/3/2015).
[4] HED is recommending for individual tolerances of 1 ppm for Kohlrabi based on the currently established tolerance for this commodity as part of crop group 5 (Vegetable, brassica, leafy). Kohlrabi is displaced by the crop group conversion noted in the footnote 3 above.

Table 2.2.2.2. Summary of Tolerance Revisions for Chlorpyrifos (40 CFR §180.342(c))[1, 2]			
Commodity/ **Correct Commodity Definition**	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Asparagus	5.0	5	Corrected values to be consistent with OECD Rounding Class Practice.

[1] This table only includes recommended revisions to established tolerances. For a complete list of all established tolerances see the IRLS in Appendix 4.
[2] Regional registrations.

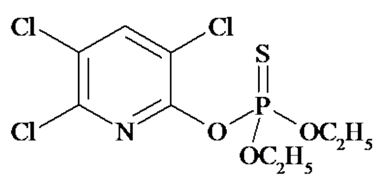
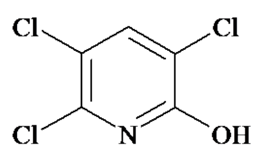
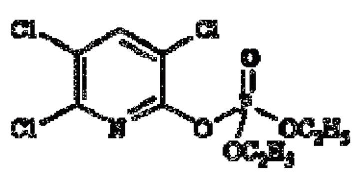
2.2.3 International Harmonization

The Codex Alimentarius Commission and Canada Pesticide Management Rgulatory Agency (PMRA) have established Maximum Residue Limits (MRLs) for chlorpyrifos. Mexico generally adopts U.S. tolerances and/or Codex MRLs for its export purposes. The residue definition for enforcemnt is harmonized for U.S. tolerances and Codex MRLs and includes parent compound chlorpyrifos only. However, Canada MRLs are for chlorpyrifos for a few commodities and for both parent chlorpyrifos and its metabolite TCP (3,5,6-trichloro-2-pyridinol) which is not a U.S. residue of concern, for other commodities.

Except for apple commodities, Canada MRLs are currently not harmonized with the U.S. tolerances because of the difference in residue definition. Codex MRLs are currently harmonized with U.S. tolerances for the following commodities: field corn grain; citrus; cranberry; egg; sorghum grain (and stover); wheat grain; and head and Chinese cabbage. HED is recommending that the current tolerances for strawberry and cotton, undelinted seed be increased to harmonize with the Codex MRLs. There are several U.S. tolerances that are not harmonized with Codex MRLs; harmonization is not currently being recommended for these commodities because the large difference in residue levels indicates that domestic and foreign use patterns are much different. A summary of the U.S. tolerances and international MRLs is included in Appendix 4.

3.0 Introduction

3.1 Chemical Identity

Table 3.1 Chlorpyrifos Degradate/ Residues of Concern Nomenclature.	
Chlorpyrifos	
IUPAC name	*O,O*-diethyl *O*-3,5,6-trichloro-2-pyridyl phosphorothioate
CAS name	*O,O*-diethyl *O*-(3,5,6-trichloro-2-pyridinyl) phosphorothioate
CAS registry number	2921-88-2
TCP Metabolite/Degradate (Residue of Concern for Canada) IUPAC Name 3,5,6 Trichloro-2-pyridinol	
Oxon Metabolite/Degradate Common Name Chlorpyrifos Oxon IUPAC Name O,O-diethyl. O-3,5,6-trichloro-2-pyridyl phosphate	

3.2 Physical/Chemical Characteristics

Technical chlorpyrifos is a white crystalline solid. Chlorpyrifos is stable in neutral and acidic aqueous solutions; however, stability decreases with increasing pH. Chlorpyrifos is practically insoluble in water, but is soluble in most organic solvents (i.e., acetone, xylene and methylene chloride). Chlorpyrifos is moderately volatile based on its vapor pressure of 1.87×10^{-5} mmHg at 25°C. See Appendix 3.

Laboratory studies show chlorpyrifos is susceptible to hydrolysis under alkaline conditions and that volatilization and photo-degradation are not likely to play a significant role in the dissipation of chlorpyrifos in the environment. Nonetheless, chlorpyrifos has been detected in air samples, and so volatilization may play more of a role in dissipation than laboratory studies indicate. The major route of dissipation appears to be aerobic and anaerobic metabolism, as well as partitioning to the soil (partition coefficient of 6040). The aerobic aquatic metabolism half-life is 30.4 days (~6% remaining in 4 months). The water peak half-lives were ~1 day in a monitoring study (MRID 44711601). Based on available data, chlorpyrifos degrades slowly in soil under both aerobic and anaerobic conditions. Degradation begins with cleavage of the phosphorus ester bond to yield 3,5,6-trichloro-2-pyridinol (TCP). Field dissipation studies show that chlorpyrifos is moderately persistent under field conditions—dissipation half-life less than 60 days. Chlorpyrifos is only slightly soluble in water (1400 ppb). However, if it reaches aquatic environments the Log K_{ow} (4.7) indicates that chlorpyrifos may bioaccumulate in fish and other aquatic organisms. A fish bioaccumulation study shows that chlorpyrifos is absorbed by fish; however, it rapidly depurates when exposure ceases.

Oxidation of chlorpyrifos to chlorpyrifos oxon could potentially occur through photolysis, aerobic metabolism, and chlorination as well as other oxidative processes. Chlorpyrifos oxon is expected to have similar fate characteristics as chlorpyrifos except chlorpyrifos oxon is more soluble in water and undergoes hydrolysis faster. The hydrolysis half-life of chlorpyrifos oxon is significantly shorter than that observed for chlorpyrifos (5 days vs 81 days). Chlorpyrifos oxon hydrolyses to form TCP. For chlorpyrifos, water purification (chlorination) has been shown to be a major route of chlorpyrifos oxon formation and degradation.

3.3 Pesticide Use Pattern

Chlorpyrifos (0,0-diethyl-0-3,5,6-trichloro -2-pyridyl phosphorothioate) is a broad-spectrum, chlorinated OP insecticide. Registered use sites include a large variety of food crops (including fruit and nut trees, many types of fruits and vegetables, and grain crops), and non-food use settings (e.g., golf course turf, industrial sites, greenhouse and nursery production, sod farms, and wood products). Public health uses include aerial and ground-based fogger adulticide treatments to control mosquitoes. There are also residential uses of roach bait products and ant mound treatments. Permanent tolerances are established (40 CFR§180.342) for the residues of chlorpyrifos in/on a variety of agricultural commodities, including meat, milk, poultry and eggs. There are also tolerances for use in food handling/service establishments (FHE or FSE). Chlorpyrifos is manufactured as granular, microencapsulated liquid, soluble concentrate liquid, water dispersible granular in water soluble packets (WSP), wettable powders in WSPs, impregnated paints, cattle ear tags, insect bait stations and total release foggers. There is a wide range of application rates and methods. Registered labels generally require that handlers use normal work clothing/baseline attire (i.e., long sleeved shirt and pants, shoes and socks) and coveralls, chemical resistant gloves, and dust/mist respirators. The REIs on the registered chlorpyrifos labels range from 24 hours to 5 days. The master use table is provided in Appendix 5.

3.4 Anticipated Exposure Pathways

Chlorpyrifos applications may be made directly to growing crops (food and feedstuffs) which may result in human exposure to chlorpyrifos in food and to chlorpyrifos or chlorpyrifos oxon in drinking water (from surface and ground water sources). Registered uses that may result in residential (non-occupational) exposures to chlorpyrifos include aerial and ground-based fogger adult mosquitocide applications and golf course turf applications. There are also potential exposures for residential bystanders who live on, work in, or frequent areas adjacent to chlorpyrifos-treated agricultural fields from spray drift and volatilization. In occupational settings, exposure may occur while handling the pesticide prior to application, as well as during application. There is also a potential for post-application exposure for workers re-entering treated fields.

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (https://www.archives.gov/files/federal-register/executive-orders/pdf/12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age and ethnic group. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Spray drift can also potentially result in post-application exposure and it was considered in this analysis. Further considerations are also currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to other types of possible bystander exposures and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

The 2014 chlorpyrifos HHRA provided summary information and weight of evidence findings integrating multiple lines of evidence from experimental toxicology and epidemiology with respect to AChE/ChE inhibition (acetylcholinesterase/cholinesterase) and neurodevelopmental outcomes. The 2014 HHRA also describes the use of a robust PBPK-PD model for PODs and refined intra-species factors. Full details of the science and data analysis that support these conclusions can be found in the 2014 chlorpyrifos HHRA (D. Drew *et al.,* D424485, 12/29/2014).

4.1 Safety Factor for Infants and Children (FQPA Safety Factor)[10]

The dietary, residential, aggregate, and non-occupational assessments have been conducted both with and without the retention of the 10X FQPA Safety Factor based on the following considerations:

- The toxicology database for chlorpyrifos is complete for deriving risk assessment PODs based on cholinesterase inhibition.
- Despite several years of study, the science addressing neurodevelopmental effects remains unresolved. Regulatory history of the scientific evaluation is contained in Appendix 2.
- Chlorpyrifos is an OP insecticide with an established neurotoxic MOA; neurotoxicity is the most sensitive effect in all species, routes, and lifestages. AChE inhibition is being used to derive the PODs for risk assessment. These PODs are protective for neurotoxic effects related to AChE inhibition and potential downstream neurotoxic effects. Although the dose response relationship of AChE inhibition across different lifestages is established quantitatively, the MOAs/AOPs for postulated neurodevelopmental effects occurring at doses below those eliciting cholinesterase inhibition have not been established.
- A literature search identified epidemiological studies with results suggesting an association between neurodevelopmental effects and exposure to chlorpyrifos even in the absence of AChE inhibition.
- There are no residual uncertainties in the exposure database. The chlorpyrifos residue chemistry database is robust. The exposure assessment in drinking water provides a conservative approach for estimating chlorpyrifos parent and oxon concentrations in ground and surface water sources of drinking water and is unlikely to underestimate exposure. The dietary (food) exposure analyses, although highly refined, incorporate conservative assumptions that are unlikely to underestimate exposures. Residue levels are based on either monitoring data reflecting actual residues found in the food supply, or high-end residues in foods. Furthermore, processing factors used were either those measured in processing studies, or default high-end factors representing the maximum concentration in the processed commodity. Residential exposure assessments use data from surrogate and chemical-specific sources and rely on the 2012 Residential Standard Operating Procedures (SOPs). Although some refinements have been incorporated into the exposure assessments, the exposure assumptions will not underestimate risks.

As discussed above and in Appendix 2, despite several years of study, the science addressing neurodevelopmental effects remains unresolved, the dietary, residential, aggregate, and non-occupational risk assessments have been conducted both with retention of the 10X Food Quality Protection Act (FQPA) safety factor (SF) and without retention of the 10X FQPA SF

[10] HED's standard toxicological, exposure, and risk assessment approaches are consistent with the requirements of EPA's children's environmental health policy (https://www.epa.gov/children/epas-policy-evaluating-risk-children).

(*i.e.*, FQPA SF reduced to 1X). Similarly, the occupational risk assessments have been conducted both with and without retention of a 10X Database Uncertainty Factor (UF_{DB}).

4.2 Dose Response Assessment

4.2.1 Durations of Exposure, Critical Windows of Exposure, & Temporality of Effects

In risk assessment, exposure is evaluated considering the toxicology profile. More specifically, a variety of toxicokinetic and toxicodynamic factors are considered when determining the appropriate exposure durations to assess for risk potential. In the case of chlorpyrifos, exposure can occur from a single event or on a single day (*e.g.*, eating a meal) or from repeated days of exposure (*e.g.*, worker, residential).

With respect to AChE inhibition, these effects can occur from a single exposure or from repeated exposures. For OPs, repeated exposures generally result in more AChE inhibition at a given administered dose compared to acute exposures. Moreover, AChE inhibition in repeated dosing guideline toxicology studies with most OPs show a consistent pattern of inhibition reaching steady state at or around 2-3 weeks of exposure in adult laboratory animals (U.S. EPA, 2002). This pattern observed with repeated dosing is a result of the amount of inhibition comes at equilibrium with production of new enzyme. As such, AChE studies of 2-3 weeks generally show the same degree of inhibition with those of longer duration (*i.e.*, up to 2 years of exposure). Thus, for most of the human health risk assessments for the OPs, the Agency is focusing on the critical durations ranging from a single day up to 21 days (*i.e.*, the approximate time to reach steady state for most OPs). As described below, PODs for various lifestages, routes, and scenarios have been derived at the acute and steady state durations.

With respect to effects on the developing brain, very little is known about the duration of chlorpyrifos exposure needed to precipitate adverse effects in the developing brain. There are critical windows of vulnerability (Rice & Barone, 2000; Rodier, 2004) with regard to toxicant effects on brain development. This vulnerable period in humans spans early pregnancy to adolescence (Rice & Barone, 2000). In fact, evidence shows that synapse formation peaks quite late in human brain development at 4-8 years of age (Glantz *et al.,* 2007). Within these vulnerable periods there are key neurodevelopmental processes (*e.g.* cell division, migration, differentiation, synaptogenesis, and myelination) and each of these is region and stage specific. Consequently, the time of toxicant exposure will be a major determinate in the spectrum of neurotoxic effects. Because of the dynamic processes in the developing brain (*i.e.*, vulnerable windows) it is difficult to determine if the effect or differences in effects is due to duration of exposure or if different vulnerable windows were affected. As such, it is impossible at this time to rule out even a single day of high exposure to chlorpyrifos having a potential adverse neurodevelopmental effect in humans.

For the chlorpyrifos risk assessment, PODs for various lifestages, routes, and scenarios have been derived at the acute and steady state durations.

4.2.2 Use of the PBPK-PD Model

Evaluation of PBPK-PD models intended for risk assessments includes a review of the model purpose, model structure, mathematical representation, parameter estimation (calibration), and computer implementation (USEPA, 2006b). The chlorpyrifos PBPK-PD model has been through several quality assurance reviews by various individuals or groups, including the Agency, and found that the model reasonably predicts both blood/urine dosimetry of chlorpyrifos and 3,5,6-trichloro-2-pyridinol (TCPy), and ChE inhibition in two controlled, deliberate oral human dosing studies (Nolan *et al.,* 1982; Kisicki *et al.,* 1999) and a dermal human study (Nolan *et al.,* 1984). The PBPK-PD model predictions for rats inhaled chlorpyrifos compare well with observed data (Hotchkiss *et al.,* 2013) with respect to chlorpyrifos, oxon, and TCPy concentrations in plasma, and ChE in plasma, RBC and brain (Poet *et al.,* 2014). Significant improvements have been made to the PBPK-PD model in response to the 2008, 2011, and 2012 SAPs, the Agency, and peer reviewers from academic journals. The Agency believes that the model is sufficiently robust for use in HHRA. Age-specific parameters are incorporated in the model to allow for lifestage-specific evaluations from infant through adulthood. Since the model accounts for human specific metabolism and physiology, using the human model obviates the need for the inter-species extrapolation factor. The deterministic model can be used to simulate an "average individual" for all age groups. As such, as described below, the Agency is using the PBPK-PD model to derive the scenario-specific PODs for all age groups (See Table 4.2.2.1.2 below).

At the 2011 SAP meeting, the Panel specifically noted the lack of maternal and fetal PK and PD compartments in the current PBPK-PD model to inform about tissue dosimetry and AChE inhibition during lactation (FIFRA SAP 2011). As described in detail below, the Agency has assessed exposure to bottle-feeding infants exposed to the oxon through water used with infant formula. With respect to chlorpyrifos or oxon exposure to infants through breast milk, any exposure to chlorpyrifos would be far lower than drinking water levels predicted by EFED. Thus, the Agency is already accounting for oral exposure to chlorpyrifos to infants via bottle-feeding and a lactation component in the PBPK-PD model is not necessary.

The SAP noted the lack of maternal and fetal PK and PD compartments in the PBPK-PD model to inform tissue dosimetry and AChE inhibition to pregnant women and their fetuses (FIFRA SAP 2011). With respect to exposure to the fetus during gestation, there are multiple studies on chlorpyrifos (Mattsson et al., 1998, 2000) and other OPs (U.S. EPA, 2006a) which show that the pregnant dam exhibits similar or more AChE inhibition than the fetus at a given dose to the dam. As such, for AChE inhibition, protecting against AChE inhibition in the pregnant female is expected to be protective for AChE inhibition in the fetus. Biomonitoring data from rats and humans support the findings of these AChE studies. Specifically, Whyatt *et al.* (2003) have shown that levels of chlorpyrifos in maternal blood are similar to the levels measured in human umbilical cord blood (Whyatt *et al.,* 2003). With respect to the pregnant dam during gestation, metabolic activities and physiological parameters can be altered during pregnancy (for citations, see Appendix 1 of D424485 (D. Drew *et al.,* 12/29/2014)). While the PBPK-PD model accounts for age-related growth from infancy to adulthood by using polynomial equations to describe tissue volumes and blood flows as a function of age, the model does not include any descriptions on physiological, anatomical and biochemical changes associated with pregnancy. Due to the uncertainty in extrapolating the current model predictions among women who may be pregnant, **the Agency is applying the standard 10X intra-species extrapolation factor for women of childbearing age.**

4.2.2.1 Derivation of Human Equivalent Doses/Concentrations

In typical risk assessments, PODs are derived directly from laboratory animal studies and inter- and intra-species extrapolations are accomplished by use of 10X factors. In the case of chlorpyrifos and its oxon, PBPK-PD modeling is being used as a data-derived approach to estimate PODs for all age groups and Data-Derived Extrapolation Factors (DDEF) for intra-species extrapolation for some groups (USEPA, 2014). The Agency typically uses a 10% response level for AChE inhibition in human health risk assessment. This response level is consistent with the 2006 OP cumulative risk assessment (USEPA, 2006a) and other single chemical OP risk assessments. As such, the model has been used to estimate exposure levels resulting in 10% RBC AChE inhibition following single day (acute; 24 hours) and 21-day exposures for a variety of exposure scenarios (see Table 4.2.2.1.2 below).

The PBPK-PD model accounts for PK and PD characteristics to derive age, duration, and route specific PODs (Table 4.2.2.1.2 below). Separate PODs have been calculated for dietary (food, drinking water), residential, and occupational exposures by varying inputs on types of exposures and populations exposed. Specifically, the following characteristics have been evaluated: duration [acute, 21 day (steady state)]; route (dermal, oral, inhalation); body weights which vary by lifestage; exposure duration (hours per day, days per week); and exposure frequency [events per day (eating, drinking)].

For each exposure scenario, the appropriate body weight for each age group or sex was modeled as identified from the Exposure Factors Handbook (USEPA, 2011) for occupational and residential exposures and from the NHANES/What We Eat in America (WWEIA) Survey[11] for dietary exposures. All body weights used are consistent with those assumed for dietary, occupational, and residential exposure assessments. The Agency assesses dietary exposures for children 6-12 years old, and children between 6-11 years old for residential exposures. For purpose of aggregate assessment, these age groups are combined. The Agency assesses dietary exposures for youths 13-19 years old, and youths between 11-16 years old for residential exposures. For purpose of aggregate assessment, these age groups are combined. The body weights used in the chlorpyrifos PBPK model are summarized in Table 4.2.2.1.1.

[11] http://www.ars.usda.gov/Services/docs.htm?docid=13793

Table 4.2.2.1.1 Body Weight Assumptions Incorporated into PBPK Model for Chlorpyrifos.

Exposure Scenario	Exposure Pathway		Population & Body Weight (kg)			
		Infants (<1 year old)	Young Children (<1 - 2 years old)	Children (Residential:6-11 years old; Dietary:6-12 years old)	Youths (Residential:11-16 years old; Dietary:13-19 years old)	Females (13 – 49 years old)
Dietary	Food and Drinking Water	4.8[1]	12.6[2]	37.1[2]	67.3[2]	72.9[2]
Residential (Contact with Treated Turf from Mosquitocide Application)	Oral		11[3]			
	Dermal			32[5]	57[6]	69[4]
	Inhalation		11[3]			69[4]
Residential (Golfing)	Dermal			32[5]	57[6]	69[4]
Non-Occupational Spray Drift	Oral		11[3]			
	Dermal					69[4]
Occupational	Dermal, Inhalation					69[4]

1 For infants from birth to < 1 year old, the Agency has selected the body weight for the youngest age group, birth to < 1 month old, 4.8 kg (Exposure Factors Handbook, Table 8-3, mean body weight for the birth to < 1 month age group).
2 NHANES/WWEIA
3 Exposure Factors Handbook, Table 8-3, mean body weight for the 1 to < 2 year old age group.
4 Exposure Factors Handbook, Table 8-5, mean body weight for females 13 to < 49 years old.
5 Exposure Factors Handbook, Table 8-3, mean body weight for the 6 to < 11 year old age group.
6 (Exposure Factors Handbook, Table 8-3, mean body weight for the 11 to < 16 year old age group).

In order to derive the scenario specific PODs, assumptions were incorporated into the PBPK model on routes of exposure, surface area exposed, etc. The following scenarios were evaluated: dietary exposure to the oxon exposures via drinking water (24-hour and 21-day exposures for infants, children, youths, and female adults); exposure to chlorpyrifos exposures via food (24-hour and 21-day exposures for infants, children, youths, and female adults); 21-day residential exposures to chlorpyrifos via skin for children, youths, and female adults; 21-day residential exposures to chlorpyrifos via hand-to-mouth ingestion for children 1- 2 years old; 21-day residential exposures to chlorpyrifos via inhalation for children 1-2 years old and female adults.

Steady state dietary exposure was estimated daily for 21 days. For drinking water exposure, infants and young childrens (infants < 1 year old, children between 1-2 years old, and children between 6-12 years old) were assumed to consume water 6 times per day, with a total consumption volume of 0.69 L/day[12]. For youths and female adults, they were assumed to consume water 4 times per day, with a total consumption volume of 1.71 L/day[13].

[12] The daily volumes consumed and number of daily consumption events for all populations are mean values by age group based on USDA What We Eat in America, NHANES survey for dietary exposures. The mean daily water consumption values for children 1- 2 years old (0.35 L/day) and children 6-12 years old (0.58 L/day), were less than that for the infants (0.69 L/day); however, the infant daily water consumption volume was selected to be protective for PBPK-PD POD derivation for these age groups.
[13] For youths 13-19 years old, the mean daily water consumption (0.93 L/day), was less than that for the female adults (1.71 L/day); however, the adult daily water consumption was also selected to be protective.

All residential steady state exposures were set to be continuous for 21 days. For all residential dermal exposures to chlorpyrifos the dermal PODs were estimated assuming 50% of the skin's surface was exposed. Exposure times for dermal exposure assessment were consistent with those recommended in the 2012 Residential Standard Operating Procedures (SOPs)[14]. For residential inhalation exposures following public health mosquitocide application, the exposure duration was set to 1 hour per day for 21 days. The incidental oral PODs for children 1 to < 2 years old for other turf activities were estimated assuming that there were six events, 15 minutes apart, per day.

In addition to dietary and residential exposures, the PBPK-PD model was also used to estimate exposure levels resulting in 10% RBC AChE inhibition following steady state occupational exposures. For occupational handlers and post-application workers, the dermal PODs were estimated assuming a body weight of 69 kg (to represent a female aged 13-49), 100% of the skin's surface was exposed for 5 days/week and the exposure duration was 8 hours/day for 21 days. For occupational handlers, the inhalation PODs were estimated exposure for 8 hours/day, 5 days/week, for 21 days.

[14] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

Table 4.2.2.1.2. Chlorpyrifos PBPK Modeled Doses (PODs) Corresponding to 10% RBC AChE Inhibition.

RA Type	Exposure Pathway (all chlorpyrifos unless noted)	Infants (< 1 yr old)		Young Children (1 - 2 years old)		Children (Residential: 6-11 years old; Dietary: 6-12 years old)		Youths (Residential: 11-16 years old; Dietary: 13-19 years old)		Females (13 – 49 years old)	
		Acute	Steady State (21 day)	Acute	Steady State (21 day)	Acute	Steady State (21 day)	Acute	Steady State (21 day)	Acute	Steady State (21 day)
Dietary	Drinking Water (oxon conc, ppb)	1,183	217	3,004	548	7,700	1,358	4,988	878	5,285	932
	Food (mg/kg/day)	0.60	0.103	0.581	0.099	0.53	0.09	0.475	0.080	0.467	0.078
Residential (Golfers)	Dermal (mg/kg/day)						25.75		13.95		11.89
Residential (Mosquitocide Application) and Spray Drift	Dermal (mg/kg/day)				134.25						23.6
	Oral (mg/kg/day)				0.101						
	Inhalation (concn. in air mg/m^3)				2.37						6.15
Occupational	Dermal (mg/kg/day)										3.63
	Inhalation (mg/kg/day)										0.138

*PODs and exposure and risk estimates for females 13-49 yrs covers all youths >13 yrs

4.2.2.2 Intra-species Extrapolation

With respect to intra-species extrapolation, the PBPK-PD model can be run in ‘variation’ mode which allows for age-specific parameters to vary across a distribution of values. The model will not be described in detail here as it is described in multiple recent publications, including a detailed report reviewed by the FIFRA SAP in 2011; summary information is provided here. All model code for the PBPK-PD variation model are available to the public.

Significant improvements have been made to the PBPK-PD model in response to the 2008, 2011, and 2012 SAPs, the Agency, and peer reviewers from academic journals in addition to the input of new data. At the 2011 SAP, the panel was critical of some aspects of how the registrant proposed to assess intra-species extrapolation. The registrant made multiple changes, including the addition of a global sensitivity analysis, improvements to the quantitative approach to evaluate population variability across individuals at a given age, and an uncertainty analysis on metabolism data from human hepatic microsomes to address variation in metabolic capabilities. .

Of the more than 120 parameters in the PBPK-PD model, 16 parameters were selected for varying in the DDEF intra-species analysis. They were selected using local and global sensitivity analyses (MRID 49248201, Dow, 2014a,b). The distributions for these 16 parameters are provided in Table 4.2.2.2.1 below. Inter-individual variations for the 16 sensitive parameters (listed above) were assumed to follow a lognormal distribution. The distributions are truncated at far extreme values only to permit the model to compute but functionally not truncated with respect to assessing human variability. References cited in the table are listed in the report “Development of Chemical Specific Adjustment Factors for Chlorpyrifos and Chlorpyrifos Oxon” (MRID number 49248201) and also provided in Dow, 2014a,b,c.

Table 4.2.2.2.1. Sixteen parameters in variation model. Extracted from Dow, 2014c.				
Parameter	**Mean value**	**Standard Deviation**	**CV**	**Variability Reference**
Total Blood Volume (L/kg body	0.08	0.0022	0.027	P3M; Price *et al.,* 2003
Plasma PON1 (µmol/hr×L)	162,000	92,000	0.57	Smith et al., 2011
Hepatic Blood Flow (L/hr×kg tissue)	50	14	0.27	Materne et al., 2000
RBC ChE Inhibition Rate (l/µmol×hr)	100	17	0.17	Dimitriadis and Syrmos,
Hepatic PON1 (µmol/hr×kg tissue)	154,000	88,000	0.57	Smith et al., 2011
Hematocrit (%)	0.45	0.031	0.068	P3M; Price *et al.,* 2003
RBC ChE Degradation Rate (l/hr)	0.01	0.0014	0.14	Chapman *et al.,* 1968
Hepatic P450 Bioactivation to Oxon (µmol/hr×kg tissue)	690	410	0.59	Smith et al., 2011
Hepatic P450 Detoxification to TCPy (µmol/hr×kg tissue)	1500	800	0.53	Smith et al., 2011
RBC ChE Reactivation Rate (l/hr)	0.014	0.0050	0.36	Mason et al., 2000
Intestinal CYP Bioactivation to Oxon (µmol/hr×kg tissue)	82	43	0.52	Obach *et al.,* 2001
Intestinal CYP Detoxification to TCPy (µmol/hr×kg tissue)	53	28	0.52	Obach *et al.,* 2001
Transfer Rate to Intestine (hr-1)	0.31	0.081	0.26	Singh et al., 2006
Volume of the Liver (L/kg body weight)	0.032	0.0010	0.032	P3M; Price *et al.,* 2003
Hepatic Carboxyl Basal Activity Rate (l/hr/kg tissue)	1,270,000	460,000	0.36	Pope *et al.,* 2005
Hepatic Carboxyl Reactivation Rate (l/hr)	0.014	0.0050	0.36	Mason et al., 2000

Of these 16 parameters, four metabolism-related parameters (hepatic CYP450 activation of chlorpyrifos to chlorpyrifos oxon, hepatic CYP450 detoxification of chlorpyrifos oxon to TCPy, hepatic PON1 detoxification of chlorpyrifos oxon to TCPy, PON1 detoxification of chlorpyrifos oxon to TCPy in plasma) were found to drive more than 80% of the total variation in RBC AChE inhibition (Table 4.2.2.2.2). The human variability for these four parameters were assessed using *in vitro* data from 30 human hepatic microsome samples and 20 human plasma samples (Smith et al., 2011). Twenty of the hepatic microsome samples came from individuals < 12 years of age; and 10 of the samples came from adults > 17 years old. Ten of the plasma sample came from individuals < 2 years of age; and 10 of the samples came from adults. Because the findings from Smith et al (2011) account for more than 80% of the total variation in RBC AChE inhibition, it was determined that evaluating the uncertainty associated with the data (i.e., small number of samples compared to the large U.S. population) from this study was important to having confidence in the DDEFs derived from the variation model. Although some other *in vitro* studies shown in Table 4.2.2.2.1 also have small numbers of samples, these parameters make relatively small contributions to the overall variability. As such, additional quantitative uncertainty analysis on these *in vitro* studies is not needed.

Table 4.2.2.2.2. Four Metabolism Related Parameters in Variation Model. Extracted from Dow, 2014c.			
hepatic CYP450 activation of chlorpyrifos to chlorpyrifos oxon	total blood volume	RBC ChE degradation rate	transfer rate of chlorpyrifos or oxon from the stomach to the intestine
hepatic PON1 detoxification of chlorpyrifos oxon to TCPy	hepatic blood flow	RBC ChE reactivation rate	volume of the liver
PON1 detoxification of chlorpyrifos oxon to TCPy in plasma	RBC AChE inhibition rate	intestinal CYP bioactivation to chlorpyrifos oxon	hepatic carboxyl basal activity rate
hepatic PON1 detoxification of chlorpyrifos oxon to TCPy	hematocrit	intestinal CYP detoxification to TCPy	hepatic carboxyl reactivation rate

The uncertainty associated with these four critical parameters were incorporated in the subsequent Monte Carlo analysis by generating 50 sets of unbounded parametric distributions using the following approach. First, the parametric bootstrap approach was used to sample 1000 values, with replacement, from the *in vitro* data. Then, this process was repeated for 50 iterations, and the resulting 50 sets of distribution all have equally probable sets of means and coefficient of variation as the observed data, except for the coefficient of variation of the plasma PON1 metabolism rate. Since the liver is the origin of PON1 in plasma, the variation of the plasma PON1 metabolism rate was set to be the same as the hepatic PON1 metabolism rate. Even though the distributions have similar means and coefficient of variation as the observed data, they included values outside of the range of the observed data because the distributions were assumed to be unbounded. These 50 sets of distributions, for each of the four parameters, were found to cover the entire range of the observed data; and the ratios of maximum value to minimum value in the simulated distributions were at least three times the ratios of maximum value to minimum value in the observed data.

According to EPA's Data-Derived Extrapolation Factor guidance, when calculating a DDEF intra-species extrapolation (USEPA, 2014), administered doses leading to the response level of interest (10% change in RBC AChE inhibition) are compared between a measure of average response and response at the tail of the distribution representing sensitive individuals. Oral doses that cause 10% RBC AChE inhibition in both adults and 6-month old infants (example provided in Figure 1 a,b) were estimated using the model. The ratio of the adult ED_{10} to the infant ED_{10} was then used to derive intraspecies extrapolation factors. In the subsequent Monte Carlo simulations, the target age group is six-month-old individuals. Some model parameters are specific to this age group (e.g., PON1 metabolism in plasma), and some parameters are scaled by body weight that reflect this age group (e.g., tissue volume). Based on the 5^{th} percentile of the distributions, the DDEF for intraspecies extrapolation is 2.8X for chlorpyrifos and 3.1X for the oxon (Dow, 2014b). Based on the 99^{th} percentile of the distributions, the DDEF for intraspecies extrapolation is 4X for chlorpyrifos and 5X for the oxon (Dow, 2014b). For this revised HHRA, the 99^{th} percentile is being used to account for sensitivities (i.e., the intra-species factor is 4X for chlorpyrifos and 5X for the oxon for all groups except women who are pregnant or may become pregnant). As shown in Figure 1b, at the 99^{th}-ile, only 1% of infants will experience 10% or greater RBC AChE inhibition at the POD.

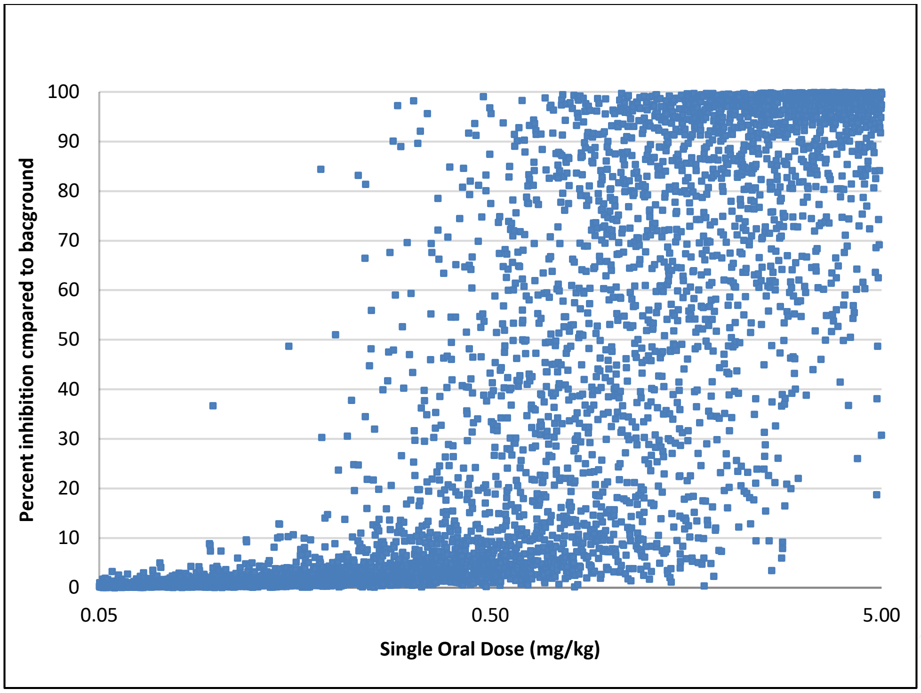


Figure 1a. Simulated population of 6 month olds for intra-species extrapolation DDEF derivation. Percent RBC AChE inhibition from exposure to single oral doses of chlorpyrifos ranging from 0.05 to 5.0 mg/kg/day (X and Y axes provided on the log scale).

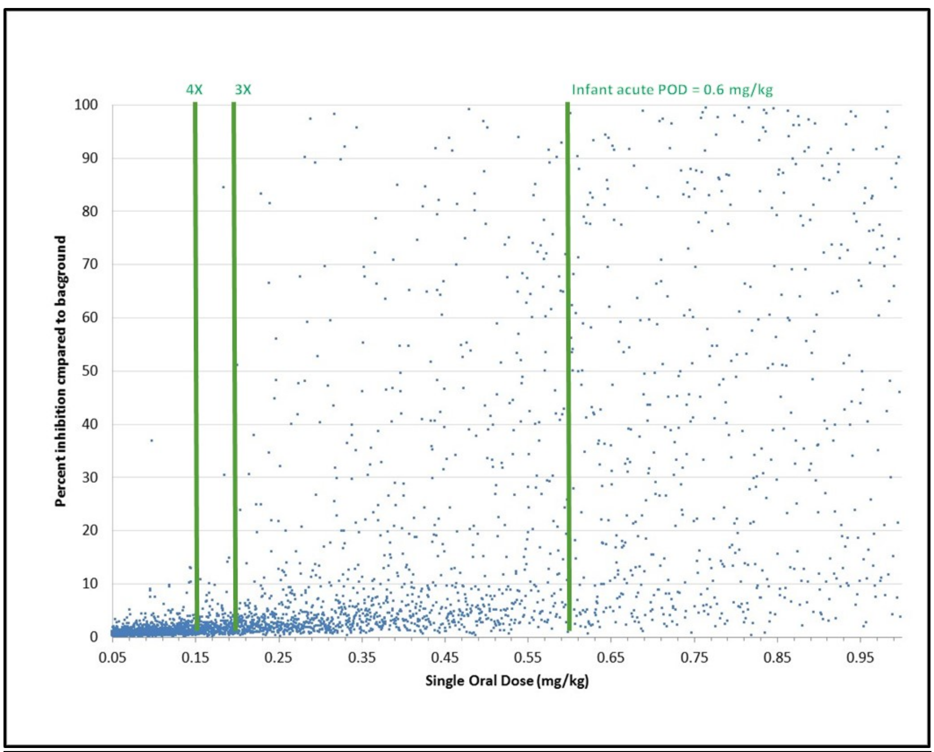


Figure 1b. Simulated population of 6 month olds for intra-species extrapolation DDEF derivation. Percent RBC AChE inhibition from exposure to single oral doses of chlorpyrifos ranging from 0.05 to 1.0 mg/kg/day. Green lines represent the infant acute POD for chlorpyrifos, the POD adjusted for the 3X and 4X intraspecies factors for the 95 and 99th-%ile, respectively.

In summary, for the chlorpyrifos HHRA, the human PBPK-PD model has been used to derive PODs for RBC AChE inhibition for various populations, durations, and routes (Table 4.2.2.1.2). As such, the interspecies factor is not needed. To account for variations in sensitivities, an intra-species factor of 4X for chlorpyrifos and 5X for the oxon is applied for all groups except women of childbearing age. For women of childbearing age, the typical 10X intra-species factor is being applied due the lack of appropriate information and algorithms to characterize physiological changes during pregnancy. Risks are being presented throughout the document assuming both the 10X FQPA SF is being retained for all subpopulations and reduced to 1X for all subpopulations. The individual and total uncertainty factors are summarized in Table 4.2.2.2.3.

Table 4.2.2.2.3 Uncertainty Factor Summary.

Uncertainty Factor	FQPA 10X Retained			FQPA 10X Reduced to 1X		
	Females	All other Subpopulations		Females	All other Subpopulations	
		Food (parent)	Drinking Water (oxon)		Food (parent)	Drinking Water (oxon)
Interspecies	1	1	1	1	1	1
Intraspecies	10	4	5	10	4	5
FQPA	10	10	10	1	1	1
Total	**100**	**40**	**50**	**10**	**4**	**5**

4.3 Endocrine Disruptor Screening Program

As required by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FFDCA), EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision for chlorpyrifos, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), chlorpyrifos is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a “naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[15] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

Chlorpyrifos is on List 1 for which EPA has received all of the required Tier 1 assay data. The Agency has reviewed all of the assay data received for the appropriate List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets (see Docket # EPA-HQ-OPP-2008-0850 for chlorpyrifos).”For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[16]

5.0 Dietary Exposure and Risk Assessment

HED had previously conducted both acute and steady state dietary (food only) exposure analyses for chlorpyrifos using DEEM and Calendex software with the Food Commodity Intake Database (FCID) (D. Drew *et al.,* D424486, 11/18/2014), respectively.

For the current assessment, the resulting acute and steady state food exposure values are compared to the PBPK-derived aPAD or ssPAD. When the dietary exposure exceeds 100% of the aPAD or ssPAD there is a potential risk concern.

All details pertaining to the assumptions, data inputs, and exposure outputs for the dietary analysis may be found in the 2014 dietary assessment memorandum (D. Drew *et al.,* D425586, 11/18/2014).

[15] See https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[16] https://www.epa.gov/endocrine-disruption

Table 5.0.1. Chlorpyrifos Population Adjusted Doses (PADs) Derived from PBPK Modeled Doses Corresponding to 10% RBC AChE Inhibition – FQPA SF 10X Retained[1].

RA Type	Infants (< 1 year old)			Children (1 – 2 Years old)			Children (6-12 Years Old)			Youths (13-19 Years Old)			Females (13-49 Years Old)		
	LOC	Acute	Steady State	LOC	Acute	Steady State	LOC	Acute	Steady State	LOC	Acute	Steady State	LOC	Acute	Steady State
Drinking Water (oxon conc, ppb)	50	23.66	4.34	50	60.08	10.96	50	154	27.16	50	99.76	17.56	100	52.85	9.32
Food (µg/kg/day)	40	15	2.6	40	15	2.5	40	13	2.3	40	12	2.0	100	4.7	0.78

1. Population Adjusted Dose (PAD) = POD ÷ LOC (including all applicable uncertainty factors). PODs for each scenario and subpopulation are provided in Table 4.2.2.1.2.

Table 5.0.2. Chlorpyrifos Population Adjusted Doses (PADs) Derived from PBPK Modeled Doses Corresponding to 10% RBC AChE Inhibition – FQPA SF Reduced to 1X[1].

RA Type	Infants (< 1 year old)			Children (1 – 2 Years old)			Children (6-12 Years Old)			Youths (13-19 Years Old)			Females (13-49 Years Old)		
	LOC	Acute	Steady State	LOC	Acute	Steady State	LOC	Acute	Steady State	LOC	Acute	Steady State	LOC	Acute	Steady State
Drinking Water (oxon conc, ppb)	5	236	43.4	5	600.8	109.6	5	1540	271.6	5	997.6	175.6	10	528.5	93.2
Food (µg/kg/day)	4	150	26	4	150	25	4	130	23	4	120	20	10	47	7.8

1. Population Adjusted Dose (PAD) = POD ÷ LOC (including all applicable uncertainty factors). PODs for each scenario and subpopulation are provided in Table 4.2.2.1.2.

5.1 Residues of Concern Summary and Rationale

The qualitative nature of the residue in plants and livestock is adequately understood based on acceptable metabolism studies with cereal grain (corn), root and tuber vegetable (sugar beets), and poultry and ruminants. The residue of concern, for tolerance expression and risk assessment, in plants (food and feed) and livestock commodities is the parent compound chlorpyrifos.

Based on evidence (various crop field trials and metabolism studies) indicating that the metabolite chlorpyrifos oxon would be not be present in edible portions of the crops (particularly at periods longer than the currently registered PHIs), it is not a residue of concern in food or feed at this time. Also, the chlorpyrifos oxon is not found on samples in the U.S. Department of Agriculture's Pesticide Data Program (USDA PDP) monitoring data. In fact, from 2007 to 2012, out of several thousand samples of various commodities, only one sample of potato showed presence of the oxon at trace levels, 0.003 ppm where the LOD was 0.002 ppm, even though there are no registered uses of chlorpyrifos on potato in the U.S.

The oxon metabolite was not found in milk or livestock tissues in cattle and dairy cow feeding studies, at all feeding levels tested, and is not a residue of concern in livestock commodities.

Oxidation of chlorpyrifos to chlorpyrifos oxon could potentially occur through photolysis, aerobic metabolism, and chlorination as well as other oxidative processes. Because of the toxicity of the oxon and data indicating that chlorpyrifos rapidly converts to the oxon during typical drinking water treatment (chlorination), the drinking water risk assessment considers the oxon as the residue of concern in treated drinking water and assumes 100% conversion of chlorpyrifos to chlorpyrifos oxon (see DWA, R. Bohaty, 09/15/2020, D459269 and 09/15/2020, D459270).

Table 5.1. Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression.

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	Chlorpyrifos	Chlorpyrifos
	Rotational Crop	Chlorpyrifos	Chlorpyrifos
Livestock	Ruminant	Chlorpyrifos	Chlorpyrifos
	Poultry	Chlorpyrifos	Chlorpyrifos
Drinking Water		Chlorpyrifos Oxon	Not Applicable

5.2 Food Residue Profile

Acute and steady state dietary (food only) exposure analyses for chlorpyrifos were conducted using the Dietary Exposure Evaluation Model (DEEM) and Calendex software with the Food Commodity Intake Database (FCID) (D. Drew, 11/18/2014, D424486, *Chlorpyrifos Acute and Steady State Dietary (Food Only) Exposure Analysis to Support Registration Review*). This software uses 2003-2008 food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). These analyses were performed for the purpose of obtaining food exposure values for comparison to the chlorpyrifos doses predicted by the PBPK-PD model to cause RBC ChEI. The acute and steady state dietary exposure analyses do not include drinking water which is assessed separately as discussed in Section 7 (Aggregate Exposure/Risk Characterization).

Both the acute and steady state dietary exposure analyses are highly refined. The large majority of food residues used were based upon PDP monitoring data except in a few instances where no appropriate PDP data were available. In those cases, field trial data or tolerance level residues were assumed. OPP's Biological and Economic Analysis Division (BEAD) provided estimated percent crop treated information. Food processing factors from submitted studies were used as appropriate.

5.3 Percent Crop Treated Used in Dietary Assessment

The acute and steady state dietary exposure assessment used percent crop treated (%CT) information from BEAD's Screening Level Usage Analysis (SLUA; May 2014). BEAD has recently issued an updated SLUA (March 2020) for chlorpyrifos which includes a comparison of the percent crop treated estimates of 2016 and 2020.[17] Those results indicate that there were no appreciable increases in estimated percent crop treated and that most reported crop commodities had a decrease in percent crop treated as well as a decrease in the average yearly amount of chlorpyrifos applied. The use of the 2014 crop treated estimates do not underestimate the dietary exposures.

5.4 Acute Dietary (Food Only) Risk Assessment

Chlorpyrifos acute (food only) dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database DEEM-FCID™, Version 3.16, which incorporates consumption data from NHANES/WWEIA. This dietary survey was conducted from 2003 to 2008. Acute dietary risk estimates are presented below for the sentinel population subgroups for acute risk assessment: infants (< 1 year old), children (1-2 years old), youths (6-12 years old) and adults (females 13-49 years old). The assessment of these index lifestages will be protective for the other population subgroups.

Acute dietary (food only) risk estimates are all <100 % of the acute PAD for food ($aPAD_{food}$) at the 99.9th percentile of exposure and are not of concern. With the 10X FQPA SF retained, the population with the highest risk estimate is females (13-49 years old) at 3.2 % $aPAD_{food}$. With the FQPA SF reduced to 1X, the acute dietary risk estimates are <1% of the $aPAD_{food}$ for all populations.

Table 5.4. Acute Dietary (Food Only) Exposure and Risk Estimates for Chlorpyrifos.

Population Subgroup	Food Exposure[1] (µg/kg/day)	$aPOD_{food}$[2] (µg/kg/day)	10X FQPA SF		1X FQPA SF	
			$aPAD_{food}$[3] (µg/kg/day)	% of $aPAD_{food}$	$aPAD_{food}$[4] (µg/kg/day)	% of $aPAD_{food}$
Infants (< 1 yr)	0.273	600	15	1.8	150	<1

[17] L. Hendrick, 03/05/2020, Updated Chlorpyrifos (059101) Screening Level Usage Analysis (SLUA)

Table 5.4. Acute Dietary (Food Only) Exposure and Risk Estimates for Chlorpyrifos.						
Population Subgroup	Food Exposure[1] (µg/kg/day)	aPOD$_{food}$[2] (µg/kg/day)	10X FQPA SF		1X FQPA SF	
			aPAD$_{food}$[3] (µg/kg/day)	% of aPAD$_{food}$	aPAD$_{food}$[4] (µg/kg/day)	% of aPAD$_{food}$
Children (1-2 yrs)	0.423	581	15	2.8	150	<1
Youths (6-12 yrs)	0.189	530	13	1.4	130	<1
Adults (Females 13-49 yrs)	0.150	467	4.7	3.2	47	<1

[1] Acute food only exposure estimates from DEEM (at 99.9th percentile). Refined with monitoring data and %CT.
[2] Acute point of departure; daily dose predicted by PBPK-PD model to cause RBC ChEI of 10% for acute dietary (food) exposures. Table 4.8.4.1.2.
[3]aPAD= acute population adjusted dose = PoD (Dose predicted by PBPK-PD model to cause 10% RBC ChEI) ÷ total UF; Total uncertainty factor =100X for females 13-49 yrs (10X intraspecies factor and 10X FQPA uncertainty factor) and 40X for other populations (4X intraspecies factor and 10X FQPA uncertainty factor). Table 5.0.1.
[4]aPAD= acute population adjusted dose = PoD (Dose predicted by PBPK-PD model to cause 10% RBC ChEI) ÷ total UF; Total uncertainty factor =10X for females 13-49 yrs (10X intraspecies factor and 1X FQPA uncertainty factor) and 4X for other populations (4X intraspecies factor and 1X FQPA uncertainty factor). Table 5.0.2.

5.5 Steady State Dietary (Food Only) Exposure and Risk Estimates

A chlorpyrifos steady state dietary (food only) exposure analysis was conducted using Calendex-FCID™. HED's steady state assessment considers the potential risk from a 21-day exposure duration using a 3-week rolling average (sliding by day) across the year. For this assessment, the same food residue values used in the acute assessment were used for the 21-day duration. In the Calendex software, one diary for each individual in the WWEIA is selected to be paired with a randomly selected set of residue values for each food consumed. The steady state analysis calculated exposures for the sentinel populations for infant, child, youths, and adult (infants <1 yr, children 1-2 yrs, youths 6-12 yrs, females 13-49 yrs). The assessment of these index lifestages will be protective for the other population subgroups.

Calendex reported dietary exposures for each population subgroup at several percentiles of exposure ranging from 10th percentile to 99.9th percentile. The dietary (food only) exposures for chlorpyrifos were all <100% ssPAD$_{food}$ (all populations, at all percentiles of exposure). Only the 99.9th percentile of exposure is presented in Table 5.5 below. Calendex exposure results for other percentiles of exposure can be found in D424486.

Steady state dietary (food only) risk estimates are all <100 % of the steady state PAD for food (ssPAD$_{food}$) at the 99.9th percentile of exposure and are not of concern. With the 10X FQPA SF retained, the population with the highest risk estimate is children (1-2 years old) at 9.7 % ssPAD$_{food}$. With the FQPA SF reduced to 1X, the steady state dietary risk estimates are <1% of the ssPAD$_{food}$ for all populations.

Table 5.5. Steady State Dietary (Food Only) Exposure and Risk Estimates for Chlorpyrifos.						
Population Subgroup	Food Exposure[1] (µg/kg/day)	$ssPoD_{food}$[2] (µg/kg/day)	10X FQPA SF		1X FQPA SF	
			$ssPAD_{food}$[3] (µg/kg/day)	% of $ssPAD_{food}$	$ssPAD_{food}$[4] (µg/kg/day)	% of $ssPAD_{food}$
Infants (< 1 yr)	0.186	103	2.6	7.2	26	<1
Children (1-2 yrs)	0.242	99	2.5	9.7	25	<1
Youths (6-12 yrs)	0.128	90	2.3	5.6	23	<1
Adults (Females 13-49 yrs)	0.075	78	0.78	9.6	7.8	<1

[1] Steady state food only exposure estimates from DEEM (at 99.9th percentile). Refined with monitoring data and %CT.
[2] Steady state point of departure; daily dose predicted by PBPK-PD model to cause RBC ChEI of 10% for acute dietary (food) exposures. Table 4.8.4.1.2.
[3]ssPAD= steady state population adjusted dose = POD (Dose predicted by PBPK-PD model to cause 10% RBC ChEI) ÷ total UF; Total uncertainty factor =100X for females 13-49 yrs (10X intraspecies factor and 10X FQPA uncertainty factor) and 40X for other populations (4X intraspecies factor and 10X FQPA uncertainty factor). Table 5.0.1.
[4] ssPAD= steady state population adjusted dose = POD (Dose predicted by PBPK-PD model to cause 10% RBC ChEI) ÷ total UF; Total uncertainty factor =10X for females 13-49 yrs (10X intraspecies factor and 1X FQPA uncertainty factor) and 4X for other populations (4X intraspecies factor and 1X FQPA uncertainty factor). Table 5.0.2.

5.6 Dietary Drinking Water Risk Assessment

The total dietary exposure to chlorpyrifos is through both food and drinking water. EFED has provided a revised drinking water assessment (DWA) for chlorpyrifos (R. Bohaty, 09/15/2020, D459269 and 09/15/2020, D459270) which includes the updated EDWCs for dietary risk assessment. A DWLOC approach is used to calculate the amount of exposure available in the total dietary 'risk cup' for chlorpyrifos in drinking water after accounting for chloropyrifos exposure from food and from residential uses. This DWLOC can be compared to the EDWCs to determine if there is a risk of concern for drinking water exposures (See D. Drew, D424485, 12/29/2014 for details on the DWLOC approach and calculations). The acute and steady state dietary exposure analyses discussed above only include food and do not include drinking water; the aggregate assessment, which does incorporate drinking water, is discussed in Section 7 (Aggregate Exposure/Risk Characterization).

6.0 Residential Exposure/Risk Characterization

Residential exposures to chlorpyrifos are currently expected from chlorpyrifos use in residential settings. Formulations/use sites registered for use in residential areas include a granular ant mound use and roach bait in child-resistant packaging. Additionally, chlorpyrifos is labeled for public health aerial and ground-based fogger ULV mosquito adulticide applications and for golf course turf applications. All residential exposures and risks were previously assessed in support of the 2014 HHRA (W. Britton, D424484, 12/29/2014) and 2016 HHRA (W. Britton, D436317, 11/3/2016). The previous assessments included evaluation of residential post-application risks from playing golf on chlorpyrifos-treated courses and from exposures which can occur following aerial and ground-based ULV mosquito adulticide usage. The potential for residential exposures from the roach bait product was determined to be negligible. Further, residential exposures from the ant mound use were also determined to be negligible since these products can only be applied professionally and direct exposure with treated ant mounds is not anticipated.

The previously assessed residential post-application assessments have been updated to incorporate the approach applied for PBPK-derivation of PODs for infants, children, and adults based on 10% RBC AChE inhibition. The results have been summarized assuming both that the FQPA SF has been retained at 10X and has been reduced to 1X. If the FQPA SF is retained, the total LOC for residential exposure assessment is 100X for adults (represented by females 13-49) and 40X for all other subpopulations, including children.

6.1 Residential Handler Exposure/Risk Estimates

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are addressed somewhat differently by HED as homeowners are assumed to complete all elements of an application without use of any protective equipment.

Based upon review of all chlorpyrifos registered uses, only the roach bait products can be applied by a homeowner in a residential setting, but the application of roach bait products has not quantitatively assessed because these exposures are negligible. The roach bait product is designed such that the active ingredient is contained within a bait station which eliminates the potential for contact with the chlorpyrifos containing bait material. Therefore, updated residential handler risks are not required for these uses.

6.2 Residential Post-Application Exposure/Risk Estimates

Residential post-application exposures are likely from being in an environment that has been previously treated with chlorpyrifos. Chlorpyrifos can be used on golf courses and as an aerial and ground based ULV mosquito adulticide application in residential areas. Post-application exposure from residential ant mount treatment was assessed qualitatively because post-application exposures to treated ant mounts are expected to be negligible.

All of the residential post-application exposure scenarios, data and assumptions, and algorithms used to assess exposures and risks from activities on golf course turf following chlorpyrifos application and from aerial and ground based ULV mosquito adulticide applications are the same as those used in the 2016 HHRA. Additionally, this updated assessment makes use of the same chemical-specific turf transferable residue (TTR) data to assess exposures and risks. In the 2016 HHRA (W. Britton, D436317, 11/03/2016), the residential post-application exposures and risks resulting from aerial and ground-based ULV mosquito adulticide applications were updated to reflect 1) the current default deposition fraction recommended for ground applied ULV mosquitocides (i.e., 8.7 percent of the application rate vs the previous 5 percent) and 2) several iterations of aerial applications modeled assuming differing winds speeds and release heights allowed by chlorpyrifos mosquitocide ULV labels. The previously assessed residential post-application assessment has been updated to incorporate the approach applied for PBPK-derivation of PODs for infants, children, and adults based on 10% RBC AChE inhibition and assuming both that the FQPA SF has been retained at 10X and has been reduced to 1X. The AgDISP (v8.2.6) model input parameters, outputs, and the algorithms used to estimate residential post-application exposures following aerial and ground based ULV mosquitocide application can be found in Appendix 7.

Combining Exposure and Risk Estimates

Since dermal, incidental oral, and inhalation exposure routes share a common toxicological endpoint, RBC AChE inhibition, risk estimates have been combined for those routes. The incidental oral scenarios (i.e., hand-to-mouth and object-to-mouth) should be considered inter-related and it is likely that they occur interspersed amongst each other across time. Combining these scenarios with the dermal and inhalation exposure scenarios would be unrealistic because of the conservative nature of each individual assessment. Therefore, the post-application exposure scenarios that were combined for children 1 < 2 years old are the dermal, inhalation, and hand-to-mouth scenarios (the highest incidental oral exposure expected). This combination should be considered a protective estimate of children's exposure to pesticides.

Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

Whether the FQPA SF is retained at 10X or reduced to 1X, there are no residential post-application risk estimates of concern for the registered uses of chlorpyrifos. If the FQPA SF is retained at 10X, the assessment of steady state residential golfing post-application exposures (dermal only) to chlorpyrifos treated turf results in no risks of concern for adults or children/youths [i.e., MOEs ≥ 40 for children 6 to < 11 years old and youths 11 to < 16 years old and MOEs ≥ 100 for adults (females 13-49)]. Additionally, the steady state post-application exposures from public health mosquitocide applications results in no combined risk estimates of concern for adults (females 13-49; dermal and inhalation exposures) and children 1 to < 2 years old (dermal, incidental oral, and inhalation exposures) (i.e., MOEs ≥ 40 for children 1 to < 2 years old and MOEs ≥ 100 for adults). If the FQPA SF is reduced to 1X, there are also no residential post-application risk estimates of concern for adults (females 13-49) or children/youths [MOEs > 4 for children 1 to < 2 years old, children 6 to < 11 years old, and children 11 to < 16 years old; and MOEs > 10 for adults (females 13-49 years old)].

The risk estimates are presented in Table 6.2.1 – Table 6.2.8.

Table 6.2.1. Steady State Residential Post-Application Exposure and Risk Estimates for Chlorpyrifos - Golf Course Uses.

Lifestage	Post-application Exposure Scenario		Application Rate[1]	State (TTR Data)	Dose (mg/kg/day)[2]	MOEs[3]
	Use Site	Route of Exposure				
Adult (Females 13-49 years old)	Golf Course Turf	Dermal	1.0 (Emulsifiable Concentrate)	CA	0.010	1,200
				IN	0.0069	1,700
				MS	0.012	1,000
				Mean	0.0095	1,200
Youths 11 to < 16 years old				CA	0.010	1,400
				IN	0.0069	2,000
				MS	0.012	1,200
				Mean	0.0096	1,500
Children 6 to < 11 years old				CA	0.012	1,900

Table 6.2.1. Steady State Residential Post-Application Exposure and Risk Estimates for Chlorpyrifos - Golf Course Uses.

Lifestage	Post-application Exposure Scenario		Application Rate[1]	State (TTR Data)	Dose (mg/kg/day)[2]	MOEs[3]
	Use Site	Route of Exposure				
				IN	0.0082	2,800
				MS	0.014	1,600
				Mean	0.011	2,000
Adult (Females 13-49 years old)			1.0 (Granular)	CA	0.0088	1,400
Youths 11 to < 16 years old					0.0088	1,600
Children 6 to < 11 years old					0.010	2,200

1 Based on the maximum application rates registered for golf course turf.
2 Dose (mg/kg/day) equations for golfing applications are provided in Appendix B of the occupational and residential exposure assessment (W. Britton, D424484, 12/29/2014). For dose estimation from exposures to golfing on treated turf, the TTR data were used. Doses have been presented for all State sites, including the mean of all state sites.
3 MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day). LOC = if the FQPA SF is retained at 10X, the total LOC for residential exposure assessment is 100X for adults (females 13-49) and 40X for all other subpopulations, including children. If the FQPA SF is reduced to 1X, the total LOC for residential exposure assessment is 10X for adults (females 13-49) and 4X for all other subpopulations, including children. See Table 4.2.2.1.2 for PODs.

Table 6.2.2. Residential Post-Application Inhalation Steady State Exposure Estimates from Chlorpyrifos ULV Aerial Mosquitocide Application - AgDISP Model.

Application Parameters	Population	Air Concentration Estimate (mg/m^3)[1]	MOE[2]
1 mph Wind Speed Dv 0.5 = 60 µm 75 Foot Release Height	Adults	0.0047	1,300
	Children 1 to <2 years old		500
10 mph Wind Speed Dv 0.5 = 40 µm 300 Foot Release Height	Adults	0.00070	8,800
	Children 1 to <2 years old		3,400

1 Air concentration estimate modeled using AGDISP v8.2.6 at breathing height of adults and children.
2 MOE = POD (mg/m^3) ÷ Dose (mg/m^3). See Table 4.2.2.1.2 for PODs.

Table 6.2.3. Residential Post-Application Inhalation Steady State Exposure Estimates from Chlorpyrifos ULV Ground Mosquitocide Application – Well Mixed Box (WMB) Model.

Population	Air Concentration Estimate (mg/m^3)[1]	MOE[2]
Adults	0.0051	1,200
Children 1 to <2 years old		460

1 Air concentration estimate modeled using the well mixed box model. The inputs and algorithms used are presented in Appendix C of D424484 (W. Britton, 12/29/2014).
2 MOE = POD (mg/m^3) ÷ Dose (mg/m^3). See Table 4.2.2.1.2 for PODs.

Table 6.2.4. Residential Post-Application Dermal Steady State Exposure Estimates Resulting from Chlorpyrifos Aerial ULV Mosquitocide Application.

Application Parameters	Lifestage	Application Rate (lb ai/A)	AgDISP Deposition Fraction[1]	Adjusted TTR[2] ($\mu g/cm^2$)	Dermal Dose[3] (mg/kg/day)	MOE[4]
1 mph Wind Speed Dv 0.5 = 60 µm 75 Foot Release Height	Adults	0.010	1.0	0.00038	0.0015	16,000
	Children 1 to < 2 Years Old				0.0026	53,000
10 mph Wind Speed Dv 0.5 = 40 µm 300 Foot Release Height	Adults	0.010	0.086	0.000033	0.00013	180,000
	Children 1 to < 2 Years Old				0.00022	610,000

1 The fraction of chlorpyrifos residue deposited following aerial mosquitocide application was determined with use of the AgDISP (v8.2.6) model.
2 TTR_t ($\mu g/cm^2$) = [(Day 0 Residue from MS TTR study ($\mu g/cm^2$) × Application Rate (0.010 lb ai/A)) ÷ Application Rate of MS TTR Study (3.83 lb ai/A))] × AgDISP Deposition Fraction. The MS TTR data was selected for use because it is the worst case and, as a result, most protective of human health.
3 Dermal Dose (mg/kg/day) = [(TTR_t ($\mu g/cm^2$) × CF1 (0.001 mg/µg) × Transfer Coefficient (180,000 cm^2/hr, adults; 49,000 cm^2/hr, children) * ET (1.5 hrs))] ÷ BW (kg).
4 MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day). See Table 4.2.2.1.2 for PODs.

Table 6.2.5. Residential Post-Application Dermal Steady State Exposure Estimates Resulting from Chlorpyrifos ULV Ground Mosquitocide Application.

Lifestage	Application Rate (lb ai/A)	Deposition Fraction[1]	Adjusted TTR[2] ($\mu g/cm^2$)	Dermal Dose[3] (mg/kg/day)	MOE[4]
Adults	0.010	1.0	0.00038	0.00013	180,000
Children 1 to < 2 Years Old				0.00022	610,000

1 Ground fraction of mosquitocide application rate deposited on turf as determined using eight published studies on ground ULV application in which deposition was measured.
2 TTR_t ($\mu g/cm^2$) = [(Day 0 Residue from MS TTR study ($\mu g/cm^2$) × Application Rate (0.010 lb ai/A)) ÷ Application Rate of MS TTR Study (3.83 lb ai/A))] × AgDISP Deposition Fraction
3 Dermal Dose (mg/kg/day) = [(TTR_t ($\mu g/cm^2$) × CF1 (0.001 mg/µg) × Transfer Coefficient (cm^2/hr - 180,000, adults; 49,000, children) × ET (1.5 hrs))] ÷ BW (kg)
4 MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day). See Table 4.2.2.1.2 for PODs.

Table 6.2.6. Residential Post-Application Steady State Incidental Oral Exposure Estimates Resulting from Chlorpyrifos ULV Aerial Mosquitocide Application.

Application Parameters	Lifestage	Application Rate (mg ai)	Dermal Exposure (mg/day)[1]	Incidental Oral Dose (mg/kg/day)[2]	MOE[3]
1 mph Wind Speed Dv 0.5 = 60 µm 75 Foot Release Height	Children 1 to < 2 Years Old	0.010	0.028	5.2×10^{-5}	1,900
10 mph Wind Speed			0.0022	4.5×10^{-6}	22,000

Dv 0.5 = 40 µm 300 Foot Release Height					

1 Dermal exposure (mg/day) as calculated for children's aerial based ULV applications using the algorithms as described in Appendix C of D424484 (W. Britton, 12/29/2014).
2 Incidental Oral Dose estimated using the algorithms as described below in Appendix C of the 2014 HHRA.
3 MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day). See Table 4.2.2.1.2 for PODs.

Table 6.2.7. Residential Post-Application Steady State Incidental Oral Exposure Estimates Resulting from Chlorpyrifos ULV Ground Mosquitocide Application.

Lifestage	Application Rate (mg ai)	Dermal Exposure (mg/day)[1]	Incidental Oral Dose (mg/kg/day)[2]	MOE[3]
Children 1 to < 2 Years Old	0.010	0.0024	4.5×10^{-6}	22,000

1 Dermal exposure (mg/day) as calculated for children's ground based ULV applications using the algorithms described in Table 6.2.5 above, and as described below in Appendix C of D424484 (W. Britton, 12/29/2014).
2 Incidental Oral Dose estimated using the algorithms as described in Appendix C of the 2014 HHRA.
3 MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day). See Table 4.2.2.1.2 for PODs.

Table 6.2.8. Combined Residential Post-Application Steady State Exposure Estimates from Chlorpyrifos Mosquitocide Applications.						
Population	**Application Parameter**	**Route of Exposure**	**Dermal or Incidental Oral Dose (mg/kg/day) or Air Concentration estimate (mg/m^3)[1]**	**MOE[2]**	**Combined Routes[3]**	**Combined MOEs[4]**
Adults (Females 13-49 years old)	Aerial ULV Mosquitocide Application 1 mph Wind Speed Dv 0.5 = 60 µm 75 Foot Release Height	Inhalation	0.0047	1,300	X	1,200
		Dermal	0.0015	16,000		
	Aerial ULV Mosquitocide Application 10 mph Wind Speed Dv 0.5 = 40 µm 300 Foot Release Height	Inhalation	0.00070	8,800	X	8,400
		Dermal	0.00013	180,000		
	Ground Mosquitocide Application – WMB	Inhalation	0.0051	1,200	X	1,200
		Dermal	0.00013	180,000		
Children 1 to < 2 years old	Aerial ULV Mosquitocide Application 1 mph Wind Speed Dv 0.5 = 60 µm 75 Foot Release Height	Inhalation	0.0047	500	X	400
		Dermal	0.0026	53,000		
		Incidental Oral	5.2×10^{-5}	1,900		
	Aerial ULV Mosquitocide Application 10 mph Wind Speed Dv 0.5 = 40 µm 300 Foot Release Height	Inhalation	0.00070	3,400	X	2,900
		Dermal	0.00022	610,000		
		Incidental Oral	4.5×10^{-6}	22,000		
	Ground Mosquitocide Application – WMB	Inhalation	0.0051	460	X	450
		Dermal	0.00022	610,000		
		Incidental Oral	4.54×10^{-6}	22,000		

1. See Tables 6.2.3 – 6.2.7 for route-specific exposure inputs and risk estimates.
2. MOE = POD (mg/m^3) ÷ Dose (mg/m^3). See Table 4.2.2.1.2 for PODs.
3. X indicates the exposure scenarios included in the combined MOE.

4. Combined MOE = 1 ÷ [(1/dermal MOE) + (1/inhalation MOE) + (1/incidental oral MOE)], where applicable.

6.3 Residential Risk Estimates for Use in Aggregate Assessment

Table 6.3 reflects the residential risk estimates that are recommended for use in the aggregate assessment for chlorpyrifos.

- Adults (females 13-49 years old): post-application dermal exposures from golfing on treated turf using MS TTR data.
- Children 11 to < 16 years old: post-application dermal exposures from golfing on treated turf using MS TTR data.
- Children 6 to < 11 years old: post-application dermal exposures from golfing on treated turf using MS TTR data.

Exposures to treated turf from mosquitocide applications are completed as stand-alone assessments since mosquitocide applications are typically only made as a result of/in response to a public health need, and require a risk mitigation/risk management determination significantly different from an assessment without a large public health benefit. Therefore, these exposures are not aggregated with exposures from food and drinking water.

Table 6.3. Recommendations for the Residential Exposures for the Chlorpyrifos Aggregate Assessment.

Lifestage	Exposure Scenario	Dose[1]			MOE[2]			
		Dermal (mg/kg/day)	Inhalation (mg/m^3)	Oral (mg/kg/day)	Dermal	Inhalation	Oral	Total
Adults (Females 13-49 Years Old)	Golf Course Turf – MS TTR Data	0.012	N/A	N/A	1,000	N/A	N/A	1,000
Children 11 to < 16 Years Old		0.012	N/A		1,200	N/A		1,200
Children 6 to < 11 Years Old		0.014	N/A		1,600	N/A		1,600

1 Dose = the highest dose for each applicable lifestage of all residential scenarios assessed. Total = dermal + incidental oral (where applicable).
2 MOE = the MOEs associated with the highest residential doses. Total = 1 ÷ [(1/Inhalation MOE) + (1/Dermal MOE) + (1/Incidental Oral MOE)], where applicable.

7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard, or the risks themselves can be aggregated. The durations of exposure identified for chlorpyrifos uses are acute and steady state. The acute aggregate assessment includes food and drinking water only. The steady state aggregate assessment includes food, drinking water, and residential exposures.

A drinking water level of comparison (DWLOC) approach to aggregate risk was used to calculate the amount of exposure available in the total 'risk cup' for chlorpyrifos oxon in drinking water after accounting for any chloropyrifos exposures from food and/or residential uses. This DWLOC can then be compared to the EDWCs to determine if there is an aggregate risk of concern. EFED has provided an updated drinking water assessment (DWA) for chlorpyrifos which includes the EDWCs for aggregate risk assessment. For chlorpyrifos, DWLOCs were calculated for both the acute and steady state aggregate assessments for infants, children, youths and adult females.

For complete details on the assumptions, results, and characterization of the drinking water analysis refer to EFED's DWA (R. Bohaty, 09/15/2020, D459269 and 09/15/2020, D459270).

7.1 Acute Aggregate Risk – DWLOC Approach

The acute aggregate assessment includes only food and drinking water. Acute DWLOCs were calculated for infants, children, youths, and adults. The DWLOCs were calculated assuming both that the FQPA SF has been retained at 10X and has been reduced to 1X. With the 10X FQPA SF retained, the lowest acute DWLOC calculated was for infants (<1 year old) at 23 ppb. With the FQPA SF reduced to 1X, the lowest acute DWLOC calculated was for infants (<1 year old) at 230 ppb.

Table 7.1.1. Acute Aggregate (Food and Drinking Water) Calculation of DWLOCs with FQPA 10X SF.[1,2]

Population	Food Exposure (chlorpyrifos)[3]		Drinking Water Exposure (chlorpyrifos oxon)[4]		Acute DWLOC with FQPA 10X[5] (ppb chlorpyrifos oxon)
	MOE	ARI	MOE	ARI	
Infants[1] (<1 yr)	2200	55	51	1.0	23
Children[1] (1-2 yrs)	1400	35	52	1.0	58
Youths[1] (6-12 yrs)	2800	70	51	1.0	150
Adults[2] (Females 13-49 yrs)	3100	31	103	1.0	51

[1] DWLOCs for infants, children and youths are calculated using the ARI (Aggregate Risk Index) approach since target MOEs are different for drinking water (chlorpyrifos oxon target MOE=50 with 10X FQPA SF retained) and for food and residential (chlorpyrifos target MOE= 40 with FQPA SF retained) exposures.

[2] DWLOCs for adults (females 13-49 yrs) are calculated using the reciprocal MOE approach since the target MOEs are the same for drinking water (chlorpyrifos oxon target MOE=100 with 10X FQPA SF retained) and for food and residential (chlorpyrifos target MOE= 100 with 10X FQPA SF retained) exposures.

[3] **FOOD:** $MOE_{food} = POD_{food}$ (µg/kg/day) (from Table 4.2.2.1.2) ÷ Food Exposure (µg/kg/day) (from Table 5.4). $ARI_{food} = [(MOE_{food})/(MOE_{target})]$.

[4] **WATER (ARI approach):** $ARI_{water} = 1/[(1/ARI_{agg}) - ((1/ARI_{food}) + (1/ARI_{dermal}))]$; Where $ARI_{agg}=1$ (Note:HED is generally concerned when calculated ARIs are less than 1).

MOE_{water} $= ARI_{water} \times MOE_{target}$.

WATER (Reciprocal MOE approach): $MOE_{water} = 1 \div [(1/MOE_{agg}) - ((1/MOE_{food}) + (1/MOE_{dermal}))]$; Where MOE_{agg} = Target MOE.

[5] **DWLOC:** DWLOC ppb= POD_{water} (ppb; from Table 4.2.2.1.2) ÷ MOE_{water}

Table 7.1.2. Acute Aggregate (Food and Drinking Water) Calculation of DWLOCs with FQPA SF Reduced to 1X.[1,2]

Population	Food Exposure (chlorpyrifos)[3]		Drinking Water Exposure (chlorpyrifos oxon)[4]		Acute DWLOC with FQPA 1X[5] (ppb chlorpyrifos oxon)
	MOE	ARI	MOE	ARI	
Infants[1] (<1 yr)	2200	55	51	1.0	230

Table 7.1.2. Acute Aggregate (Food and Drinking Water) Calculation of DWLOCs with FQPA SF Reduced to 1X.[1,2]					
Population	**Food Exposure (chlorpyrifos)[3]**		**Drinking Water Exposure (chlorpyrifos oxon)[4]**		**Acute DWLOC with FQPA 1X[5] (ppb chlorpyrifos oxon)**
	MOE	**ARI**	**MOE**	**ARI**	
Children[1] (1-2 yrs)	1400	35	52	1.0	600
Youths[1] (6-12 yrs)	2800	70	51	1.0	1,500
Adults[2] (Females 13-49 yrs)	3100	31	10	1.0	530

[1] DWLOCs for infants, children and youths are calculated using the ARI (Aggregate Risk Index) approach since target MOEs are different for drinking water (chlorpyrifos oxon target MOE= 5 with FQPA SF reduced to 1X) and for food and residential (chlorpyrifos target MOE= 4 with FQPA SF reduced to 1X) exposures.
[2] DWLOCs for adults (females 13-49 yrs) are calculated using the reciprocal MOE approach since the target MOEs are the same for drinking water (chlorpyrifos oxon target MOE= 10 with FQPA SF reduced to 1X) and for food and residential (chlorpyrifos target MOE= 10 with FQPA SF reduced to 1X) exposures.
[3] **FOOD:** $MOE_{food} = POD_{food}$ (μg/kg/day) (from Table 4.2.2.1.2) ÷ Food Exposure (μg/kg/day) (from Table 5.4).
$ARI_{food} = [(MOE_{food})/(MOE_{target})]$.
[4] **WATER (ARI approach):** $ARI_{water} = 1/[(1/ARI_{agg}) - ((1/ARI_{food}) + (1/ARI_{dermal}))]$; Where $ARI_{agg}=1$ (Note:HED is generally concerned when calculated ARIs are less than 1).
MOE_{water} = $ARI_{water} \times MOE_{target}$.
WATER (Reciprocal MOE approach): $MOE_{water} = 1 \div [(1/MOE_{agg}) - ((1/MOE_{food}) + (1/MOE_{dermal}))]$; Where MOE_{agg} = Target MOE.
[5] **DWLOC:** DWLOC ppb= POD_{water} (ppb; from Table 4.2.1.2) ÷ MOE_{water}

7.2 Steady State Aggregate Risk – DWLOC Approach

The steady state aggregate assessment includes dietary exposures from food and drinking water and dermal exposures from residential uses. Treated golf course turf represent the highest residential dermal exposures. Aggregate DWLOCs are presented below for the population subgroups of infants (< 1 year old), children (1-2 years old), youths (6-12 years old), and adults (females 13-49 years old). The assessment of these index lifestages is protective for the other population subgroups, including youths 11 to < 16 years old. The DWLOCs were calculated assuming both that the FQPA SF has been retained at 10X and has been reduced to 1X. The lowest steady state DWLOC calculated was for infants (<1 year old) at 4.0 ppb if the FQPA SF is retained at 10X and the lowest steady state DWLOC calculated was for infants (< 1 year old) at 43 ppb if the FQPA SF is reduced to 1X.

Table 7.2.1. Steady State Aggregate (Food, Drinking Water, Residential) Calculation of DWLOCs with FQPA 10X SF.[1,2]							
Population	**Food Exposure (chlorpyrifos)[3]**		**Residential Exposure (chlorpyrifos)[4]**		**Drinking Water Exposure (chlorpyrifos oxon)[5]**		**Steady State DWLOC with FQPA 10X[6] (ppb chlorpyrifos oxon)**
	MOE	**ARI**	**MOE**	**ARI**	**MOE**	**ARI**	
Infants[1] (<1 yr)	550	14	NA	NA	54	1.1	4.0
Children[1] (1-2 yrs)	410	10	NA	NA	55	1.1	9.9
Youths[1] (6-12 yrs)	700	18	1,600	40	44	1.1	21

Table 7.2.1. Steady State Aggregate (Food, Drinking Water, Residential) Calculation of DWLOCs with FQPA 10X SF.[1,2]

Population	Food Exposure (chlorpyrifos)[3]		Residential Exposure (chlorpyrifos)[4]		Drinking Water Exposure (chlorpyrifos oxon)[5]		Steady State DWLOC with FQPA 10X[6] (ppb chlorpyrifos oxon)
	MOE	ARI	MOE	ARI	MOE	ARI	
Adults[2] (Females 13-49 yrs)	1040	10	1,000	10	124	1.2	7.5

[1] DWLOCs for infants, children and youths are calculated using the ARI (Aggregate Risk Index) approach since target MOEs are different for drinking water (chlorpyrifos oxon target MOE=50 with 10X FQPA SF retained) and for food and residential (chlorpyrifos target MOE= 40) exposure.
[2] DWLOCs for adults (females 13-49 yrs) are calculated using the reciprocal MOE approach since the target MOEs are the same for drinking water (chlorpyrifos oxon target MOE=100 with 10X FQPA SF retained) and for food and residential (chlorpyrifos target MOE= 100 with 10X FQPA SF retained) exposure.
[3] **FOOD:** $MOE_{food} = POD_{food}$ (µg/kg/day) (from Table 4.2.2.1.2) ÷ Food Exposure (µg/kg/day) (from Table 5.5).
$ARI_{food} = [(MOE_{food})/(MOE_{target})]$.
[4] **RESIDENTIAL:** $MOE_{residential} = 1 \div (1/\text{Dermal MOE})$, (see Table 6.3).
[5] **WATER (ARI approach):** $ARI_{water} = 1/[(1/ARI_{agg}) - ((1/ARI_{food}) + (1/ARI_{residential}))]$; Where $ARI_{agg}=1$ (Note:HED is generally concerned when calculated ARIs are less than 1).
$MOE_{water} = ARI_{water} \times MOE_{target}$.
WATER (Reciprocal MOE approach): $MOE_{water} = 1/[(1/MOE_{agg}) - ((1/MOE_{food}) + (1/MOE_{residential}))]$; Where MOE_{agg} =Target MOE.
[6] **DWLOC:** DWLOC ppb= PoD_{water} (ppb; from Table 4.2.2.1.2) $/MOE_{water}$

Table 7.2.2. Steady State Aggregate (Food, Drinking Water, Residential) Calculation of DWLOCs with FQPA SF Reduced to 1X.[1,2]

Population	Food Exposure (chlorpyrifos)[3]		Residential Exposure (chlorpyrifos)[4]		Drinking Water Exposure (chlorpyrifos oxon)[5]		Steady State DWLOC with FQPA 1X[6] (ppb chlorpyrifos oxon)
	MOE	ARI	MOE	ARI	MOE	ARI	
Infants[1] (<1 yr)	550	140	NA	NA	5.0	1.0	43
Children[1] (1-2 yrs)	410	102	NA	NA	5.0	1.0	110
Youths[1] (6-12 yrs)	700	180	1,600	400	4.0	1.0	230
Adults[2] (Females 13-49 yrs)	1040	104	1,000	100	10	1.0	91

[1] DWLOCs for infants, children and youths are calculated using the ARI (Aggregate Risk Index) approach since target MOEs are different for drinking water (chlorpyrifos oxon target MOE=5 with FQPA SF reduced to 1X) and for food and residential (chlorpyrifos target MOE= 4 with FQPA SF reduced to 1X) exposure.
[2] DWLOCs for adults (females 13-49 yrs) are calculated using the reciprocal MOE approach since the target MOEs are the same for drinking water (chlorpyrifos oxon target MOE= 10 with FQPA SF reduced to 1X) and for food and residential (chlorpyrifos target MOE= 10 with FQPA SF reduced to 1X) exposure.
[3] **FOOD:** $MOE_{food} = POD_{food}$ (µg/kg/day) (from Table 4.2.2.1.2) ÷ Food Exposure (µg/kg/day) (from Table 5.5).
$ARI_{food} = [(MOE_{food})/(MOE_{target})]$.
[4] **RESIDENTIAL:** $MOE_{residential} = 1 \div (1/\text{Dermal MOE})$, (see Table 6.3).
[5] **WATER (ARI approach):** $ARI_{water} = 1/[(1/ARI_{agg}) - ((1/ARI_{food}) + (1/ARI_{residential}))]$; Where $ARI_{agg}=1$ (Note:HED is generally concerned when calculated ARIs are less than 1).
$MOE_{water} = ARI_{water} \times MOE_{target}$.
WATER (Reciprocal MOE approach): $MOE_{water} = 1/[(1/MOE_{agg}) - ((1/MOE_{food}) + (1/MOE_{residential}))]$; Where MOE_{agg} =Target MOE.
[6] **DWLOC:** DWLOC ppb= PoD_{water} (ppb; from Table 4.2.2.1.2) $/MOE_{water}$

8.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Spray drift is a potential source of exposure to those nearby pesticide applications. This is particularly the case with aerial application, but, to a lesser extent, spray drift can also be a potential source of exposure from the ground application methods (e.g., groundboom and airblast) employed for chlorpyrifos. Sprays that are released and do not deposit in the application area end up off-target and can lead to exposures to those it may directly contact. They can also deposit on surfaces where contact with residues can eventually lead to indirect exposures (*e.g.*, children playing on lawns where residues have deposited next to treated fields). The potential risk estimates from these residues can be calculated using drift modeling coupled with methods employed for residential risk assessments for turf products.

In the 2011 occupational and residential exposure assessment, the potential risks to bystanders from spray drift and exposure from volatilization were identified as possible concerns. Spray drift is the movement of aerosols and volatile components away from the treated area during the application process. The potential risks from spray drift and the impact of potential risk reduction measures were assessed in July 2012 (J. Dawson *et al.,* D399483, 07/13/2012). This evaluation supplemented the 2011 assessment where limited monitoring data indicated risks to bystanders. To increase protection for children and other bystanders, chlorpyrifos technical registrants voluntarily agreed to lower application rates and to other spray drift mitigation measures (R. Keigwin, 2012). As of December 2012, spray drift mitigation measures and use restrictions appear on all chlorpyrifos agricultural product labels (including a restriction to nozzles and pressures that produce a medium to coarse droplet size). Spray drift risk estimates have been re-presented here for children and adults using endpoints based on 10% RBC AChE inhibition and PODs derived with a PBPK model; and assuming both that the FQPA SF has been retained at 10X and has been reduced to 1X.

If the FQPA SF is retained at 10X, there were no dermal risk estimates of concern from indirect spray drift exposure to chlorpyrifos at the field edge for adults (females 13-49 years old) (MOEs $\geq$ 100). For children 1 to < 2 years old, there were no combined (dermal + incidental oral) risk estimates of concern from indirect spray drift exposure to chlorpyrifos (MOEs $\geq$ 40), except for two scenarios. For aerial applications at 2.3 lb ai/A, a distance of 10 feet results in MOEs not of concern. However, the 2012 agreement between EPA and the technical registrants (R. Keigwin, 2012) indicates that buffer distances of 80 feet for coarse or very coarse droplets and 100 feet for medium droplets for aerial applications are required for application rates $\geq$ 2.3 lb ai/A. For airblast applications > 3.76 lb ai/A, distances of 10 to 25 feet results in MOEs not of concern (LOC = 40). However, the 2012 agreement between EPA and the technical registrants (R. Keigwin, 2012) indicates that buffer distances of $\geq$ 25 feet and medium to coarse drops are required for airblast applications at rates >3.76 lb ai/A. Therefore, there are no risk estimates of concern incorporating the agreed-upon buffer distances and droplet sizes/nozzle types by the EPA and the technical registrants in 2012.

If the FQPA SF is reduced to 1X, there were no dermal risk estimates of concern from indirect spray drift exposure to chlorpyrifos at the field edge for adults (females 13-49 years old) (MOEs $\geq$ 10) and no combined (dermal + incidental oral) risks for children 1 to < 2 years old at the field edge (MOEs $\geq$ 4).

<table>
<tr><th colspan="8">Table 8.1. Summary of Spray Drift Distances from the Field Edge for Chlorpyrifos MOEs to be > LOCs with 10X FQPA SF Retained.[1]</th></tr>
<tr><th rowspan="3">Application Rate (lb ai/A)</th><th rowspan="3">Nozzle Droplet Type/ Canopy Density</th><th colspan="3">Adult Buffer Summary</th><th colspan="3">Children 1 to < 2 Years Old Buffer Summary (Dermal + Incidental Oral)</th></tr>
<tr><th colspan="3">Distance (Feet) from the Field Edge Needed For MOE > LOC of 100</th><th colspan="3">Distance (Feet) from the Field Edge Needed for MOE > LOC of 40</th></tr>
<tr><th>Aerial[2]</th><th>Groundboom[2]</th><th>Airblast</th><th>Aerial[2]</th><th>Groundboom[2]</th><th>Airblast</th></tr>
<tr><td>6.0</td><td rowspan="9">Medium/ Coarse for Aerial and Ground-boom
Sparse for Airblast</td><td rowspan="5">NA</td><td>NA</td><td rowspan="9">0</td><td rowspan="5">NA</td><td>NA</td><td>25</td></tr>
<tr><td>4.3</td><td rowspan="8">0</td><td rowspan="8">0</td><td>10</td></tr>
<tr><td>4.0</td><td>10</td></tr>
<tr><td>3.76</td><td>10</td></tr>
<tr><td>3.0</td><td rowspan="5">0</td></tr>
<tr><td>2.3</td><td rowspan="4">0</td><td>10</td></tr>
<tr><td>2.0</td><td rowspan="3">0</td></tr>
<tr><td>1.5</td></tr>
<tr><td>1.0</td></tr>
</table>

1 Per December 2012 spray drift mitigation memorandum, aerial application of greater than 2 lb ai/A is only permitted for Asian Citrus Psylla control, up to 2.3 lb ai/A.
2 NA = not allowable.

<table>
<tr><th colspan="8">Table 8.2. Summary of Spray Drift Distances from the Field Edge for Chlorpyrifos MOEs to be > LOCs with FQPA SF Reduced to 1X.[1]</th></tr>
<tr><th rowspan="3">Application Rate (lb ai/A)</th><th rowspan="3">Nozzle Droplet Type/ Canopy Density</th><th colspan="3">Adult Buffer Summary</th><th colspan="3">Children 1 to < 2 Years Old Buffer Summary (Dermal + Incidental Oral)</th></tr>
<tr><th colspan="3">Distance (Feet) from Field Edge Needed for MOE > LOC of 10</th><th colspan="3">Distance (Feet) From Field Edge Needed for MOE > LOC of 4</th></tr>
<tr><th>Aerial[2]</th><th>Groundboom[2]</th><th>Airblast</th><th>Aerial[2]</th><th>Groundboom[2]</th><th>Airblast</th></tr>
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Sparse for Airblast</td><td rowspan="5">NA</td><td>NA</td><td rowspan="9">0</td><td rowspan="5">NA</td><td>NA</td><td rowspan="9">0</td></tr>
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</table>

1 Per December 2012 spray drift mitigation memorandum, aerial application of greater than 2 lb ai/A is only permitted for Asian Citrus Psylla control, up to 2.3 lb ai/A.
2 NA = not allowable.

9.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

In January 2013, a preliminary assessment of the potential risks from volatilization was conducted.[18] The assessment evaluated the potential risks to bystanders, or those who live and/or work in proximity to treated fields, from inhalation exposure to vapor phase chlorpyrifos and chlorpyrifos-oxon emitted from fields following application of chlorpyrifos. The results of the January 2013 assessment indicated that offsite concentrations of chlorpyrifos and

[18] R. Bohaty, C. Peck, A. Lowit, W. Britton, N. Mallampalli, A. Grube. Chlorpyrifos: Preliminary Evaluation of the Potential Risks from Volatilization. 1/31/13. U.S. EPA Office of Chemical Safety and Pollution Prevention. D399484, D400781.

chlorpyrifos-oxon may exceed the target concentration based on the toxicological endpoints used at that time.[19]

One significant area of uncertainty described in the preliminary assessment was the use of the aerosolized chlorpyrifos inhalation toxicity study -- as opposed to chlorpyrifos vapor -- for evaluation of lung AChE resulting from field volatilization. Because field volatilization is the production and release of vapor into the atmosphere after sprays have settled on treated soils and plant canopies, the vapor, rather than the aerosol, is the relevant form for evaluation of bystander volatilization exposures. However, EPA lacked chlorpyrifos vapor toxicity data at the time it conducted the preliminary volatilization assessment in 2013. Following the release of the preliminary volatilization assessment, DAS conducted, high quality nose-only vapor phase inhalation toxicity studies for both chlorpyrifos and chlorpyrifos-oxon[20] to address this uncertainty.

In June 2014, a reevaluation of the 2013 preliminary volatilization assessment was conducted to present the results of the vapor studies and their impact. In the vapor studies, female rats were administered a saturated vapor, meaning that the test subjects received the highest possible concentration of chlorpyrifos or chlorpyrifos-oxon which can saturate the air in a closed system. At these saturated concentrations, no statistically significant inhibition of AChE activity was measured in RBC, plasma, lung, or brain at any time after the six-hour exposure period in either study. Under actual field conditions, indications are that exposures to vapor phase chlorpyrifos and its oxon would be much lower as discussed in the January 2013 preliminary volatilization assessment.

Because these new studies demonstrated that no toxicity occurred even at the saturation concentration, which is the highest physically achievable concentration, then there are no anticipated risks of concern from exposure to the volatilization of either chlorpyrifos or chlorpyrifos oxon. In June 2014, the January 2013 volatilization assessment was revised to reflect these findings.[21]

10.0 Cumulative Exposure/Risk Characterization

OPs, such as chlorpyrifos, share the ability to inhibit AChE through phosphorylation of the serine residue on the enzyme leading to accumulation of acetylcholine and ultimately cholinergic

[19]EPA MRID# 48139303**:**Acute Inhalation Exposure of Adult Crl:CD(SD) Rates to Particulate Chlorpyrifos Aerosols: Kinetics of Concentration-Dependent Cholinesterase (ACHE) Inhibition in Red Blood Cells, Plasma, Brain and Lung; Authors: J. A. Hotchkiss, S. M. Krieger, K. A. Brzak, and D. L. Rick; Sponsor: Dow AgroSciences LLC.

[20]W. Irwin. Review of Nose-Only Inhalation of Chlorpyrifos Vapor: Limited Toxicokinetics and Determination of Time-Dependent Effects on Plasma, Red Blood Cell, Brain and Lung Cholinesterase Activity in Femal CD(SD): Crl Rats. U.S. EPA Office of Chemical Safety and Pollution Prevention. 6/25/14. D411959. TXR# 0056694. EPA MRID# 49119501.

W. Irwin. Review of Nose-Only Inhalation of Chlorpyrifos-Oxon Vapor: Limited Toxicokinetics and Determination of Time-Dependent Effects on Plasma, Red Blood Cell, Brain, and Lung Cholinesterase Activity in Female CD(SD):Crl Rats. U.S. EPA Office of Chemical Safety and Pollution Prevention. 6/25/14. D415447. TXR# 0056869. EPA MRID# 49210101.

[21] W. Britton. W. Irwin. J. Dawson. A. Lowit. E. Mendez. Chlorpyrifos:Reevaluation of the Potential Risks from Volatilization in Consideration of Chlorpyrifos Parent and Oxon Vapor Inhalation Toxicity Studies. 6/25/2014. U.S. EPA Office of Chemical Safety and Pollution Prevention. D417105.

neurotoxicity. This shared MOA/AOP is the basis for the OP common mechanism grouping per OPP's *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999). The 2002 and 2006 CRAs used brain AChE inhibition in female rats as the source of dose response data for the relative potency factors and PODs for each OP, including chlorpyrifos. Prior to the completion of Registration Review, OPP will update the OP CRA on AChE inhibition to incorporate new toxicity and exposure information available since 2006.

OPP has conducted the chlorpyrifos human health risk assessment both with retention of the 10X FQPA SF and without retention of the 10X FQPA SF (*i.e.*, FQPA SF reduced to 1X) due to uncertainties associated with neurodevelopmental effects in children and exposure to OPs. There is a lack of an established MOA/AOP for the neurodevelopment outcomes which precludes the Agency from formally establishing a common mechanism group per the *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999) based on that outcome. Moreover, the lack of a recognized MOA/AOP and other uncertainties with exposure assessment in the epidemiology studies prevent the Agency from establishing a causal relationship between OP exposure and neurodevelopmental outcomes. As part of an international effort, the ORD has been developing a battery of NAMs for evaluating developmental neurotoxicity. Information from these NAMs may be used in the future as part of the weight of evidence evaluation of neurodevelopmental toxicity potential for OPs. These NAMs will be presented, using the OPs as a case study, to the Federal Insecticide, Fungicide, and Rodenticide (FIFRA) Scientific Advisory Panel (SAP) in September 2020. The Agency will also continue to evaluate the epidemiology studies associated with neurodevelopmental outcomes and OP exposure prior to the release of the revised DRA. During this period, the Agency will determine whether or not it is appropriate to apply the guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* for the neurodevelopment outcomes.

11.0 Occupational Exposure/Risk Characterization

11.1 Occupational Handler Exposure and Risk Estimates

The term handlers is used to describe those individuals who are involved in the pesticide application process. There are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of a chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event. Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from chlorpyrifos use. For purpose of occupational handler assessment, the parent chlorpyrifos is the relevant compound.

Current labels generally require that handlers use normal work clothing (i.e., long sleeved shirt and pants, shoes and socks) and coveralls, chemical resistant gloves, and dust/mist respirators. Also, some products are marketed in engineering controls such as water-soluble packets. In order to determine what level of personal protection is required to alleviate risk concerns and to ascertain if label modifications are needed, steady state exposure and risk estimates were updated for occupational handlers of chlorpyrifos for a variety of scenarios at differing levels of personal protection including engineering controls.

The previously assessed occupational handler assessments have been updated to incorporate the approach applied for PBPK-derivation of PODs for adults based on 10% RBC AChE inhibition. The results have been summarized assuming both that the database uncertainty factor has been retained at 10X and has been reduced to 1X. If the database uncertainty factor is retained, the total LOC for occupational exposure assessment is 100X for adults (represented by females 13-49). If the database uncertainty SF is reduced to 1X, the total LOC for occupational exposure assessment is 10X for adults (represented by females 13-49). The occupational handler scenarios, exposure assumptions and inputs have not changed since the previous assessment[22].

Combining Exposures/Risk Estimates:

Dermal and inhalation risk estimates were combined in this assessment, since the toxicological endpoint, RBC AChE inhibition, is the same for these exposure routes.

Summary of Occupational Handler Non-Cancer Exposures and Risk Estimates

Detailed result tables are provided in Appendix 10.

In this assessment for the non-seed treatment scenarios, a total of 288 occupational handler exposure scenarios were assessed. Using the updated PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the database uncertainty 10X SF has been retained (LOC = 100), 119 scenarios are of concern with label-specified personal protective equipment (PPE; baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs < 100). Risks of concern for 45 additional exposure scenarios could potentially be mitigated if engineering controls are used. If the database uncertainty 10X SF is reduced to 1X (LOC = 10), 19 scenarios are of concern with label-specified PPE (baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs < 10). Risks of concern for 15 additional scenarios could potentially be mitigated if engineering controls are used.

For the seed treatment scenarios, a total of 93 scenarios were assessed (40 short-term primary handler scenarios + 40 intermediate-term primary handler scenarios + 13 short- and intermediate-term planting scenarios). Assuming the 10X database uncertainty factor has been retained (LOC = 100), 12 short-term exposure and 10 intermediate-term scenarios are of concern with label-specified PPE (baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs < 100) for primary handlers; there are no short- or intermediate scenarios of concern for seed planters. Assuming the 10X database uncertainty factor has been reduced to 1X (LOC = 10), there are no short- or intermediate-term risk estimates of concern with label-specified PPE (baseline attire, chemical resistant gloves, coveralls, and a PF10 respirator) (MOEs > 10) for primary handlers or seed planters.

[22] Some occupational handler exposure inputs have changed since the previous ORE assessments were completed in 2011 (W. Britton, D388165, 06/27/2011), 2014 (W. Britton, D424484, 12/29/2014), and 2016 (W. Britton, D436317, 11/03/2016) (e.g., amount of seed treated per day, seed planted per day). The changes to the inputs are not expected to result in significant changes to the risk estimates and have not been updated at this time.

11.2 Occupational Post-Application Exposure and Risk Estimates

11.2.1 Dermal Post-Application Exposure and Risk Estimates

Detailed result tables are provided in Appendix 11.

A series of assumptions and exposure factors served as the basis for completing the occupational post-application risk assessments; these assumptions and exposure factors remain unchanged from the previous assessment (W. Britton, D424484, 12/29/2014).

The 2011 and 2014 occupational and residential exposure assessments incorporated 7 Chemical-specific DFR studies. These studies used 5 different formulations and were conducted on 12 different crops. Specifically, the DFR studies examined the use of 1) emulsifiable concentrate formulations on sugarbeets, pecans, citrus, sweet corn, cotton, and turf; 2) wettable powder formulations on almonds, apples, pecans, cauliflower, tomato and turf; 3) granular formulations on sweet corn and turf; 4) a total release aerosol formulation on ornamentals; and 5) a microencapsulated liquid formulation on ornamentals. The submitted studies were reviewed by HED. Despite limitations, HED recommended the use of all or some of the data in the studies to assess post-application risks to chlorpyrifos except for the tomato DFR data. Summaries for all DFR studies can be referenced in Appendix I of D424484 (W. Britton, 12/29/2014).

The current assessment uses the same DFR data and crop pairings as the previous occupational and residential exposure assessments. For example, DFR data for an individual crop was applied to that specific crop, as well as to crops in the same crop grouping (e.g., cauliflower data was used for cauliflower and all other cole crops). For other crops in which no crop-specific or crop group-specific data are available, the DFR data for the crop deemed the closest match were used as surrogates to calculate potential exposure (e.g., cauliflower data were also used for strawberries, cranberries, and leafy vegetables). Additionally, whenever possible, a label use was assessed using DFR data for the same formulation type. A full description of the criteria for selection of DFR data for assessment of post-application exposures to individual crops/crop groupings can be referenced in Section 2.4.3 of D388165 (W. Britton, 06/27/2011).

<u>Summary of Occupational Post-Application Dermal Exposure and Risk Estimates</u>

Current labels require a Restricted Entry Interval (REI) of 24 hours from most crops and activities, but in some cases such as tree fruit, REIs are up to 5 days after application. Using the updated PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the UF_{DB} of 10X has been retained, the majority of the post-applications scenarios are not of concern 1 day after application (REI = 24 hours). However, for some activities such as irrigation, hand harvesting, scouting, and thinning result in risks of concern up to as many as 10 days following application for the non-microencapsulated formulations and > 35 days for the microencapsulated formulation.

Using the updated PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the UF_{DB} has been reduced to 1X, the majority of the post-application risk estimates are not of concern 1 day after application (REI = 24 hours).

Table 11.2.1. Chlorpyrifos Occupational Post-application Exposure and Risk Summary.

Crop Group	Crop	App. Rate (lbs ai/A)	DFR Data Source	DFR Study Location	Estimated REI Range (days) (Dermal LOC = 10)	Estimated REI Range (days) (Dermal LOC = 100)
Berry: Low	Strawberry	1.0	MRID 42974501 (cauliflower WP)	AZ	0	0 - 4
	Cranberry	1.5			0	0 - 5
Field and Row Crops: Low to Medium	Clover (Grown for Seed)	1.9	MRID 44748102 (sugar beet EC)	MN	1	1
				OR	0	1
	Perennial Grass Seed Crops	1.0	MRID 44748102 (sugar beet EC)	MN	0	1
				OR	0	1
	Alfalfa	1.0	MRID 44748102 (cotton EC)	TX	0 – 1	1
	Cotton[1]	1.0	MRID 44748102 (cotton EC)	CA	0	0
				MS	0	0 – 1
				TX	0	0 – 1
	Peppermint/ Spearmint	2.0	MRID 44748102 (sugar beet EC)	MN	0 - 1	1
				OR	0	0 – 1
	Wheat	1.0	MRID 44748102 (sugar beet EC)	CA	0	0 - 1
				MN	0	0 - 1
	Soybean	1.0	MRID 44748102 (cotton EC)	MS	0	0 – 1
	Sugar Beet	1.0	MRID 44748102 (sugar beet EC)	CA	0	0 – 1
				MN	0	0 – 1
				OR	0	0 – 1
Field and Row Crops: Tall	Corn: Sweet; Corn: Field, Including Grown for Seed	1.5	MRID 44748102 (sweet corn EC)	IL	0 – 1	0 – 3
				MN	0 – 1	0 – 3
				OR	0 – 1	0 – 2
	Corn: Sweet; Corn: Field, Including Grown for Seed	1.0	MRID 44748102 (sweet corn EC)	IL	0 – 1	0 – 2
				MN	0 – 1	0 – 2
				OR	0 – 1	0 – 2
	Sorghum	1.0	MRID 44748102 (sweet corn EC)	IL	0	0 – 1
				MN	0	0 – 1
	Sunflowers	1.5	MRID 44748102 (sweet corn EC)	IL	0	1
				MN	0	1
Tree Fruit: Deciduous	Apples, Cherries, Peaches, Pears, Plums, Prunes, Nectarines	2.0	MRID 44748101 (apple WP)	CA	0	1
				WA	0	1 – 2
				NY	0	1 – 2

Table 11.2.1. Chlorpyrifos Occupational Post-application Exposure and Risk Summary.						
Crop Group	**Crop**	**App. Rate (lbs ai/A)**	**DFR Data Source**	**DFR Study Location**	**Estimated REI Range (days) (Dermal LOC = 10)**	**Estimated REI Range (days) (Dermal LOC = 100)**
	(Dormant and Delayed Dormant)					
	Nectarine & Peaches (Dormant and Delayed Dormant)	3.0	MRID 44748101 (apple WP)	CA	0	1
				NY	0	2 - 3
	Cherries (Sour)	4.0	MRID 44748101 (apple WP)	CA	0 – 1	1 – 5
				WA	0 – 2	2 – 6
				NY	0 – 3	2 – 6
Tree Fruit: Evergreen	Conifer Trees and Christmas Tree Plantations	1.0	MRID 43062701 (citrus EC)	CA (scouting, harvesting seed cone, irrigation)	0	0 – 1
			MRID 44839601 (turf EC)	MS (harvesting/ seedling production)	0	0
	Citrus	6.0 (CA and AZ)	MRID 43062701 (citrus EC)	CA	0	0 – 2
		4.0	MRID 43062701 (citrus EC)	CA	0	0
Forestry	Hybrid Cottonwood/ Poplar Plantations (Dormant and Delayed Dormant)	2.0	MRID 44748101 (apple WP)	WA	0 – 1	2 – 4
				NY	0 – 1	2 – 4
	Deciduous Trees (Plantations and Seed Orchards)	1.0	MRID 44748101 (apple WP)	CA	0	0 – 1
				WA	0	0 – 1
				NY	0	0 – 1
Tree Nuts[2]	Almonds	2.0	MRID 44748101 (almond WP)	CA (arid)	0	1
	Almonds (Dormant and Delayed Dormant)	4.0	MRID 44748101 (almond WP)	CA (arid)	0	1 – 3
	Filberts, Pecans, Walnuts	2.0	MRID 44748101 (pecan EC)	GA	0	0
				LA	0	0
				TX	0	0

Table 11.2.1. Chlorpyrifos Occupational Post-application Exposure and Risk Summary.						
Crop Group	**Crop**	**App. Rate (lbs ai/A)**	**DFR Data Source**	**DFR Study Location**	**Estimated REI Range (days) (Dermal LOC = 10)**	**Estimated REI Range (days) (Dermal LOC = 100)**
	Filberts & Walnuts (Dormant and Delayed Dormant)[3]	2.0	MRID 44748101 (pecan EC)	GA	0	0
Ornamentals/ Nurseries (Outdoor Only)	Deciduous Trees in Nurseries and Orchards Except Apples (Dormant and Delayed Dormant) Non-bearing Apple Trees	1.0	MRID 44748101 (apple WP)	CA	0	0
				WA	0	1
				NY	0	0
Ornamentals/ Nurseries (Outdoor Only)	Non-bearing Fruit and Nut Trees (Almonds, Citrus, Filbert, Cherry, Pear, Plum/Prune)	4.0	MRID 43062701 (citrus EC)	CA	0	0
	Non-bearing Fruit Trees (Peach, Nectarine)	3.0	MRID 44748101 (apple WP)	CA	0	1
				NY	0	2
	Non-bearing Fruit Trees (Apple)	2.0	MRID 44748101 (apple WP)	CA	0	1
				NY	0	1
	Conifers in Nurseries	1.0	MRID 43062701 (citrus EC)	CA	0	0
Field and Row Crops: Low to Medium (Outdoor Only)	Ornamentals	2.0	MRID 44748102 (sugar beet EC)	CA	0 – 1	1 – 5
				MN	0 – 1	1 – 3
				OR	0 – 1	1 – 2
Vegetable: Root and Tuber	Carrot	0.94	MRID 44748102 (sugar beet EC)	CA	0	0 – 1
				MN	0 – 1	0 – 1
	Radish	1.0	MRID 44748102 (sugar beet EC)	MN	0 – 1	0 – 1
Vegetable: Fruiting	Pepper	1.0	MRID 44748102 (cotton EC)	CA	0	0 – 2
				MS	0 – 1	1
				TX	0 – 1	1
Vegetable: Head and Stem Brassica	Broccoli, Brussel Sprouts, Cabbage, and Cauliflower	1.0	MRID 42974501 (cauliflower WP)	AZ	0	0 – 10
Vegetable: Leafy	Bok Choy, Collards, Kale, Kohlrabi	1.0	MRID 42974501 (cauliflower WP)	AZ	0	0 – 6
	Asparagus	1.0	MRID 44748102 (sugar beet EC)	CA	0	0 – 1

Table 11.2.1. Chlorpyrifos Occupational Post-application Exposure and Risk Summary.						
Crop Group	**Crop**	**App. Rate (lbs ai/A)**	**DFR Data Source**	**DFR Study Location**	**Estimated REI Range (days) (Dermal LOC = 10)**	**Estimated REI Range (days) (Dermal LOC = 100)**
Stalk and Stem: Vegetable				MN	0 – 1	1
				OR	0	0 – 1
	Non-bearing Pineapple	2.0	MRID 44748102 (cotton EC)	MS	0	1
Vine/ Trellis	Grapes (Dormant and Delayed Dormant) Grapes (Post-harvest and Prior to Budbreak)	2.0	MRID 43062701 (citrus EC)	CA	0	1
Turf	Turf for Sod and Seed	3.76	MRID 44829601 (turf EC and WP)	CA	0	1
				IN	0	1
				MS	0	1
	Turf for Golf Course	1.0	MRID 44829601 (turf EC and WP)	CA	0	0
				IN	0	0
				MS	0	0
Granular Applications						
Field and Row Crops: Low to Medium	Soybeans	1.0	MRID 44748102 (sweet corn G)	IL	0	0
	Sugar Beet	2.0	MRID 44748102 (sweet corn G)	IL	0	0
				OR	0	0 – 1
	Peanuts	4.0	MRID 44748102 (sweet corn G)	IL	0	0 – 1
Field and Row Crops: Tall	Corn, Sweet; Corn, Field; Corn, Grown for Seed	2.0	MRID 44748102 (sweet corn G)	IL	0	0 – 1
				OR	0 – 1	0 – 1
Nursery	Woody Ornamentals (In Container and Field Grown) – Preharvest	6.0 (Note: all other ornamental application rates are either 1.1 or 1.0 lb ai/A)	MRID 44748102 (sweet corn G)	IL	0	0
				OR	0	0
Turf	Turf for Sod or Seed	1.0	MRID 44829601 (turf G and fertilizer)	CA	0	0
	Golf Course				0	0
Microencapsulated Formulation Application						

Table 11.2.1. Chlorpyrifos Occupational Post-application Exposure and Risk Summary.						
Crop Group	**Crop**	**App. Rate (lbs ai/A)**	**DFR Data Source**	**DFR Study Location**	**Estimated REI Range (days) (Dermal LOC = 10)**	**Estimated REI Range (days) (Dermal LOC = 100)**
Nursery (Microencap. Formulations)	Ornamentals – Nurseries and Greenhouses	1.4	MRID 46722702 (smooth ornamentals ME)	Greenhouse	0 - 3	1 to > 35
Greenhouse						
Greenhouse (Total Release Fogger and. Liquid Concentrate Formulations)	Ornamentals – *Liquid Concentrates*	2	MRID 46722701 (hairy ornamentals ME)	Greenhouse	0 – 1	1 – 5
	Commercial Ornamentals, Greenhouse Production: Bedding Plants, Cut Flowers, Flowering Hanging Baskets, Potted Flowers, Ornamentals, Trees and Shrubs – *Total Release Foggers*	0.29	MRID 46722701 (hairy ornamentals ME)	Greenhouse	0	0 – 2

1. Mechanical harvesting (tramper) activities are not anticipated to result in significant chlorpyrifos exposures due to the 14-day pre-harvest interval (PHI).
2. Exposure during nut sweeping and windrowing results from contact with soil, for which transfer coefficients are currently unavailable. Assessment options include requesting exposure data or a qualitative comparison with a post- application exposure scenario assumed to result in higher exposure. Note that dislodgeable soil residue would be needed for an exposure assessment, as this would be the media contacted by worker's performing this activity. A study monitoring such exposure is available (Exposure of Workers During Reentry into Pecan Groves Treated with Super-Tim 80WP, Griffin Corporation, 1994; EPA MRID 43557401), however has yet to be evaluated for derivation of transfer coefficients.
2. Transfer coefficients for dormant pruning are unavailable. Assessment options include requesting exposure data or a qualitative comparison with a post-application exposure scenario assumed to result in higher exposure. Note that dislodgeable branch or bark residue would be needed for an exposure assessment, as this would be the surface contacted by workers performing this activity.

11.2.2 Dermal Post-Application Exposure and Risk Estimates: Chlorpyrifos Oxon

Chlorpyrifos is activated by desulfuration, reacting in bioactivation to the more toxic and potent AChE inhibitor, chlorpyrifos oxon. The oxon is highly unstable due to rapid deactivation through hydrolytic cleavage by a process called dearylation which releases TCP. Workers reentering an indoor environment (i.e., greenhouses) previously treated with chlorpyrifos could potentially be exposed to the oxon as chlorpyrifos degrades. Available exposure data indicate chlorpyrifos oxon may form in indoor environments.[23] Toxicity adjustment factors (TAFs) were used to estimate the potency of chlorpyrifos oxon relative to chlorpyrifos. HED determined the oxon to be between 11.9 (acute) and 18 (chronic) times more toxic than the parent.

Dermal exposure to the oxon on foliar surfaces from reentry into an outdoor environment (e.g., field crops and orchards) previously treated with chlorpyrifos is not anticipated and, therefore, has not been assessed. No occupational exposure studies (handler, post-application, or DFR) were identified that quantified the levels of oxon present in the environment. However, a search of open literature for the 2011 assessment resulted in 4 plant metabolism studies which measured surface residues. Three plant metabolism studies[24] measured leaf surface residues of the oxon in outdoor environments that were either well below the parent, not detectable, or detected at a level just above the level of detection (LOD). The potential for exposure to the oxon is further minimized due to rapid deactivation of the oxon to TCP. Further, the dietary exposure risk assessment[25] conducted in support of registration review concludes the following, "all residues in food are assumed to be parent chlorpyrifos since the chlorpyrifos oxon is not typically found in foods in monitoring data or crop field trials."

The 4th plant metabolism study, a tomato and green bean metabolism study conducted in a greenhouse, was less definitive than the other three plant metabolism studies regarding oxon presence; therefore, there is concern that the formation of the oxon may be greater and its deactivation to TCP slower in greenhouses when compared to the outdoor environment. The study results indicate that oxon residue is from 9 to 14X less than the parent from fruit analyzed on the day of application in flat and asymmetric roof greenhouses. The proportion of oxon to parent is less for all days which measurable levels were observed (all but 8 and 15 days after application). The oxon was detected until day 5 with levels between 5 and 6X below that of the parent. It should be noted that residues of chlorpyrifos and oxon were measured from analysis of whole fruit samples. HED typically assesses occupational post-application exposure and risk based upon the potential for transfer from surface residues. The whole fruit samples, which include surface residues, as well as residues which may have been contained within the fruit

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[23] J.L. Martinez Vidal, et al. 1998. Diminution of Chlorpyrifos and Chlorpyrifos Oxon in Tomatoes and Green Beans Grown in Greenhouses. J. of Agric. and Food Chem. 46 (4), 1440–1444.

[24] Iwata, Y. et al. 1983. Chlorpyrifos Applied to California Citrus: Residue Levels on Foliage and On and In Fruit. J. Agric. Food Chem. 31(3), 603-610.

H. Jin and G.R. Webster. 1997. Persistence, Penetration, and Surface Availability of Chlorpyrifos, Its Oxon, and 3,5,6-Trichloro-2-pyridinol in Elm Bark. 45(12), 4871-4876.

R. Putnam, et al. 2003. The Persistence and Degradation of Chlorthalonil and Chlorpyrifos in a Cranberry Bog. J. Agric. Food Chem. 51(1), 170-176.

[25] D. Drew. Chlorpyrifos: Acute and Steady State Dietary (Food Only) Exposure Analysis to Support Registration Review. 11/18/2014. U.S. EPA Office of Chemical Safety and Pollution Prevention. D424486.

sample, may overestimate the amount of oxon on the fruit surface. Regardless, the 2011 occupational and residential exposure assessment recommended additional data to measure the chlorpyrifos and oxon residues on leaf surfaces following treatment with a liquid formulation in greenhouses in order to address these uncertainties and more accurately address the risk potential for exposure from occupational reentry into greenhouses treated with chlorpyrifos. To date, no data have been submitted to address these uncertainties. As a result, HED has assessed occupational dermal post-application exposures in greenhouses using conservative assumptions of oxon formation.

In order to account for the formation of and potential increased toxicity from exposure to chlorpyrifos oxon, a total toxic residue approach was applied which combines chlorpyrifos and chlorpyrifos oxon (expressed as toxicity equivalents). The total toxic residue approach[26] estimates the chlorpyrifos oxon equivalent residues by 1) assuming a specific fraction of the measured chlorpyrifos dislodgeable foliar residues are available as the oxon and 2) factoring in the relative potency of chlorpyrifos oxon with use of a TAF. It was conservatively assumed that 5% (0.05) of the total chlorpyrifos present as DFR in greenhouses is available for worker contact during post-application activities. This assumption is based on a review of available TTR and DFR data for other OPs where both the parent and metabolite were measured in residue samples. Five percent was found to be the high-end value for the percent of parent that metabolized during the course of the residue studies. The chronic TAF (which is appropriate for steady state assessment) of 18 was derived from BMD analysis of inhibition of RBC AChE in adult female rats (adult male rats not examined) observed in the repeated phase of the CCA study. Once predicted, these total toxic (dislodgeable foliar) residues are used to estimate exposures from post-application activities in greenhouse and risks are estimated with used of the steady state POD for occupational exposures, 3.63 mg/kg/day.

Summary of Occupational Post-Application Dermal Exposure and Risk Estimates with Use of Total Toxic Residue Approach

Due to uncertainty regarding the formation of chlorpyrifos oxon in greenhouses, HED also estimated risks for reentry into treated greenhouses (all 4 formulations) for the parent chlorpyrifos plus chlorpyrifos oxon using a total toxic residue approach. When the total toxic residue approach is used and with the updated PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming a 10X UF_{DB} has been retained, MOEs are not of concern 0 to 6 days after treatment for non-microencapsulated formulations. For the microencapsulated formulation, MOEs are not of concern 3 to > 35 days after treatment (the completion of the monitoring period), depending on the exposure activity considered.

When the total toxic residue approach is used and with the updated PBPK-derived steady state PODs based on 10% RBC AChE inhibition and assuming the 10X UF_{DB} has been reduced to 1X, there are no risk estimates of concern with the current labeled REI (24 hours), except for the microencapsulated formulation. For the microencapsulated formulation, MOEs are of concern 0 to > 35 days after treatment (the completion of the monitoring period), depending on the exposure activity considered.

[26] Total DFR ($\mu g/cm^2$) = [Chlorpyrifos DFR ($\mu g/cm^2$) * TAF] + [Chlorpyrifos DFR ($\mu g/cm^2$)]

Table 11.2.2.1. All Formulations - Summary of Post-Application Risk Assessment for Total Toxic Residue (Chlorpyrifos + Chlorpyrifos Oxon) Using Chlorpyrifos -Specific DFR Data.						
Crop Group	**Crop**	**App Rates (lbs. ai/ acre)**	**DFR Data Source**	**DFR Study Location**	**Estimated REI Range (days) (Dermal LOC = 10)**	**Estimated REI Range (days) (Dermal LOC = 100)**
Nursery	Ornamentals – Nurseries and Greenhouses	0.0070 lb ai/gal 1.4 lb ai/A	MRID 46722702 (smooth ornamentals ME)	Greenhouse	0 to >35	3 to > 35
Field and Row Crops – Low to Medium	Ornamentals – Nurseries and Greenhouses	2.0	MRID 44748102 (sugar beet EC)	CA	0 – 1	1 – 6
				OR	0 – 1	1 – 2
				MN	0 – 1	1 – 5
Nursery	Ornamentals - Greenhouse	0.29	DFR: MRID 46722701 (hairy ornamentals -aerosol)	Greenhouse	0 – 1	0 – 5

Restricted Entry Interval

Chlorpyrifos is classified as Toxicity Category II via the dermal route and Toxicity Category IV for skin irritation potential. It is not a skin sensitizer. There were some risk estimates of concern related to contacting chlorpyrifos treated foliage both outdoors and in greenhouses; therefore, HED is recommending that the REI be revised on the label to address those concerns.

Table 11.2.2.2. Acute Toxicity Profile: Chlorpyrifos.				
Guideline No.	**Study Type**	**MRID(s)**	**Results**	**Toxicity Category**
870.1100	Acute Oral (rat)	44209101	LD_{50} = 223 mg/kg (M & F)	II
870.1200	Acute Dermal (rabbit)	44209102	LD_{50} ≥ 5000 mg/kg (M & F)	IV
870.1300	Acute Inhalation (rat)	00146507	LC_{50} > 0.2 mg/L (M & F)	II[1,2]
870.2400	Primary Eye Irritation (rabbit)	44209103	Minimum to mild irritant	IV
870.2500	Primary Skin Irritation (rabbit)	44209104	Mild irritant	IV
870.2600	Dermal Sensitization (guinea pig)	44209105	Non-Sensitizing (Buehler Method)	N/A

[1] Study classified as Supplementary (TXR 0004633, S. Saunders, 08/26/1985)
[2] Study requirement waived and Toxicity Category II assigned (TXR 5001957, M. Hashim, 12/20/1997)

11.2.3 Inhalation Post-Application Exposure and Risk Estimates

There are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (https://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for chlorpyrifos.

In addition, the Agency is continuing to evaluate the available post-application inhalation exposure data generated by the Agricultural Reentry Task Force. Given these two efforts, the Agency will continue to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments.

The Worker Protection Standard for Agricultural Pesticides contains requirements for protecting workers from inhalation exposures during and after greenhouse applications through the use of ventilation requirements. [40 CFR 170.110, (3) (Restrictions associated with pesticide applications)].

A post-application inhalation exposure assessment is not required as exposure is expected to be negligible. Seed treatment assessments provide quantitative inhalation exposure assessments for seed treaters and secondary handlers (i.e., planters). It is expected that these exposure estimates would be protective of any potential low-level post-application inhalation exposure that could result from these types of applications. As described in Section 4, a quantitative occupational post-application inhalation risk assessment is not required for chlorpyrifos or chlorpyrifos oxon due to the lack of toxicity from the vapor phase of these chemicals, even at the saturation concentration.

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13.0 List of Appendices

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Appendix 1: Summary of OPP's ChE Policy and Use of BMD Modeling

OPP's ChE policy (USEPA, 2000[27]) describes the way ChE data are used in human health risk assessment. The following text provides a brief summary of that document to provide context to points of departure selected.

AChE inhibition can be inhibited in the central or peripheral nervous tissue. Measurements of AChE or cholinesterase (ChE) inhibition in peripheral tissues (e.g., liver, diaphragm, heart, lung etc) are rare. As such, experimental laboratory studies generally measure brain (central) and blood (plasma and red blood cell, RBC) ChE. Blood measures do not represent the target tissue, per se, but are instead used as surrogate measures for peripheral toxicity in studies with laboratory animals or for peripheral and/or central toxicity in humans. In addition, RBC measures represent AChE, whereas plasma measures are predominately BuChE. Thus, RBC AChE data may provide a better representation of the inhibition in target tissues. As part of the dose response assessment, evaluations of neurobehavior and clinical signs are performed to consider the dose response linkage between AChE inhibition and apical outcomes.

Refinements to OPP's use of ChE data have come in the implementation of BMD approaches in dose response assessment. Beginning with the OP CRA, OPP has increased its use of BMD modeling to derive PODs for AChE inhibiting compounds. Most often the decreasing exponential empirical model has been used.

OPP does not have a defined benchmark response (BMR) for OPs. However, the 10% level has been used in the majority of dose response analyses conducted to date. This 10% level represents a 10% reduction in AChE activity (i.e., inhibition) compared to background (i.e., controls). Specifically, the BMD_{10} is the estimated dose where ChE is inhibited by 10% compared to background. The $BMDL_{10}$ is the lower confidence bound on the BMD_{10}.

The use of the 10% BMR is derived from a combination of statistical and biological considerations. A power analysis was conducted by the Office of Research and Development (ORD) on over 100 brain AChE datasets across more than 25 OPs as part of the OP CRA (USEPA, 2002). This analysis demonstrated that 10% is a level that can be reliably measured in the majority of rat toxicity studies. In addition, the 10% level is generally at or near the limit of sensitivity for discerning a statistically significant decrease in ChE activity in the brain compartment and is a response level close to the background brain ChE level. With respect to biological considerations, a change in 10% brain AChE inhibition is protective for downstream cholinergic clinical signs and apical neurotoxic outcomes. With respect to RBC AChE inhibition, these data tend to be more variable than brain AChE data. OPP begins its BMD analyses using the 10% BMR for RBC AChE inhibition but BMRs up to 20% could be considered on a case by case basis as long as such PODs are protective for brain AChE inhibition, potential peripheral inhibition, and clinical signs of cholinergic toxicity.

[27] USEPA (2000) Office of Pesticide Programs, US Environmental Protection Agency, Washington DC 20460. August 18, 2000 Office of Pesticide Programs Science Policy of The Use of Data on Cholinesterase Inhibition for Risk Assessments of Organophosphorous and Carbamate Pesticides.

Appendix 2: Summary of Regulatory and Scientific Activities to Address Uncertainty Around Neurodevelopmental Effects

1. Regulatory Context & History:

Historically, data on the AChE inhibition has been the critical effect used to derive points of departure (PODs) for OPs, including chlorpyrifos. The Registration Eligibility Decision (RED) for chlorpyrifos was completed in 2006 and relied on AChE inhibition results from laboratory animals to derive PODs but retained the FQPA 10X Safety Factor due to concerns over age-related sensitivity and uncertainty associated with potential neurodevelopmental effects observed in laboratory animals. Since that time, numerous epidemiology, laboratory animal, and mechanistic studies have evaluated the hypothesis that chlorpyrifos exposure results in adverse effects on the developing brain. This body of studies has raised concerns that EPA's historical practice of using AChE inhibition as the critical effect for deriving PODs may not be protective of neurodevelopmental outcomes.

EPA-OPP initiated a science evaluation of the potential effects on neurodevelopment in 2007 following the receipt of a petition from Pesticide Action Network of North America (PANNA) and Natural Resources Defense Council (NRDC) seeking revocation of all tolerances and cancellation of all FIFRA registrations of products containing chlorpyrifos. EPA has three times presented approaches and proposals to the Federal Insecticide, Fungicide, Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP).[28] for evaluating epidemiologic, laboratory animal, and mechanistic data exploring the possible connection between *in utero* and early childhood exposure to chlorpyrifos and adverse neurodevelopmental effects. The SAP's reports have rendered numerous recommendations for additional study and sometimes conflicting advice for how EPA should consider (or not consider) the epidemiology data in conducting EPA's registration review human health risk assessment for chlorpyrifos. For over a decade, EPA has evaluated the scientific evidence surrounding the different health effects associated with chlorpyrifos. Despite these efforts, unresolved scientific questions remain. EPA has continued to pursue some aspects of these uncertainties but has not found resolution.

2. Previous Risk Assessments, Peer Review & Public Process:

The public process surrounding science issues on chlorpyrifos and in the PANNA/NRDC petition has been extensive and began with the September 2008 FIFRA SAP. The 2008 SAP evaluated the Agency's preliminary review of available literature and research on epidemiology in mothers and children following exposures to chlorpyrifos and other OPs, laboratory studies on animal behavior and cognition, AChE inhibition, and mechanisms of action (USEPA, 2008). The 2008 FIFRA SAP recommended that AChE inhibition remain as the source of data for the PODs but noted that despite some uncertainties, the Columbia Center for Children's Environmental Health (CCCEH) epidemiologic studies were "indeed quite strong and provided extremely valuable information (p. 35, FIFRA SAP, 2008)" and "concluded that the Columbia

[28] FIFRA SAP is a federal advisory committee created by Congress through FIFRA and is the primary venue for external, independent scientific advice to the EPA on major health and safety issues related to pesticides:

study is epidemiologically sound and that there is minimal selection and information bias (p. 32, FIFRA SAP, 2008)."

In 2010, EPA developed the Draft "Framework for Incorporating Human Epidemiologic & Incident Data in Health Risk Assessment" which describes the use of the Bradford Hill Criteria as modified in the Mode of Action Framework to integrate epidemiology information with other lines of evidence. The draft epidemiology framework was reviewed favorably by the FIFRA SAP in 2010. As suggested by the FIFRA SAP, EPA did not immediately finalize the draft epidemiology framework but instead used the document in several pesticide evaluations prior to making revisions and finalizing. OPP's epidemiology framework was finalized in December 2016[29] (USEPA, 2016).

In 2011, EPA released the preliminary human health risk assessment for chlorpyrifos[30]. The preliminary assessment used red blood cell (RBC) AChE inhibition from laboratory rats as the critical effect for extrapolating risk. The preliminary assessment also used the standard 10X factors for inter- and intra-species extrapolation. The 10X FQPA SF was removed with a note to the public that a weight of evidence (WOE) as described in the Draft "Framework for Incorporating Human Epidemiologic & Incident Data in Health Risk Assessment" evaluation would be forthcoming.

In 2011, EPA convened a meeting of the FIFRA SAP to review the PBPK-PD model for chlorpyrifos. The panel made numerous recommendations for the improvement of the model for use in regulatory risk assessment, including the inclusion of dermal and inhalation routes. From 2011-2014, Dow AgroSciences, in consultation with EPA, refined the PBPK-PD model for use in the revised human health risk assessment.

In 2012, the Agency convened another meeting of the FIFRA SAP to review the latest experimental data related to AChE inhibition, cholinergic and non-cholinergic adverse outcomes, including neurodevelopmental studies on behavior and cognition effects. The Agency also performed an in-depth analysis of the available chlorpyrifos biomonitoring data and of the available epidemiologic studies from three major children's health cohort studies in the U.S., including those from the CCCEH, Mt. Sinai and CHAMACOS. The Agency explored plausible hypotheses on mode of actions/adverse outcome pathways (MOAs/AOPs) leading to neurodevelopmental outcomes seen in the biomonitoring and epidemiology studies. The 2012 Panel described the Agency's epidemiology review as "very clearly written, accurate" and "very thorough review". The 2012 Panel went further to note that "The Panel believes that the [Agency's] epidemiology review *appropriately concludes* that the studies show some consistent associations relating exposure measures to abnormal reflexes in the newborn, pervasive development disorder at 24 or 36 months, mental development at 7-9 years, and attention and behavior problems at 3 and 5 years of age….." [*italics added*]. Although the 2012 Panel noted that the RBC AChE inhibition remained the most robust dose-response data, the 2012 Panel expressed significant concerns about the degree to which 10% AChE inhibition is protective for neurodevelopmental effects pointing to evidence from epidemiology, *in vivo* animal studies, and

[29] https://www3.epa.gov/pesticides/EPA-HQ-OPP-2008-0316-DRAFT-0075.pdf
[30] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0025

in vitro mechanistic studies, and urged the EPA to find ways to use the CCCEH cord blood data (pp. 50-52, FIFRA SAP, 2012).

In 2014, EPA released the revised human health risk assessment. The revised assessment used the chlorpyrifos PBPK-PD model for deriving human PODs for RBC AChE inhibition, thus obviating the need for the inter-species extrapolation factor and providing highly refined PODs which accounted for gender, age, duration and route specific exposure considerations. The PBPK-PD model was also used to develop data derived intra-species factors for some lifestages. The 10X FQPA SF was retained based on the outcome of the 2012 FIFRA SAP and development of a WOE analysis on potential for neurodevelopmental outcomes according to OPP's *Framework for Incorporating Human Epidemiologic & Incident Data in Risk Assessments for Pesticides*.

Based on the aggregate human health risks identified in 2014, a proposed rule (PR) for revoking all tolerances of chlorpyrifos was published in the Federal Register on November 6, 2015 (80 FR 69079). The 2014 human health risk assessment (HHRA), which used the 10% RBC AChE inhibition endpoint, was the basis for the proposed tolerance revocation for chlorpyrifos since a determination of 'reasonable certainty of no harm' could not be met due to risks identified from drinking water using a national-scale assessment.

In 2015, EPA conducted additional hazard analyses using data on chlorpyrifos levels in fetal cord blood reported by the CCCEH study investigators. The Agency convened another meeting of the FIFRA SAP in April 2016 to evaluate a proposal of using cord blood data from the CCCEH epidemiology studies as the source of data for PODs. The 2016 SAP did not support the "direct use" of the cord blood and working memory data for deriving the regulatory endpoint due in part to lack of raw data from the epidemiology study, insufficient information about timing and magnitude of chlorpyrifos applications in relation to cord blood concentrations at the time of birth, uncertainties about the prenatal window(s) of exposure linked to reported effects, and lack of a second laboratory to reproduce the analytical blood concentrations.

Despite their critiques regarding uncertainties in the CCCEH studies, the 2016 SAP expresses concern throughout the report that 10% RBC AChE inhibition is not sufficiently protective of human health. Specifically, the Panel stated that it "agrees that both epidemiology and toxicology studies suggest there is evidence for adverse health outcomes associated with chlorpyrifos exposures below levels that result in 10% red blood cell (RBC) acetylcholinesterase (AChE) inhibition (i.e., toxicity at lower doses) (p. 18, FIFRA SAP, 2016)." This statement is repeated multiple times throughout the 2016 SAP report (e.g., pp. 22, 25, 39-40, and 53, FIFRA SAP, 2016).

The 2016 SAP was supportive of the EPA's use of the PBPK model as a tool for assessing internal dosimetry from typical OPP exposure scenarios using peer reviewed exposure assessment approaches (e.g., food, water, residential, occupational). The 2016 SAP recommended the use of a time weighted average (TWA) blood concentration of chlorpyrifos for the CCCEH study cohort as the PoD for risk assessment (p. 36, 42, 45, FIFRA SAP, 2016) and EPA's 2016 chlorpyrifos HHRA followed this approach.

3. Regulatory and Scientific Activities Since 2016

In March 2017, EPA denied the NRDC/PANNA petition to revoke all tolerances and cancel all FIFRA registrations of products containing chlorpyrifos. In the 2017 denial, EPA noted that "further evaluation of the science is warranted to achieve greater certainty as to whether the potential exists for adverse neurodevelopmental effects to occur from current human exposures to chlorpyrifos." The denial went on to state that EPA "will not complete the human health portion of the registration review or any associated tolerance revocation of chlorpyrifos without first attempting to come to a clearer scientific resolution on those issues." Since that time, EPA has continued to pursue acquisition of the raw data from new laboratory animal studies and the epidemiology studies conducted by Columbia University; evaluated the new laboratory animal studies with results suggesting effects on the developing brain occur at doses lower than does that cause AChE inhibition; and evaluated whether or not additional statistical analysis, including bias analysis, would be useful in characterizing the epidemiology results.

3.1 Transparency in Regulatory Decision Making: Availability of Raw Data

For conventional pesticides, like chlorpyrifos, EPA receives numerous toxicology studies in laboratory animals conducted according to OCSPP[1] and OECD[2] guidelines to comply with pesticide registration data requirements listed in the 40CFR Part 158. Most of these studies are conducted in accordance with Good Laboratory Practice (GLP), as set forth in 40 CFR Part 160. In accordance with GLP regulations, registrants certifying compliance with Good Laboratory Practice are required to retain the raw data from these toxicology studies. Raw data must also be retained by pesticide producers pursuant to EPA's Books and Records regulations (40 CFR section 169.2(k)) and EPA must, upon request, be furnished with (or given access to) such records (see sections 160.15 and 169.3). These toxicology studies (including the raw data, if it is in EPA's possession) used by EPA in human health risk assessment can, in turn, be obtained through a Freedom of Information Act request as long as the person affirms under FIFRA section 10(g) that he or she will not provide the data to a multinational pesticide producer. As such, EPA and stakeholders interested in pesticide risk assessment have high expectations with regard to the transparency of data used to develop hazard assessment and characterization. Although for most conventional pesticides, EPA uses the guideline studies submitted by pesticide registrants, there are some cases where studies from the open scientific literature are used. In those situations, in line with EPA's commitment to transparency, EPA often makes an effort to obtain the raw data from the investigators. EPA will often, but not always, receive such requested information.

- With regard to the new laboratory animal studies (reviewed by Mendez, 2020, D457378), EPA contacted the primary investigators in July-August 2018. Dr. Russell Carr from Mississippi State University kindly provided the requested information. However, none of the others provided EPA with the raw data.

- With regard to the raw data from CCCEH, EPA has a history of requesting this information as detailed on EPA's website (https://www.epa.gov/ingredients-used-

[1] https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances
[2] http://www.oecd.org/env/ehs/testing/oecdguidelinesforthetestingofchemicals.htm

pesticide-products/chlorpyrifos-epas-seven-year-quest-columbias-raw-data). Throughout 2018, EPA continued to pursue the raw data from CCCEH but to no avail. See Attachment 1.

3.2 Review of New Laboratory Animal Studies

Chlorpyrifos has numerous studies in laboratory animals evaluating effects on behavior and learning in young animals exposed during gestation and/or post-natal period. Beginning with the 2008 preliminary evaluation, EPA evaluated the open literature studies in 2008 in a preliminary evaluation, in 2012 in a comprehensive systematic review of the literature, and again in 2016 with additional studies. EPA has consistently concluded, with support from the FIFRA SAP, that these studies provide evidence of the potential effects on the developing brain from exposure to chlorpyrifos but that they lack robustness for using as PODs for extrapolating human health risk. Moreover, until recently, the dose levels used in these animal behavior studies typically were only high enough to elicit AChE inhibition. The newest studies have used lower doses, including some below doses required to elicit 10% AChE inhibition.

In 2018, the California Department of Pesticide Regulation (CDPR) proposed to adopt a regulation designating chlorpyrifos as a toxic air contaminant (TAC) in California[31]. As part of this determination, CDPR developed its "Final Toxic Air Contaminant Evaluation of Chlorpyrifos Risk Characterization of Spray Drift, Dietary, and Aggregate Exposures to Residential Bystanders[32]." The CDPR risk characterization document cites five new laboratory animal studies not previously reviewed by EPA (Gomez-Gimenez *et al.,* 2017, 2018; Silva *et al*., 2017; Lee *et al.,* 2015; Carr *et al.,* 2017). CDPR is using these studies as the main source of information for their new POD for acute oral exposure (Table 23 in CDPR, 2018). EPA-OPP in consultation with the Office of Research and Development, has reviewed these five studies (Mendez, 2020, D457378) in accordance with OPP's Guidance for Considering and Using Open Literature Toxicity Studies to Support Human Health Risk Assessment.[33]
In short, EPA concludes that the Gomez-Gimenez et al (2017, 2018) and Silva et al (2017) papers are of unacceptable quality due to a number of deficiencies described in Mendez, 2020, D457378. Lee et al (2015) is considered acceptable but only for use qualitatively as some key deficiencies surrounding the assignment of pups from litters were noted. EPA finds the Carr et al (2017) study to be of high quality and provides strong support for the conclusion that effects on the developing brain may occur below a dose eliciting 10% AChE inhibition. Using the raw data provided by Dr. Carr, EPA conducted an independent statistical analysis of these results[34]. EPA's statistical analysis confirms the conclusions of Carr et al (2017) that young rats exposed to chlorpyrifos, at doses lower than those eliciting brain AChE inhibition, spent significantly less time in the dark container prior to emerging as compared to the control group.

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[31] https://www.cdpr.ca.gov/docs/emon/pubs/tac/tacpdfs/chlorpyrifos/proposed_determination_chlorpyrifos.pdf
[32] https://www.cdpr.ca.gov/docs/emon/pubs/tac/tacpdfs/chlorpyrifos/final_eval_chlorpyrifos_tac.pdf
[33] https://www.epa.gov/sites/production/files/2015-07/documents/lit-studies.pdf
[34] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0939

EPA-OPP continues to view the laboratory animal studies as part of the weight of the evidence surrounding the effects on the developing brain. Despite the strength of the new Carr paper, EPA continues to conclude these studies are not robust enough for deriving a POD.

3.3 Potential for Additional Statistical Analysis of CCCEH Studies

One of the areas of additional evaluation by EPA was a consideration of whether additional statistical analyses would be useful in characterizing the epidemiology results.

As described by Lash et al (2014[35]), quantitative bias analysis (QBA) evaluates nonrandom errors that may affect the results and interpretation of epidemiological studies. The purpose is to estimate the potential magnitude and direction of biases and to quantify the uncertainty about these biases. EPA held a series of conference calls with Dr. Timothy Lash at Emory University about the CCCEH studies. Dr. Lash is a recognized expert in this area. These conference calls and associated activities are described in the docket[36]. Some stakeholders have identified the limited blood lead testing in the CCCEH cohort to be an area of uncertainty and potential unresolved confounder in the epidemiology results. Dr. Lash noted that given that lead abatement was conducted by New York City prior to the start of the CCCEH study that this was not a major concern for him. Dr. Lash initially identified potential selection bias in the interpretation of working memory IQ from Rauh et al (2011) as a possible area for QBA. Upon further evaluation of this issue, it was determined that a QBA would not be useful or possible since working memory was only evaluated in children at age 7 but not at other ages.

EPA has recently pursued some additional questions about the statistical analysis conducted in CCCEH papers[37]. In Rauh et al (2011), CCCEH investigators log-transformed the working memory composite score but not log-transforming the chlorpyrifos exposure in the data analysis. EPA asked the investigators why this was done. The researchers explained that the natural log-transformation was applied to the outcome variables to stabilize the variance and improve the linear model fit. EPA inquired about further sensitivity analysis and if any model-fit diagnostics were available. CCCEH investigators responded that they did perform various transformations of the data in an exploratory mode but did not publish or further detail these results or share the results of these exploratory analyses with EPA.

EPA also recently asked CCCEH investigators about the impact of including/excluding extremely high exposure data points. The CCCEH investigators noted that there are three subjects with non-missing data had chlorpyrifos levels above 25 pg/g. These three subjects were not included in the final model because one subject with 63 pg/mg was a highly influential observation (outlier) and drastically impacted inference and the data from the two other subjects were too sparse and the splines too unstable in this region. The CCCEH investigators did not share the results of these exploratory analyses with EPA.
Although EPA does not have a specific reason to believe that CCCEH have inappropriately handled the data or statistical analysis, without the availability of the raw data, EPA remains

[35] Lash TL, Fox MP, MacLehose RF, Maldonado G, McCandless LC, Greenland S. 2014. Good practices for quantitative bias analysis. Int J Epidemiol. 2014 Dec;43(6):1969-85. doi: 10.1093/ije/dyu149. Epub 2014 Jul 30.
[36] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0939
[37] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0939

unable to verify the reported findings of the CCCEH papers. Moreover, EPA and interested stakeholders are unable to conduct alternative statistical analyses to evaluate the robustness and appropriateness of the approaches used by the investigators.

4. FQPA 10X Safety Factor for the 2020 Human Health Risk Assessment

The Food Quality Protection Act (FQPA, 1996) requires EPA in making its "reasonable certainty of no harm" finding, that in "the case of threshold effects, *an additional tenfold margin of safety* for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account *potential pre- and postnatal toxicity and completeness of data with respect to exposure and toxicity to infants and children*." The statute goes on to state that "the Administrator may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children."

Over the last decade, EPA has used several different approaches for assessing the human health risk to chlorpyrifos. EPA began registration review with a 2011 preliminary assessment using a traditional risk assessment based on laboratory animal data with standard 10X inter- and inter-species extrapolation factors but without the FQPA 10X SF. The 2014 revised human health risk assessment applied the PBPK-PD model to derive PODs for 10% RBC AChE inhibition which obviated the need for the inter-species factor and applied the FQPA 10X SF based on uncertainty identified regarding the potential for chlorpyrifos to effect neurodevelopment. In 2016, EPA used the PBPK model to derive an internal human POD based on the TWA for blood concentrations to women potentially exposed to chlorpyrifos from residential uses voluntarily cancelled in 2000. Despite the distinct differences in approach, EPA's acute and chronic population adjusted doses (PADs) in the 2011 and 2014 risk assessments are quite similar. Specifically, in the 2011 preliminary assessment, the acute and chronic PADs were 0.0036 mg/kg/day and 0.0003 mg/kg/day respectively, whereas in the 2014 revised assessment, the acute and chronic PADs are 0.005 mg/kg/day and 0.0008 mg/kg/day for females ages 13-49, respectively. In the 2016 assessment and using a PBPK model to derive a TWA for blood concentrations to women potentially exposed to chlorpyrifos from residential uses voluntarily cancelled, a PAD of 0.00005 mg/kg/day was calculated which is approximately an order of magnitude lower than the 2011 and 2014 assessments.

In conclusion, despite several years of study, peer review, and public process, the science addressing neurodevelopmental effects remains unresolved. Therefore, the dietary, residential, aggregate, and non-occupational risk assessments have been conducted with retention of the 10X Food Quality Protection Act (FQPA) safety factor (SF) and without retention of the 10X FQPA SF (*i.e.*, FQPA SF reduced to 1X). Similarly, the occupational risk assessments have been conducted both with and without retention of a 10X UF_{DB}.

Appendix 2 Attachment 1: Summary of Regulatory and Scientific Activities to Address Uncertainty Around Neurodevelopmental Effects

Despite a stated public commitment to "share all data gathered," CCCEH has not provided EPA with the data used in the CCCEH epidemiology studies. In the summer of 2015, Dr. Dana Barr of Emory University (formerly of CDC) provided the EPA with limited raw urine and blood data in her possession from the three cohorts. However, the files provided from Dr. Barr are not useful for the EPA's current purpose of assessing risk to chlorpyrifos. The EPA does not have any of the other measurements of the children in the cohort (e.g., chlorpyrifos blood data, interviews, test or IQ scores). CCCEH researchers have asserted that the pesticide component of the cohort study was privately funded, not federally funded, and therefore disclosure of underlying data is not required. EPA has described its efforts to acquire the CCCEH data on its website (https://www.epa.gov/ingredients-used-pesticide-products/chlorpyrifos-epas-seven-year-quest-columbias-raw-data).

Some recent requests include[38].

- April 19, 2016: EPA letter to Linda P. Fried, Dean, Mailman School of Public Health
- May 18, 2016: Linda P. Fried, Dean, Mailman School of Public Health letter to EPA
- June 27, 2016: EPA letter to Linda P. Fried, Mailman School of Public Health
- January 17, 2017: USDA letter to EPA citing Scientific Integrity Policy
- January 2, 2018: EPA letter to Linda Fried, once again requesting dataset
- January 8, 2018: Email from Linda Fried saying EPA needs to "clarify the information requests"

Throughout 2018, EPA continued to request the raw data from Columbia University:

- February 1, 2018: Teleconference and email to Howard Andrews regarding continued interest in reviewing the raw data and questions regarding statistical analysis of the Columbia dataset[39]
- February 6, 2018: Email from Howard Andrews requesting additional details on EPA's questions regarding the statistical analysis of the Columbia dataset
- March 26, 2018: Email to Howard Andrews with additional questions regarding statistical analysis of the Columbia dataset
- May 31, 2018: Teleconference with Howard Andrews regarding statistical analysis of Columbia dataset and reiterated request for the raw dataset
- June 27, 2018: Teleconference with Howard Andrews regarding raw dataset and CCCEH concern about the identification of study participants[40]

Following the June 2018 conference call with CCCEH, EPA contacted the CDC in July 2018 to discuss HIPAA and data de-identification issues as it relates to the CCCEH. The CDC

[38] Links to each letter can be found on https://www.epa.gov/ingredients-used-pesticide-products/chlorpyrifos-epas-seven-year-quest-columbias-raw-data.
[39] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0939
[40] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0937

representative noted that even after taking out personally identifiable information (PII) from the dataset, the data that remain can still pose identification issues because of the possibility of linking it with information currently in the public domain. The CDC representative further noted there are some datasets that cannot be deidentified given the nature of the data and specified that geographic location is one of the variables that makes something highly identifiable. In the case of CCCEH, the study participants live within a small geographical range with New York City. The CDC representative noted that for those cases, there is the possibility of allowing the data to be viewed in a secure data center[41].

Since June 2018, EPA has not made further attempts at obtaining or viewing the raw data from CCCEH.

[41] https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0850-0936

Appendix 3: Physical/Chemical Properties

Physical/Chemical Properties of Chlorpyrifos.		
Parameter	Value	Reference
Melting point/range	41.5-42.5 ºC	Chlorpyrifos IRED
pH	NR	
Density (21ºC)	1.51 g/mL	
Water solubility (25°C)	1.05 mg/L	
Solvent solubility (20°C)	Acetone >400 g/L Dichloromethane >400 g/L Methanol 250 g/L Ethyl acetate >400 g/L Toluene >400 g/L n-hexane >400 g/L	
Vapor pressure, (25°C)	1.87×10^{-5} torr[1]	
Dissociation constant, pK_a	NR	
Octanol/water partition coefficient, $Log(K_{OW})$	4.7	
UV/visible absorption spectrum	NR	

NR – not reported.

[1] R. Bohaty, June 2011, D368388 and D389480, *Chlorpyrifos Drinking Water Assessment for Registration Review* (CRF assessment, Oct. 16, 2009 product chemistry BC 2062713)

Appendix 4: Current U.S. Tolerances and International Residue Limits for Chlorpyrifos

Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US	**Canada**		**Mexico**[2]	**Codex**[3]
40CFR180.342 chlorpyrifos *per se* (*O,O* -diethyl *O* -(3,5,6-trichloro-2-pyridyl) phosphorothioate	*O,O*-diethyl-*O*-(3,5,6-trichloro-2-pyridyl) phosphorothioate (apples, grapes, tomatoes) *O,O*-diethyl-*O*-(3,5,6- trichloro-2-pyridyl) phosphorothioate, including the metabolite 3,5,6-trichloro-2-pyridinol (citrus fruits; fat, kidney, and liver of cattle; kiwifruit; peppers; rutabagas; green onion subgroup (crop subgroup 3-07B); meat and meat byproducts of cattle (calculated on the fat content))			Chlorpyrifos. The residue is fat soluble.
Commodity[1,]	Tolerance (ppm) /Maximum Residue Limit (mg/kg)			
	US	Canada	Mexico[2]	Codex[3]
Alfalfa, forage	3.0			
Alfalfa, hay	13			5 alfalfa fodder
Almond	0.2			0.05
Almond, hulls	12			
Apple	0.01	0.01		1 pome fruits
Apple, wet pomace	0.02			
Banana	0.1			2
Beet, sugar, dried pulp	5.0			
Beet, sugar, molasses	15			
Beet, sugar, roots	1.0			0.05
Beet, sugar, tops	8.0			
Cattle, fat	0.3	1		
Cattle, meat	0.05	1		1 (fat)
Cattle, meat byproducts	0.05	1		0.01 cattle, kidney and liver
Cherry, sweet	1.0			
Cherry, tart	1.0			
Citrus, dried pulp	5.0			
Citrus, oil	20			
Corn, field, forage	8.0			
Corn, field, grain	0.05	0.05		0.05 maize
Corn, field, refined oil	0.25			0.2 maize oil, edible
Corn, field, stover	8.0			10 maize fodder (dry)
Corn, sweet, forage	8.0			

Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US	**Canada**		**Mexico**[2]	**Codex**[3]
Corn, sweet, kernel plus cob with husk removed	0.05	0.05		0.01 sweet corn (corn-on-the-cob)
Corn, sweet, stover	8.0			
Cotton, undelinted seed	0.2			0.3 cotton seed
Cranberry	1.0			1
Cucumber	0.05	0.05		
Egg	0.01			0.01 (*)
Fig	0.01			
Fruit, citrus, group 10	1.0	1		1
Goat, fat	0.2			
Goat, meat	0.05			
Goat, meat byproducts	0.05			
Hazelnut	0.2			
Hog, fat	0.2			
Hog, meat	0.05			0.02 (fat)
Hog, meat byproducts	0.05			0.01 (*) pig, edible offal
Horse, fat	0.25			
Horse, meat	0.25			
Horse, meat byproducts	0.25			
Kiwifruit	2.0	2		
Milk, fat (Reflecting 0.01 ppm in whole milk)	0.25			0.02 milk
Nectarine	0.05	0.05		
Onion, bulb	0.5	0.2		0.2
Peach	0.05	0.05		0.5
Peanut	0.2			
Peanut, refined oil	0.2			
Pear	0.05			1 pome fruits
Pecan	0.2			0.05 (*)
Pepper	1.0	1		2 peppers sweet including pimento or pimiento); 20 peppers chili, dried
Peppermint, tops	0.8			
Peppermint, oil	8.0			
Plum, prune, fresh	0.05			0.5 plums (including prunes)
Poultry, fat	0.1			
Poultry, meat	0.1			0.01 (fat)
Poultry, meat byproducts	0.1			0.01 (*) poultry, edible offal
Pumpkin	0.05			
Radish	2.0			
Rutabaga	0.5	0.5		
Sheep, fat	0.2			

Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US	**Canada**		**Mexico**[2]	**Codex**[3]
Sheep, meat	0.05			1 (fat)
Sheep, meat byproducts	0.05			0.01 sheep, edible offal
Spearmint, tops	0.8			
Spearmint, oil	8.0			
Sorghum, grain, forage	0.5			
Sorghum, grain, grain	0.5			0.5
Sorghum, grain, stover	2.0			2 sorghum straw and fodder, dry
Soybean, seed	0.3			0.1 soya bean (dry)
Strawberry	0.2			0.3
Sunflower, seed	0.1	0.1		
Sweet potato, roots	0.05			
Turnip, roots	1.0			
Turnip, tops	0.3			
Vegetable, brassica, leafy, group 5	1.0			2 Broccoli 1 Cabbages, head 0.05 Cauliflower 1 Chinese cabbage (type pe-tsai)
Vegetable, legume, group 6 except soybean	0.05	0.05 lentils		0.01 common bean (pods and/or immature seeds); peas (pods and succulent=immature seeds)
Walnut	0.2			0.05 (*)
Wheat, forage	3.0			
Wheat, grain	0.5			0.5
Wheat, straw	6.0			5 wheat straw and fodder, dry
Prepared 05/19/2020 D. Drew				

[1] Includes commodities listed in the CFR as of 5/19/2020. The 40CFR 180.342 (a) (3) also stipulates that "a tolerance of 0.1 part per million is established for residues of chlorpyrifos, per se, in or on food commodities (other than those already covered by a higher tolerance as a result of use on growing crops) in food service establishments where food and food products are prepared and served, as a result of the application of chlorpyrifos in microencapsulated form."
[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.
[3] * = absent at the limit of quantitation. (fat) = to be measured on the fat portion of the sample.

Tolerances with regional registrations

Commodity	Parts per million	Canada	Codex
Asparagus	5.0		
Grape	0.01	0.01	0.5

Appendix 5: Master Use Summary Document

Table A.5. Summary of Current Chlorpyrifos Usage

Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
AGRICULT-URAL FARM PREMISES Livestock housing and holding areas (such as hog barns, empty chicken houses, dairy areas, milkrooms, calf hutches, calving pens and parlors).		✓		Indoor general surface spray	backpack sprayer; high and low sprayer (pressure or volume)	0.075 lb a.i./ 1000 ft sq 1.2 EC, ME	[14.4] NS	NA	12	NA	NA	NS	NS		Only permitted for use in poultry houses
ALFALFA		✓		At plant	groundboom	1.0 G	1.0	1.0	[1] NS	1	21	24	[10] NS	Missouri only	Lower PHI permitted for EC rates 0.33 lb a.i./A (7 d) and 0.67 lb a.i./A (14 d) e.g. Reg. No. 62719-591 Stand is in production 3-5 years. Planted ¼” to ½” deep.

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
		✓		Foliar	aerial or ground/ broadcast, chemigation	1.0 EC	[4.0] NS	4.0	[4] NS	4	21	24	10		Lower PHI permitted for EC rates 0.33 lb a.i./A (7 d) and 0.67 lb a.i./A (14 d) *e.g.*, Reg. No. 62719-591 Multiple harvests (or cuttings) per year when used for feed/fodder and 1 harvest per year when grown for seed. Cuttings occur about every 30 days. Only 1 crop cycle per year but up to 9 cuttings, varies by geography.
				Total		**1.0**	**5.0**	**5.0**	**[5] NS**	**5**	**21**	**24**	**[10] NS**		Represents Missouri scenario otherwise 4.0 lb a.i./A per is max.

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
ALMOND		✓		**dormant/ delayed dormant**; broadcast	aircraft, airblast	2.0 WDG, WP	2.0	NA	1	NA	NA	24	10	Restricted use in California.	
		✓		**foliar**; broadcast	aircraft, airblast	2.0 WDG,WP	6.0	NA	3	NA	14		10		
		✓		pre-plant, foliar; **trunk spray/drench or pre-plant dip**	handheld, backpack, drench/dip, handgun, and low-pressure hand wand	2.5 (3.0/100 gal) WDG	2.5	NA	1	NA	14		NS		
		✓		Dormant/ delayed dormant; foliar; **orchard floors** broadcast	ground boom, handgun, chemigation	4.0 EC*	4.0	NA	2	NA	14		10	Restricted use in California. Only one dormant application can be made.	
				Total	**--**	**4.0**	**14.5**	**NA**	**7**	**NA**	**14**		**NS**		Excludes nursery applications (See general "Fruits" listing)
APPLE		✓		**dormant/ delayed dormant**; broadcast	aircraft, airblast	2.0 EC 2.0 WDG 1.5 WP	2	2.0	1	1	NA	24/ 4 d	10d		Reflects spray drift mitigation measures.

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		pre-plant, foliar; **trunk spray/drench or pre-plant dip**; ground	handheld, backpack, drench/dip, handgun, and low-pressure hand wand	1.5 (1.5 lb ai/100 gal) WDG	1.5	NA	1	1	28	4d	NS	Use permitted in states east of the Rockies except Mississippi.	
				Total		**2.0**	**3.5**		**2**						
ASPARAGUS		✓		Foliar, pre-harvest; broadcast	aircraft, ground boom	1.0 EC, WDG	1.0	1.0	1	1	1	24	10		
		✓		Postharvest, broadcast	aircraft, ground boom	1.0 EC, WDG	2.0	2.0	2	1	1	24	10		
					granular soil band treatment ground boom	1.5 G	3.0	3.0	2	2	180	24	[10] NS	Permitted in California, the Midwest, and the Pacific Northwest 19713-505, 19713-521, 5481-525, 62719-34, 83222-34	Do not apply more than 3.0 lb a.i./A between harvests.
				Total		**1.5 G**	**3.0 G 2.0**	**3.0 G 2.0**	3	3	1	24	10		

Table A.5. Summary of Current Chlorpyrifos Usage

Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
BEANS		✓		Preplant; Seed treatment	Seed Treatment	*0.016-0.348* 0.000798 lb ai/lb seed ME *0.013-0.272* 0.000625 lb ai/lb seed WP *0.012-0.253* 0.00058 lb ai/lb seed EC	NS	[0.348] NS	NS	[1] NS	NS	NS	NS	ME is SLN only for ID	Italics highlight the range of application rates depending on the number of seeds per lb and the number of seeds planted per acre. Seeding rate information provide by BEAD.[4]
BEEF/RANGE/ FEEDER CATTLE (MEAT)/ DAIRY CATTLE (NON-LACTATING)				Summer, late fall, spring; impregnated collar/tag	Animal treatment (ear tag)	0.0066 lb/animal	[0.0099] NS	NA	3	NA	NS	NS	NS		Reg. No. 39039-6 Cattle ear tags are assumed to last 4-6 months Two tags per animal at 0.0033 lb a.i./tag in the summer and one tag per animal at 0.0033 lb a.i./A.
BEETS (UNSPECIFIED; TABLE OR SUGAR)		✓		At plant, soil band treatment	Ground boom	1.0 EC	NS	1	NS	1		24		Allowed in Oregon Court ordered	Minimum Incorporation: 2 inches

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
"grown for seed"														buffer of 60 ft for ground chlorpyrifos application is required for "affected waterways".	
		✓		Preplant, soil incorporated treatment	Broadcast/ ground boom	1.9 EC	NS (2.8 ID)	NS	1	NS				Allowed in Oregon and Idaho	OR-09007; 62719-591 ID-090002; 62719-591
				Total		**1.9**	**NS**	**NS**	**NS**	**NS**		**24**			One or the other type of application.
SUGAR BEETS		✓		Preplant, soil incorporated treatment	Broadcast/ ground boom	1.0 EC 2.0 G	3.0	2.0	1	1	NA	24	10		Minimum Incorporation: 1 inch
		✓		At plant, soil band treatment	Broadcast/ ground boom	1.0 EC, WDG 2.0 G	3.0	2.0	1	1	30	24	10		
		✓		Post plant, soil band	Broadcast/ ground boom	2.0 G	3.0	2.0	1	1	30	24	10		
		✓		Post-emergence band treatment; broadcast	Broadcast/ ground boom	1.0 EC, WDG	3.0	1.0	3	1	30	24	10		

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		broadcast	Aircraft, ground boom, chemigation	1.0 EC, WDG	3.0	1.0	3	1	30	24	10		EC is not for use in MS
				Total		**1.0 EC 2.0 G**	**4.0**	**[4.0] NS**	**3**	**[3] NS**	**30**	**24**	**10**		One granular application at 2.0 a.i./A and two liquid applications at 1.0 a.i./A per year. Also assumed per crop cycle.
CARROT Grown for Seed (INCLUDING TOPS)		✓		Foliar pre-bloom broadcast	aircraft, ground boom	0.94 EC	0.94	1	1	1	7	24	NA	Oregon and Washington Court ordered buffer of 60 ft for ground and 300 ft for aerial application is required for “affected waterways”.	OR090011 SLN Expires: 12/31/2018 WA090011 SNL Expires: 12/31/2016 Carrots take two years to produce seed. All commercial production of the carrot (vegetable) takes place in the first year when the plant

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
															is nowhere near blooming.
CHERRIES		✓		**dormant/ delayed dormant**; broadcast	aircraft, airblast	2.0 WDG, EC 1.5 WP	2.0	NA	1	NA	NS	24	10		
		✓		**foliar**; broadcast	airblast	4.0 EC	10.0	NA	5	NA	14	24	10		Tart cherry only
					aircraft	2.0									Reflects spray drift mitigation
		✓		Foliar, post-harvest; **trunk spray/drench**	handheld, backpack, drench/dip, handgun, and low-pressure hand wand	2.5 (3.0/100 gal) WDG, EC	2.5	NA	1	NA	2	24	[10] NS		Only some labels specify a 10 d MRI.
				Total	**--**	**4.0**	**4.5 (sweet)** **14.5 (tart only)**		**6**						Excludes nursery applications (See general "Fruits" listing) The foliar applications only apply to tart cherries, thus, sweet cherry scenarios (*e.g.*, Pacific NW) annual

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
															application rate would be 4.5 lb total a.i./year.
CHRISTMAS TREE PLANTATIONS		✓		**foliar**; broadcast	helicopter, orchard blast	1.0 EC, WDG, WP	3.0	NA	3	NA	[0] NS	24	7	Aerial applications via helicopter are only permitted in Washington and Oregon.	
		✓		post-harvest; **Stump Treatment**	handheld, backpack, drench/dip, handgun, and low-pressure hand wand	2.5 (3.0/100 gal) EC, WDG	2.5	NA	1	NA	NA		7		
				Total		**2.5**	**5.5**		**4**						
CITRUS		✓		**foliar**; broadcast	airblast, ground boom	6.0 WP, WSP, EC	7.5	NA	2	NA	35 (21 for low rates)	5d	30 (10 for low rates)	6.0 lb a.i. /A is only permitted in California and Arizona. The max single rate in other states is restricted to 4 lb a.i./A.	
		✓			aircraft	2.3 WP, WSP, EC					21	5	10	Florida, California,	Aerial application used

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
														and potentially Texas	to control psyllid, the vector for citrus greening. Reflects spray drift mitigation
		✓		foliar; **orchard floors broadcast**	ground boom, chemigation, handheld, backpack, drench/dip, handgun, and low-pressure hand wand	1.0 G*, WSP, EC	3.0	NA	3	NA	28	24/ 5 d	10		
				Total	**--**	**6.0**	**10.5**		**5**						Registered labels permit both foliar and soil applications in the same orchard. Total excludes nursery applications (See general “Fruits” listing)
CLOVER (GROWN FOR SEED)		✓		Preplant	Ground boom	1.9 EC	1.9	1.9	1	1	NS	24	NA	Use only permitted in Oregon.	OR-0900100; master label: 62719-591

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		Post-Plant Foliar	aircraft and ground boom										Either a preplant or post plant application is allowed.
COLE CROPS (EXCLUDES CAULIFLOWER AND BRUSSELS SPROUTS)		✓		Preplant, soil incorporated treatment	Ground boom	2.0 EC, WDG, G	4.0	2.0	2	1	30	24	10		Min. incorporation: 2 inches
		✓		At plant, soil band treatment	Ground boom					1					One granular application permitted per year.
		✓		Post plant	Ground boom					1					
		✓		Foliar Established Plantings, soil sidedress treatment	Ground boom					1					
		✓		Foliar, broadcast	Aircraft, ground boom, chemigation	1.0 EC, WDG, WP	4.0	3.0	4	3	21		10		Multiple crops per year are possible in some locations.
				Total			**8.0**	**5**	**6**	**4**					Some labels restrict the yearly application rate to 3 lb a.i./A.

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
															The maximum number of crops per year is 2.
BRUSSELS SPROUTS		✓		At plant, soil band treatment	Ground boom	2.0 EC; G	2.0	[2.0] NS	2	1	21	24	10		
		✓		Preplant, soil incorporated treatment	Ground boom										Minimum incorporation is 2 inches
		✓		Post plant, soil application	Ground boom	2.25 EC, G	2.25	[2.25] NS							
		✓		Foliar broadcast	Aircraft, Ground boom	1.0 EC	[5.3] NS	3.0	NS	3			10		83222-20, 84930-7, 86363-3 specify a 7-day MRI. All other labels specify a 10-day MRI. The PHI stated 84930-7 is conflicting [p. 4 (21 days and p. 19 (30 days)]
				Total		**2.3**	**5.3**		**NS**		**21**	**24**	**7**		Assume one application of either at plant, preplant, or post plant followed with additional

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
															foliar applications.
CAULI-FLOWER		✓		At plant, soil band treatment	Ground boom	2.0 EC 2.3 G	2.0 EC 2.25 G	NS	[1] NS	1	21	3d	10		Only one granular application.
		✓		Preplant, soil incorporated treatment	Ground boom	2.3 G 2.0 EC	2.3	NS	[1] NS	1	30, EC, 21 G				Minimum incorporation is 2 inches
		✓		Post plant, soil application	Ground boom										
		✓		Foliar broadcast	aircraft, ground boom	1.0 EC	[5.3] NS	3.0	NS	3	21		10		
				Total		**2.3**	**5.3**	**[5.3] NS**	**NS**	**[4] NS**	**21**	**24**	**10**		Assume one application at either plant, preplant, or post plant followed with additional foliar applications.
COMMERCIAL /INSTITUTION-AL/ INDUSTRIAL PREMISES/ EQUIP. (INDOOR)				Broadcast	Product Container	0.4373 lb a.i./100 sq ft 190.5 G	NS	NA	NS	NA	NA	NS	NS		For treatment of fire ants
				Crack and Crevice/Void	Sprayer/ Injection	0.0625 lb a.i./1000 sq ft	NS	NA	NS	NA	NA	NS	NS		499-419

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Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
Non-food areas of manufacturing, industrial, and food processing plants; warehouses; ship holds; railroad boxcars.						2.7 ME									
				Crack and Crevice/Spot	Sprayer/ Injection	0.0424 lb/gal ME	NS	NA	NS	NA	NA	NS	7		
COMMERCIAL /INSTITUTIONAL /INDUSTRIAL PREMISES/EQUIP. (OUTDOOR) Outdoor commercial use around non-food areas of manufacturing, industrial, and food processing plants; warehouses; ship holds; railroad boxcars				Soil broadcast	Low and High Pressure, Backpack, Handgun Sprayers	0.0247 lb a.i./1000 sq ft 1.1 ME	NS	NA	NS	NA	NA	NS	NS		
				Directed spray		0.1132 lb a.i./1000 sq ft 4.9 ME	NS	NA	NS	NA	NA	NS	NS		Specific to: Inside and outside dumpsters and other trash holding containers, trash corrals and other trash storage areas.
				Crack and Crevice/void/ general outdoor		0.0424 lb/gal ME	NS	NA	NS	NA	NA	NS	7		
CONIFERS AND DECIDUOUS TREES;		✓	?	**foliar**; broadcast	Ground boom	1.0 EC	3	NA	6	NA	7	24	7		

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
PLANTATION, NURSERY		✓	?	foliar; **stump treatment**	backpack, drencher, low pressure hand wand	0.3 EC	0.3	NA	1	NA	7	24	7		
				Total		**1.0**	**3**	**NA**	**6**	**NA**	**7**	**24**	**7**		The total number of applications assumed is either 3 foliar applications or 2 foliar applications with one stump treatment.
CORN (ALL)		✓		Preplant	ground/ **soil incorporated** conservation tillage, in furrow, broadcast, chemigation, soil band	3.0 EC 2.0 G	3.0	3.0	NS	3	NA	24/ 5 EC	10		19713-520, 19713-599, 33658-26, 34704-857, 72693-11, 83222-20 The minimum incorporation depth is 2 inches.
					soil incorporated aerial conservation tillage	2.0 EC, G									

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
		✓			ground/ conservation tillage, in furrow, broadcast, chemigation, soil band	1.0 EC 2.0 G	3.0	3.0	NS	3	21		10		19713-520
		✓		Storage or preplant seed treatment	Seed treatment	*0.001-0.021* 0.000625 lb a.i./ lb seed WP *0.1-1.9* 0.058 lb a.i./ lb seed FC	[?] NS	[1.9] NS	[?] NS	1	NS	NS	NS		Italics highlight the range of application rates depending on the number of seeds per lb and the number of seeds planted per acre. Seeding rate information provide by BEAD.[4]
		✓		At plant	soil incorporated, conservation tillage	2.0 G	[?] NS	3.0	[?] NS	3	21	24	10		
		✓		Post emergence	Aerial or ground, broadcast, chemigation	1.5 EC 1.0 WDG	NS	3.0	NS	3	21	24/ 5d (EC	10		A brush on max single rate is permitted at 1.0 lb ai/a (72693-11)

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		Foliar	Aerial or ground/ broadcast, granule, seed and chemigation	1.5 EC	3.0	3.0	NS	3	21		10		
				Total		**3.0**	**8.1**	**8.1**	**NS**	**4**	**21**		**10**		Two granular applications are allowed with a maximum single rate of 1.0 lb a.i./A or one granular application at 2 lb a.i./A. Total with seed treatment PHI: 21 d except Delaware and Florida (7 d)
COTTON		✓		Storage or preplant seed treatment	Seed treatment	*0.8-2.2* 0.00116 lb/lb seed EC	[2.2] NS	[2.2] NS	[1] NS	1	NS	NS	NS		264-932 Rates in italics highlight the potential range of application rates depending on the number of seeds per lb and the number

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
															of seeds planted per acre. Seeding rate information provide by BEAD.[2]
		✓		Foliar	aerial, chemigation, ground boom	1.0 EC, WDGP	3	3.0	3	3	14	24	10		Except MS
				Total		**1.0**	**3.2**	**3.2**	**3**	**3**	**14**	**24**	**10**		1.6 lb a.i./A is max single rate (seed treatment) **Total with seed treatment** 1 crop cycle per year assumed
CRANBERRY		✓		Foliar	aircraft, ground boom/ broadcast and chemigation	1.5 EC, WDG	3.0	NA	2	NA	60	24	10	Not for use in Mississippi.	Do not apply to bogs when flooded.
CUCUMBER		✓		Storage or preplant seed treatment	Commercial seed treatment	*0.4* 0.00058 lb/lb seed EC	NS	0.1	2	1	NS	NS	NS		Seeding rate information provide by BEAD.[2] 264-932, 62719-221, CA040004 Per registrant 2 CCs per year

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
FIGS		✓		**dormant/ delayed dormant**; soil application	ground boom	2.0 WDG, EC	2.0	NA	1	NA	217	4 d	NS	Use is restricted to California only.	Incorporation to 3 inches is suggested but not required following application.
FILBERTS/ HAZELNUT		✓		**dormant/ delayed dormant**; broadcast	aircraft, airblast	2.0 WP	2.0	NA	1	NA	14	24	10		
		✓		**foliar**; broadcast	aircraft, airblast	2.0 WDG, WP, EC	6.0	NA	3	NA	14		10		Some labels specify a retreatment interval of 10 days.
				Total		**2.0**	**6.0**	**NS**	**3.0**	**NA**	**14**	**24**	**10**		Excludes nursery applications (See general "Fruits" listing)
FOOD PROCESSING PLANT PREMISES (NONFOOD CONTACT)				When needed, crack and crevice treatment, spot treatment		0.0424 lb/ gal ME	NS	NA	NS	NA	NA	NS	7		53883-264, 84575-3 Spot Treatment: Do not exceed two square feet per individual spot.
FOREST PLANTINGS (REFORESTAT			✓	Foliar, broadcast	ground boom	1.0 EC	6.0	NA	6	NA		24	7		

Table A.5. Summary of Current Chlorpyrifos Usage

Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate: Per Year lb a.i./A	Maximum Application Rate: Per CC[2] lb a.i./A	Maximum Application Number: Per Year	Maximum Application Number: Per CC[2]	PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
ION PROGRAMS) (TREE FARMS, TREE PLANTATION, ETC.)															
			✓	Foliar, stump treatment	direct spray, drencher	0.34 EC	6.0	NA	[18] NS	NA			7		
FOREST TREES (SOFTWOODS, CONIFERS)			✓	Foliar, broadcast	ground boom, drencher	0.61 EC	3.6	NA	NS	NA	24		7		
			✓	Foliar, stump treatment	direct spray	[3.6] 2.4 lb a.i./100 gal EC	3.6	NA	NS	NA			7		Application rate is provided as a dilution factor.
FRUITS & NUTS Non-bearing (not to bear fruit within 1 year) fruit trees in nurseries (includes: almonds, citrus, filbert, apple, cherry, nectarine, peach, pear, plum, prune).		✓		Foliar-Non-bearing nursery broadcast	High/low volume spay/ handheld sprayer/power sprayer	4.0 EC	4.0	NA	NS	NA	14	NS	7		For nectarines and peaches, the use is restricted to one application of no more than 3 lb a.i./A per cc. For apples, the max rate is 2 lb a.i./A per crop cycle and the use is restricted to 1 application (either canopy or trunk drench) per year.

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Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
															Example label, 62719-254
		✓		Foliar-Non-bearing nursery trunk drench	drencher, high- and low-pressure sprayer	2.0 WDG	2.0	NA	NS	1	14		7		
				Total		**4.0**	**6.0**								Maximum Single Rates: 3.0 (nectarines and peaches) 2.0 (apples) Maximum Yearly Rates: 3.0 (nectarines and peaches) 2.0 (apples)
GINSENG (MEDCINAL)		✓		Preplant, post-emergence	Ground, soil broadcast	2.0 G	2.0	NA	1	NA	365	24	NA	Permitted in Michigan and Wisconsin	MI110006,WI110003) Minimum incorporation: 4 inches Application should be followed by rainfall or overhead watering. Valid until June 29, 2016.

Table A.5. Summary of Current Chlorpyrifos Usage

Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
GOLF COURSE TURF				When needed, soil broadcast/ spot treatment	Ground, low pressure	1.0 EC	2.0	NA	2	NA		24	NS		
				Foliar, broadcast,	Ground boom, handgun, low pressure and backpack	1.0 EC, G, B	2.0	NA	2	NA			NS		Chemigation not allowed for the EC formulation.
					Tractor drawn spreader, push type spreader, belly grinder	1.0 G						[24] NS	7		
				Mound treatment	Granule applicator	1.0 G	2.0	NS	2	NS		NS	7		
				Total		**2.0**	**2.0**	**NA**	**2**	**NA**	**NS**		**NS**		
GRAPES		✓		Dormant/ Delayed Dormant (pre-bloom)	Ground boom, broadcast, drench high/low spray volume	1.0 WDG, EC	1.0	1	1	NA	35	24	NS	East of the continental divide only.	Do not use in conjunction with soil surface applications for grape borer control.
		✓				2.0 EC	2.0	1	1	NA	35			Permitted in Colorado, Idaho, and Washington	CO080008, ID090004, WA090002 Master label: 62719-591

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		Foliar	Ground/ broadcast, basal spray and drench (soil treatment)	2.25 EC	2.25	1	1	NA	35		NS	Permitted east of the continental divide.	
		✓				1.0 EC	3.0	3	3	NA	35		NS	California	CA080010
		✓		Postharvest, dormant/ delayed dormant	Ground boom, broadcast	2.0 EC	2.0	1	1	NA	NS		NS	California	CA080009
				Total		**2.25**	**2.25**	**1**			**35**	**24**	**NS**	Permitted east of the continental divide.	
						2.0	**5.0**	**4**			**NS**		**NS**	California	
GRASS FORAGE/ FODDER/HAY		✓		Foliar, broadcast	Aircraft, ground boom, chemigation	1.0 EC	3.0	NA	3	NA	NS	24		Permitted in Nevada, Oregon, Washington, and Idaho	NV080004, NV940002, OR090009, WA090010, ID090003
GREENHOUSE		✓		early evening, aerosol, fog or fumigation	Total release fogger	0.029 0.0066 lb a.i./1000 sq. ft PL	NS	NA	NS	NA	NS	NS	2		
HOUSEHOLD/ DOMESTIC DWELLINGS INDOOR PREMISES	✓			When needed	Bait station	0.0003 lb/bait station	NS	NA	NS	NA	NA	NS	NS		9688-67

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Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
HYBRID COTTONWOOD/ POPLAR PLANTATIONS		✓		Foliar, dormant, delayed dormant; broadcast	High volume (dilute) Low volume (concentrate)	1.9 EC	[2.0] NS	6.0	[1] NS	3		24	7	Washington	WA090004 Energy wood plantations may be harvested as often as every 2-3 years; pulpwood 5-10 years; and saw timber 15-20 years. (Arkansas production guide). In Washington the crop takes 2-8 years
LEGUME VEGETABLES		✓		Preplant, soil treatment	Ground boom	1.0 EC, WDG	1.0	NA	1	NA	NS	24	NA		No MRI because application only once a year
		✓		At planting, soil treatment	Ground boom	1.0 EC, WDG	1.0	NA	1	NA	NS		NA		
				Total		**1.0**	**1.0**	**NA**	**1**	**NA**	**NS**	**24**	**NS**		Assumed either a preplant or an at plant treatment.
MINT/ PEPPERMINT/ SPEARMINT		✓		Preplant soil incorporated	Aerial or ground/ broadcast	2.0 EC, WDG	[2.0] NS	2.0	[1] NS	1	90	24	NA	No use in Mississippi.	19713-599, 33658-26, 34704-857, 67760-28, 84229-25,

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
															84930-7, OR940027 MRI NA due to once per crop cycle application
		✓		Post-emergence, Postharvest, Foliar	Chemigation, ground/ airblast	2.0 EC	2.0	2.0	[1] NS	2	90		NS	No use in Mississippi.	Postharvest application retreatment not specified on some labels.
				Total		**2.0**	**4.0**	**4.0**	**2.0**	**3**	**90**	**24**	**NS**		Labels allow one growing season application including pre-plant and one post-harvest application per season.
MOSQUITO CONTROL; HOUSEHOLD/ DOMESTIC DWELLINGS OUTDOOR PREMISES; RECREATION AL AREAS	✓			When needed; broadcast	Ultra-low volume air and ground	0.01 EC	0.26	NA	26	NS	NA	NS	24 h	In Florida: Do not apply by aircraft unless approved by the Florida Dept of Ag.	Aerial applications may be made at altitudes ranging from 75-300 ft (see labels for specifics).

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
															For use by federal, state, tribal or local government officials or by persons certified in the appropriate category or authorized by the state or tribal lead regulatory agency.
NECTARINE		✓		**dormant/ delayed dormant** broadcast	airblast, handgun	3.0 WDG, EC	3.0	NA	1	NA	NS	24/ 4d	10		83222-20 others at 2 lb a.i./a
					Aircraft	2.0 WDG, EC									Updated to reflect spray drift mitigation.
		✓		pre-plant, foliar; **trunk spray/drench or pre-plant dip**	Handgun, low pressure backpack, dip	2.5 (3.0/100 gal) WDG, EC	2.5	NA	1	NA	14		5		There is no application retreatment interval specified on some of the label. The application rate is provided as a dilution factor.

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
				Total		**3.0**	**5.5**	**NA**	**2**	**NA**					Some labels limit the amount a.i./A per year. Multiple types of applications can occur such as preplant, trunk drench and dormant, delayed dormant applications. Excludes nursery applications (See general "Fruits" listing)
NONAGRICULTURAL OUTDOOR BUILDINGS/STRUCTURES to and around outside surfaces of nonresidential buildings and structures. Permitted areas of use include				Outdoor general surface/ Band (may be better if called perimeter)	Ground sprayer/ band sprayer	1.0 EC	NS	NA	NS	NA	NA	NS	NS		

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
fences, pre-construction foundations, refuse dumps, outside of walls, and other areas where pests congregate or have been seen															
NURSERY-STOCK: : Ornamental nursery stock annuals, perennials and woody plants being grown in the field, in ball and burlap or in containers outdoor and in greenhouses				Dormant/ Delayed Dormant	high spray	3.0 EC	3.0	NA	1	NA		24	NS		
				Preplant	Ground boom, soil incorporated	4.0 EC, WP	NS	NA	NS	NA					
				foliar, soil directed	Tractor drawn spreader, push type spreader, belly grinder, gravity fed	1.1 G									

Table A.5. Summary of Current Chlorpyrifos Usage

Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
					backpack, spoon										
				Total		**4.0**	**CBD**		**3**						
ONIONS		✓		Post plant (seeding) Broadcast	Ground boom	1.0 EC	1.0	NS	2	NS	60	24	NS		
		✓		At plant, soil drench or basal spray	Ground boom	1.0 EC, WDG, G	1.0		1						2-inch incorporation
				Total		2.0	2.0		2		60	24	NS		
ORNAMENTAL AND/OR SHADE TREES, HERBACEOUS PLANTS		✓		Foliar broadcast	Ground boom, air blast, handgun, low- and high-pressure hand wands	2.0 EC, WP 1.0 G, B	2.0	NA	[2] NS	NA	NS	24	NS		Some labels include an MRI of 7 days.
		✓		Dormant /Delayed Dormant	Handgun, low pressure and backpack	3.0 EC	3.0	NA	1	NA	NS		7		Low volume spray permitted for concentrated solutions and lower rates.
ORNAMENTAL LAWNS AND TURF, SOD FARMS (TURF)		✓		When needed, broadcast, soil or spot treatment	ground boom (WP only), high pressure hand wand	3.76 EC, WP	7.52	NA	2	NA	NS	24	NS		
		✓		NS	Tractor drawn spreader, push type spreader, belly grinder	1.0 B	2.0	NA	2	NA	NS	24	NS		Bait is used for fire ant control.

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
ORNAMENTAL NON-FLOWERING PLANTS		✓		Foliar, broadcast, soil drench	Chemigation, ground boom, low and high pressure handwand, handgun, backpack sprayer, sprinkling can	0.007/gal ME	NS	NA	12	NA	NA	24	NS		Application rate provided as a dilution factor. Restricted use—occupational only
ORNAMENTAL WOODY SHRUBS AND VINES				Foliar broadcast	Ground boom, air blast, handgun, low- and high-pressure sprayer, backpack	2.0 EC, WDG 0.01 lb/gal EC	2.0 0.01 lb/gal	NA	[1] NS	NA	NS	24	NS		Several labels do not restrict the application rate in lb a.i./A. Examples include 16.5 lb/100 gal (228-625) and 1.0 lb/100 gal (829-280).
				Dormant/ delayed dormant		1.0 EC 0.005 lb/gal EC	1.0	NA	[1] NS	NA					
				Preharvest	Tractor drawn spreader, push type spreader, belly grinder	6.0 G	6.0	NA	[1] NS	NA					
				Preplant, potted, bailed-and	groundboom, handgun, low- and high-	1.0 EC	NS	1	NS	1					

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Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
				burlapped, containerized	pressure sprayer, backpack, drench										
				Pretransplant	groundboom	4.0 WP	[48.0] NS	4	12	4					
				Total		**6.0 G 4.0 WP**	**CBD**		**CBD**						
PEACH		✓		**dormant/ delayed dormant** broadcast	airblast	3.0 EC 2.0 WDG	3.0	NA	1	NA	10	24/ 4d	NS		83222-20 (all other labels restrict to 2 lb ai/a)
					aircraft,	2.0 EC 2.0 WDG							NS		Updated to reflect spray drift mitigation.
		✓		**Post-harvest** broadcast	airblast	2.5 (3.0/100 gal) EC	2.5	NA	1	NA	NA		NS	Permitted in Georgia and South Carolina	GA0400001, SC040001 SLN Expires:
					aircraft	2.0 (3.0/100 gal) EC	2.0								GA0400001, SC040001 SLN Expires: Updated to reflect spray drift mitigation
		✓		pre-plant, foliar;	handheld, backpack, drench/dip,	2.5 (3.0/100 gal) WDG	2.5	NA	1	NA	14	5	NS		Some labels do not specify minimum

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
				trunk spray/drench or pre-plant dip; ground	handgun, and low-pressure hand wand										retreatment interval.
				Total		**3.0**	**5.5**	**NA**	**3**	**NA**	**NA**	**24**	**NS**		It is possible that multiple types of applications can occur such as soil, foliar and/or post-harvest and dormant/ delayed dormant applications. Excludes nursery applications (See general "Fruits" listing)
						3.0	**8.0**	**NA**	**3**	**NA**	**NA**	**24**	**NS**	Permitted in Georgia and South Carolina	
PEANUT		✓		Preplant	Aerial or ground/ broadcast	2.0 EC, WDG	[4.0] NS	4.0	[2] NS	2	NA	24	10	Do not apply aerial in Mississippi	Assumes one crop cycle per year.
		✓		At plant, post plant		4.0 G	[4.0] NS	4.0	2	2	21	24	10		
		✓		At pegging		2.0 G EC, WDG	[4.0] NS	4.0	2	[2] NS	21	24	10		

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
				Total		**4.0 G 2.0 EC, WDG**	**4.0**	**4.0**	**2**	**2**	**10**	**24**	**10**		
PEAR		✓		**dormant/ delayed dormant** broadcast	aircraft, airblast	2.0 WDG, EC	2.0	NA	1	NA	NA	24	NA	Restricted use in California.	83222-20 allows 3.0 lb a.i./ A; however, this does not match the 2001 RED.
		✓		**Post-harvest** broadcast	aircraft, airblast	2.0 WDG, EC	2.0	NA	1	NA	NA	24	NS	Permitted in California, Oregon and Washington.	
				Total		**2.0 WDG, EC**	**4.0**	**NA**	**2**	**NA**	**NA**	**24**	**NS**		Multiple types of applications may occur in within a year in California, Oregon and Washington such as a post-harvest application and a dormant, delayed dormant. Excludes nursery applications

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
															(See general "Fruits" listing)
PEAS		✓		Preplant Seed treatment	Seed Treatment	0.30 0.000625 lb/lb seed WP 0.28 0.00058 lb/lb seed EC	NS	NS	NS	NS	NS	NS	NS		There is a range of potential application rates depending on the number of seeds per lb and the number of seeds planted per acre. Seeding information provide by BEAD.[2]
PECANS		✓		**dormant/ delayed dormant** broadcast	aircraft, airblast	2.0 EC, WDG	2.0	NA	1	NA	14	24	10		66222-19 and 66222-233
		✓		**foliar**; broadcast	airblast	4.3 EC, WDG	6.3	NA	3	NA	14	24	10		Some labels require a 28 d PHI
					aircraft	2.0 EC, WDG									Updated to reflect spray drift mitigation.
		✓		foliar; **orchard floors broadcast**	Ground boom, chemigation	4.3 EC, WDG	4.3	NA	2	NA	14	24	10		

Table A.5. Summary of Current Chlorpyrifos Usage																
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
				Total		**4.3**	**12.6**	**NA**	**6**	**NA**	**14**	**24**	**10**		Considers multiple type of applications (*e.g.*, dormant, foliar broadcast, and orchard floor) but excluding nursery For nursery applications (See general "Fruits" listing)
PEPPER		✓		Foliar	Ground broadcast	1.0 WDG	[8] NS	8.0	[8] NS	8	7	24	10	Permitted in Florida	FL040005; 1 crop cycle per year.
PINEAPPLE		✓		Post plant	Ground boom, broadcast	2.0 EC	6.0	6.0	3	NA	365	24	30	Permitted in Hawaii	HI090001 SNL Expires: March 29, 2014. Do not make applications beyond three months after planting.
PLUM/ PRUNE		✓		**dormant/ delayed dormant**; broadcast	Aircraft, airblast	2.0 EC, WDG	2.0	NA	1	NA	NA	24/ 4d	10		

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		foliar; **trunk spray/drench**	handheld, backpack, drench/dip, handgun, and low-pressure hand wand	2.5 3.0/100 gal WDG	2.5	NA	1	NA	NA		10		
				Total		**2.5**	**4.5**	NA	2	NA					Excludes nursery applications (See general "Fruits" listing)
POULTRY LITTER		✓		When needed, animal bedding/litter treatment.	Sprayer	0.07126 a.i./1000 sq ft 3.1 ME	NS	NA	NS	NA	NA		NS		53883-264, 84575-3
PUMPKIN		✓		Preplant Seed treatment	Seed treatment	0.3 0.00058 lb /lb seed WP	[0.3] NS	[1] NS	[1] NS	1	NS	NS	NS	California maximum single rate 0.000625 lb a.i./lb.	There is a range of potential application rates depending on the number of seeds per lb and the number of seeds planted per acre. Seeding information provide by BEAD.[4]

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
RADISH		✓		Foliar	Broadcast ground	1.0 EC	NS	1	NS	1	NS	24	NS	permitted in Oregon	OR090012 on radish grown for seed. Label valid until December 31, 2012. (per registrant SLN still valid)
		✓		Preplant	Soil incorporation ground	3.0 EC	12.0	3	4	1	NS	NS	10		
		✓		At plant/post-plant	In furrow drench/ treatment	3.0 EC 2.8 G	[15.0] NS	3	[5] NS	1	30, EC, 7, G	24	10		Only one granular application permitted.
				Total		**3.0**	**[22.0] NS**	**2**	**[9] NS**						Only one preplant or at plant application is assumed.
RIGHTS OF WAY, ROAD MEDIANS				When needed, soil broadcast	Granular or low-pressure wand	1.0 EC, G, Bait	[2.0] NS	NA	2	NA	NA	NS	7		Apply when needed
RUTABAGA		✓		Preplant	Chemigation, Groundboom	2.4 EC, WDG	[4.8] NS	2.4	[2] NS	1	30	24	10		
					Aerial	2.0 EC, WDG		2.0							Updated to reflect spray drift mitigation.

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		At plant/post-plant	In furrow drench/ treatment	2.4 EC, G WDG	4.8	2.4	[2] NS	1	7	24	10	Disallowed in California and Arizona.	Two crop cycles per year
				Total		**2.4**	**[9.6] NS**	**4.8**	**[4] NS**	**2**		**24**	**10**		
SEWER MANHOLE COVERS AND WALLS				When needed	Low pressure	0.31 lb/manhole RTU	NS	NA	NS	NA	NA	NA	NS		3 pints product/ manhole
SEED ORCHARD TREES		✓		**foliar**; broadcast	Ground boom	1.0 EC	3.0	3.0	NS	NA	30	24	7		62719-575, 62719-615
		✓			High volume sprayer	2.5 0.01 a.i./tree 0.02 EC	2.5	NS	[1] NS	NA	30	24	7		Cone worm treatment (62719-575 and 62719-615) Treatment of 1000 trees per acre would results in a single application rate of 10 lb a.i./a. DAS: 1000 is a bit high, typically for orchards 312 trees per acre
		✓		foliar; **stump treatment**	backpack, drencher, low	0.3 EC	0.3	1.0	NS	NA	30	24	7		62719-575, 62719-615

Table A.5. Summary of Current Chlorpyrifos Usage

Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
					pressure hand wand,										
				Total		**1.0**	**5.8**	**3**	**NS**	**NA**	**30**	**24**	**7**		The total number of applications assumed is either three foliar applications or two foliar applications with one stump treatment.
SORGHUM GRAIN		✓		Seed Treatment	Seed treatment	[0.0009] 0.01-0.0024 lb ai/ 100 lbs seed EC	0.01	0.01	[1] NS	1	NA	NS	NS		264-932
		✓		Preplant Soil Directed	Ground Spreader/T Band	1.5 G	1.5	1.5	[1] NS	1	60	24	10		
		✓		Foliar/Post emergent	Ground, Aerial, Chemigation	1.0 EC, WDG	1.5	[1.5] NS	[1] NS	3	30	24	10		PHI varies across labels
				Total		**3.3 G 1.0 EC, WDG**	**3.01**	**3.01**	**[3] CBD**	**3**	30	24	10		One crop cycle per year.
SOYBEAN		✓		foliar , post-emergence soil broadcast	broadcast ground, aerial, chemigation	1.0 EC, WDG	3.0	3.0	3	3	28	24	14		One crop cycle per year.

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
		✓		At plant/post plant treatment; soil band	ground boom	2.2 G 1.0 EC	3.0	3.0	1 (G), 3 (EC)	1 (G), 3 (EC)	28	24	10		
				Total		**1.0 EC, WDG 2.2 G**	**3.0**	**3.0**	**3**	**3**					One crop cycle per year.
STRAW-BERRIES		✓		Pre-plant	Aerial or ground/ broadcast	2.0 EC	2.0	**NS**	1	NS	NA	24	10	No use in Mississippi	33658-26
		✓		Foliar	Aerial or ground/ broadcast, foliar spray	1.0 EC, WDG	2.0	**NS**	2	**NS**	21	24	10		Two applications (2 lb ai) for all products per cc.
		✓		Post-harvest	Ground directed spray	1.0 EC, WDG	2.0	**NS**	2	**NS**	21		14		
				Total		**2.0**	**4.0**		**3**						One preplant application and two foliar and/or postharvest application permitted per year.
SUNFLOWER		✓		At plant	Aerial/ground	2.0 G	3.0	3.0	[1] NS	1	42	24	10		Per registrant 1 cc per year

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Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
		✓		Preplant		2.0 EC, WDG	3.0	3.0	[1] NS	1	42		10		2 inches min incorporation
		✓		Post emergent or foliar		1.5 EC, WDG	3.0	3.0	[2] NS	2	42		10		
				Total		**2.0**	**5.0**	**5.0**	**3**	**3**					Assumed either an at plant or preplant application followed with two foliar applications. One crop cycle per year
SWEET POTATO		✓		Preplant, soil broadcast	Aircraft, ground boom	2.1 G, EC, WDG	2.1	NS	1	1	125	24		LA090002, MS080007, NC090001 permits 60 PHI	
					Aircraft	2.0 G, EC, WDG									Updated to reflect spray drift mitigation.
TOBACCO		✓		Preplant	Aircraft, ground boom	2.0 EC, G, WDG	2.0	NS	1	1	7	24	NA		
TRITICALE		✓		Storage Commercial Slurry Seed Treatment	Seed treatment	0.003 0.0024 lb ai/ 100 lbs seed EC	[0.003] NS	[1] NS	[1] NS	[1] NS	NA	[10] NS	[10] NS		264-932 Seeding information provide by BEAD.[4] One crop cycle per year.

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
TURNIP		✓		Preplant	soil incorporation/ ground boom, handgun	2.3 G, WDG	[4.6] NS	2.3	[2] NS	1	30	24	10		Minimum incorporation: 2 inches.
		✓		Post plant	Soil incorporation/ ground boom, handgun	2.3 G, WDGP	[4.6] NS	2.3	[2] NS	1	30	24	10		Minimum incorporation: 2 inches.
				Total		**2.3**	**4.6**	**2.3**	**2**	**1**	**30**	**24**	**10**		Assumed either a preplant or post plant application. Two crop cycles per year
UTILITIES For use in and around telecommunications, power, utilities and railroad systems equipment: Buried cables, cable television pedestals, cables, pad-mounted electric power transformers, telephone cables, underground				When needed, broadcast	Product container	190.5 G 0.44 lb ai./100 sq ft (see comments)	NS	NS	NS	NS	NS	NS	NS		Applications permitted as needed. Reg. Nos. 13283-14, 13283-17 Broadcast product onto the ground covering the area of the pad location, plus a two-foot perimeter around the outside of the pad location.

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Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
vaults, telecommunications equipment, power and utilities equipment															
WALNUTS		✓		**dormant/ delayed dormant**; broadcast	Aircraft, airblast	2.0 EC, WDG	2.0	NA	1	NA	14	24	10		62719-301 (12 lb a.i./A)
		✓		**foliar**; broadcast	aircraft, airblast, chemigation	2.0 EC, WDG	4.0	NA	2	NA	14		10		Some labels do not specify retreatment interval.
		✓		foliar; **orchard floors broadcast**	Ground boom, chemigation	4.0 EC, WDG	4.0	NA	1	NA	14		10		
				Total		**4.0**	**10.0**		**4**						Excluding nursery applications; includes dormant, foliar broadcast, and orchard floor. For nursery applications (See general “Fruits” listing)

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	Residential	Agricultural	Forestry	Timing; Application Type	Method/ Equipment	Maximum Single Application Rate by Formulation[1] (lb a.i./A)	Maximum Application Rate		Maximum Application Number		PHI (days)[3]	REI (hours)[3]	MRI (days)[3]	Geographic Restrictions	Comments
							Per Year lb a.i./A	Per CC[2] lb a.i./A	Per Year	Per CC[2]					
WIDE AREA/ GENERAL OUTDOOR TREATMENT For ants and other misc. pests.	✓	✓		when needed, Broadcast	Ground sprayer	0.5084 lb ai/100 gal EC	[1.02] NS	NA	2	NA	NA	NS	NS		66222-19
				when needed, Drench	Drench	1	NS	NA	NS	NA	NA		NS		228-624
						[1] 8.2 lb a.i/100 gal EC	NS	NA	NS	NA	NA		NS		228-625
				Total		[1]	NS	NA	NS	NA	NA				
WHEAT		✓		Slurry Seed Treatment	Seed treatment	0.003 0.0024 lb ai/ 100 lbs seed EC	[0.006] NS	1	[2] NS	1	NA	NA	NA	Only for use in AZ, CA, CO, ID, KS, MN, MO, NE, NM, NV, ND, OK, OR, SD, TX, UT, WA and WY	Seeding information provide by BEAD.[4]
		✓		Foliar, soil treatment	Ground, broadcast	0.5 EC	[8.0] NS	4.0	[2] NS	1	14/ 28	24	14		PHI: 14 forage or hay, 28 grain or straw
		✓		Post-emergence foliar	Ground, Aerial, Chemigation	1.0 EC	[4.0] NS	2.0	[4] NS	2	14/ 28		NS		Label states 1.0 lb ai/A for cereal leaf beetles and then state max rate 0.5 lb ai/A in restriction). Some labels restrict no more than 2 applications per crop/season PHI 14 forage or hay, 28 grain or straw

Table A.5. Summary of Current Chlorpyrifos Usage															
Crop/Site	**Residential**	**Agricultural**	**Forestry**	**Timing; Application Type**	**Method/ Equipment**	**Maximum Single Application Rate by Formulation[1] (lb a.i./A)**	**Maximum Application Rate**		**Maximum Application Number**		**PHI (days)[3]**	**REI (hours)[3]**	**MRI (days)[3]**	**Geographic Restrictions**	**Comments**
							Per Year lb a.i./A	**Per CC[2] lb a.i./A**	**Per Year**	**Per CC[2]**					
				Total		**[1] 4.0 EC**	[12.006]	**[6.003] 5.0**	[8] NS	[4] 2					MO otherwise 2.0 plus seed treatment
WOOD PROTECTION TREATMENT TO BUILDINGS/ PRODUCTS OUTDOOR				When needed, Wood surface treatment	Low pressure handwand, backback sprayer, paintbrush	16.65 lb/10,000 sq ft 0.17 lb a.i./gal EC	NS	NA	NS	NA	NS	NS	NS		
						0.08 lb ai/gal EC, RTU EC, ME	NS	NA	NS	NA	NS	NS	NS		Apply 1 gal per 100 sq ft of wood

1. EC - emulsifiable concentrate; WDG – water dispersible granular in water soluble packet; WP – wettable power in water soluble packet; B – bait (granular), G – granular; ME – microencapsulated; RTU – ready to use.
2. Reported as per crop cycle or per season
3. PHI – Preharvest interval; REI – reentry interval; MRI – Minimum retreatment interval
4. Becker, J.; Ratnayake, S. Acres Planted per Day and Seeding Rates of Crops Grown in the United States, U.S. EPA OPP/BEAD, 2011; example calculations provided below:
   Beans: 0.00058 lb a.i./lb seed / 960 seeds/lb seed x 418,176 seeds/A [pgs. 19, 81 (beans, succulent)]
   Corn: 0.000625 lb a.i./lb seed / 1,800 seeds/lb seed x 59,739 seeds/A [pgs. 24, 81 (corn, sweet)]
   Cotton: 0.00116 lb a.i./lb seed / 4,500 seeds/lb seed x 85,00 seeds/A [pgs. 13, 81]
   Cucumber: 0.00058 lb a.i./lb seed / 12,000 seeds/lb seed x 80,418 seeds/A [pgs. 25, 81]
   Peas: 0.000625 lb a.i./lb seed / 1,361 seeds/lb seed x 653,400 seeds/A [pgs. 34, 82]
   Pumpkin: 0.00058 lb a.i./lb seed / 1,600 seeds/lb seed x 7,260 seeds/A [pgs. 37, 82]
   Sorghum: 0.001 lb a.i./lb seed / 11,000 seeds/lb seed x 100,000 seeds/A [pgs. 16, 39]
   Triticale: 0.003 lb a.i./100 lb seed / 109 lb seed/A [pg.16]
   Wheat: 0.003 lb a.i./100 lb seed /116 lb seed/A [pg. 16]
   [ ] indicate assumptions that are made when the information is not specified but can be inferred

Appendix 6: Review of Human Research

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from PHED 1.1; the AHETF database; the Outdoor Residential Exposure Task Force (ORETF) database; the ARTF database; ExpoSAC Policy 14 (SOPs for Seed Treatment); the 2012 Residential SOPs: Lawns/Turf, Outdoor Fogging/Misting Systems; registrant-submitted exposure monitoring studies MRIDs 44180401, 44301301, 44793301, 44829601, 42974501, 43062701, 44748101, 44748102, 46722701, and 46722702; and published literature studies are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency.

Appendix 7: Residential Mosquito ULV Spreadsheets

See attached spreadsheets:
- Appendix 7_1_Adult Worst Case Aerial Mosquito ULV applications.xlsx
- Appendix 7_2_Adult Best Case Aerial Mosquito ULV applications.xlsx
- Appendix 7_3_Child Worst Case Aerial Mosquito ULV applications.xlsx
- Appendix 7_4_Child Best Case Aerial Mosquito ULV applications.xlsx
- Appendix 7_5_Adult Ground Mosquito ULV applications.xlsx
- Appendix 7_6_Child Ground Mosquito ULV applications.xlsx

Appendix 8: Residential Post-Application Golfing Spreadsheet

See attached spreadsheet:
- Appendix 8_Chlorpyrifos Residential Golfer Postapp.xlsx

Appendix 9: Spray Drift Spreadsheets

See attached spreadsheets:
- Appendix 9_1_Adult Drift with MS TTR Data _ 6 lb ai through 3.xlsx
- Appendix 9_2_Adult Drift with MS TTR Data _ 2 lb ai and below.xlsx
- Appendix 9_3_Child Drift with MS TTR Data _ 6 lb ai through 3.xlsx
- Appendix 9_4_Child Drift with MS TTR Data _ 2_3 lb ai through 1_0.xlsx

Appendix 10: Occupational Handler Spreadsheets

See attached spreadsheets:
- Appendix 10_1_Chlorpyrifos Occup Handler Risk Estimates.xlsx
- Appendix 10_2_Occ Seed Treatment.xlsx

Appendix 11: Occupational Post-Application Spreadsheets

See attached spreadsheet:
- Appendix 11_Occupational Postapp.xlsx