

FEDERAL COURT

BETWEEN:

SAFE FOOD MATTERS INC.
and PREVENT CANCER NOW

Applicants

and

ATTORNEY GENERAL OF CANADA
and MINISTER OF HEALTH

Respondents

AFFIDAVIT OF DR. ELAINE MACDONALD
(Affirmed March 7, 2022)

I, Dr. Elaine MacDonald, of the City of Toronto, in the Province of Ontario, AFFIRM AS FOLLOWS:

A. Introduction

1. I am employed as a Program Director and Senior Scientist at Ecojustice Canada. Before this, I was a senior scientist at Ecojustice Canada. More details about my work are included in my affidavit affirmed January 19, 2022 (“**First MacDonald Affidavit**”).
2. The purpose of this affidavit is to set out the key documents, as contained in the Certified Tribunal Records served in Court File Nos. T-956-21 and T-121-22, relevant to the issues raised in the December 21, 2021 decision (the “**Amended Decision**”). The regulatory history of chlorpyrifos up to October 2021 is set out in the First MacDonald Affidavit. This affidavit provides information that occurred after the May 13, 2021 cancellation and phase-out

decision (the “**May 13, 2021 Phase-out Decision**”) and provides supplementary information and context for the Amended Decision. I have personal knowledge of the facts stated in this affidavit, except where those facts are stated to be based on information and belief in which case I believe them to be true.

3. Unless otherwise stated I have personally obtained, requested and/or downloaded regulatory documents from the Canada.ca website, the websites of applicable international agencies and associated online public registries, including those sourced to the affidavit of Elizabeth Gabel affirmed November 17, 2021 (“**Gabel Affidavit**”).
4. I have reviewed the Certified Tribunal Record for Court File No. T-956-21 (“**CTR**”), of which certain documents are described below. The respondents first served the CTR on August 17, 2021. A revised CTR was served on September 20, 2021, and a further revised public version was served on November 15, 2021. This affidavit summarizes certain documents contained in the November 15, 2021 CTR which are referenced as “CTR Doc” or “CTR Docs”. Most of these are excerpted in Exhibit D of the First MacDonald Affidavit. Excerpts from the CTR which are not included in the First MacDonald Affidavit are attached to this affidavit as **Exhibit “A”**.
5. I have also reviewed the Certified Tribunal Record served on February 7, 2022 in Court File No. T-121-22, which I refer to herein as the “**Supplementary CTR**”.

B. Events leading up to the May 13, 2021 Phase-out Decision

6. In 2019 and 2021 the PMRA issued a data call-in for human health information on the risks of chlorpyrifos. The events surrounding the 2019 and 2021 data call-ins for chlorpyrifos products are described in the First MacDonald Affidavit:
 - paragraphs 51-68 describe PMRA correspondence on concern about drinking water data deficiencies leading up to the data call-in; see also **First MacDonald Affidavit, Exhibit C** for a summary chart of data call-in requests on drinking water data and reported deficiencies, and PMRA's own summary in CTR Doc 026, attachment, pp. 8-9, reproduced at **First MacDonald Affidavit, Exhibit D**;
 - paragraphs 90-93 describes PMRA data call-ins for mosquito adulticide and greenhouse ornamental uses, for which the data received was ultimately rejected;
 - paragraphs 115-117 describes the 2021 human health data call-in; see also associated CTR Docs 003, 012, 026 (attachment), 103, 142, 145, 198 (attachment), 209 (attachment), 211 (attachment), 212, 400, 404, 406, 408, 409, 506, 507, 508, reproduced at of the **First MacDonald Affidavit, Exhibit D**; and
 - the Affidavit of Margaret Sears affirmed November 2, 2021 also describes the 2021 human health data call-in at paragraphs 36-38.
7. These data call-ins provided the basis for the May 13, 2021 Phase-out Decision.
8. The data requested by the PMRA was based in large part on the data used in the most recent EPA and EFSA assessments, including data associated with the development of toxicology endpoints, greenhouse and mosquito occupational risks, chlorpyrifos oxon, genotoxicity and other hazards identified in those assessments. Details of how the PMRA used the EFSA and EPA assessments to craft the data call-in are included in **CTR Docs 125-129, 131-138** and **143**, reproduced in Exhibit A to this affidavit.

9. The May 13, 2021 Phase-out Decision was the first time to my knowledge that the public was notified about the three year cancellation or phase-outs for all uses for a large number of registrations. After the environmental risk assessment, fourteen registrations had end use products with acceptable uses that would continue indefinitely,¹ and/or cancelled canola and garlic uses where the cancellation would be delayed for two years.² Between three and five registrations were fully cancelled (all uses) under the environmental risk assessment on a three-year phase out.³ The active registrations that were not fully cancelled at the end of the environmental risk assessment are listed at the end of the May 6, 2021 Science Management Committee briefing note supporting the May 13, 2021 Phase-out Decision (**CTR Doc 433, attachment 1, Table 1; CTR Doc 425** reproduced at Exhibit D of the First MacDonald Affidavit)
10. It is not clear if the Amended Decision purports to apply only to the four listed products. While the Amended Decision states that other registrations were either cancelled in the environmental risk assessment or discontinued, as noted above, a large number of registrations would have had to be discontinued between December 2020 and May 2021.
11. The CTR contains records of discontinuance requests or other contextual documents for some, but not all, of these registrations.⁴ I am advised by Charlotte Ireland, paralegal working with counsel for the applicants, and believe it to be true that she submitted an access to information request (A-2021-000382) in June 2021 for these documents. In response to this access

¹ Registration numbers 23704, 23705, 33113, 14879, 29650, 21997, 27479, and 32768 (CTR Doc 433). These products had label amendments for the remaining uses that would be implemented over 24 months. In CTR Doc 425 numbers 31113, 33356, are also listed.

² Registration numbers 23705, 33113, 14879, 29650, 27479, 32768, 52831, 29984, 33356, and 30985 had canola and garlic uses which would not be cancelled until December 2022, and then followed by a three-year phase-out (CTR Doc 433). In CTR Doc 425 numbers 25831 and 30985 are also listed.

³ Registration numbers 31417, 20944, 16458, 24648, 33295. In CTR Doc 433, attachment 1, 31417 and 33295 are listed as fully cancelled, all uses, but these are not included in the chart at CTR Doc 425. These are both manufacturing uses.

⁴ For example, registration number 33295 was discontinued as a result of not responding to the 2019 data call-in.

request, Ms. Ireland was provided with a list of registration documents from 2019-2021. This spreadsheet is attached as **Exhibit “B”**.

12. In September 2021 Ms. Ireland narrowed the request to include specific documents from this list under access request number A-2021-000964. In October 2021, a 260-day extension was “required” by the PMRA to provide these documents due to third party consultation; this extension letter is provided at **Exhibit “C”**. The CTR does not include many of the documents listed in Exhibit B. Further details are provided in section L of the First MacDonald Affidavit from paragraphs 134-139 and associated exhibits.
13. Registrations cancelled as a result of the 2019 data call-in were not subject to a re-evaluation update, and appeared to be included in the update provided in the May 13, 2021 Phase-out Decision as this was the first time the public would have known about the cancellations. This is confirmed by the attached chart in the briefing note to the cancellation decision (**First MacDonald Affidavit, Exhibit D, CTR Doc 433**). The four products listed in the Amended Decision are listed as having an April 12, 2021 discontinuation application that was “registered” on the public registry (see **First MacDonald Affidavit, Exhibit L**).⁵ It is therefore unclear why only these four registrations are highlighted in the Amended Decision. All registrations of chlorpyrifos that were active in 2020 have the same three-year phase-out period: the one described in the May 13, 2021 Phase-out Decision.
14. The PMRA has a policy entitled DIR2018-01: “Policy on Cancellations and Amendments Following Re-evaluation and Special Review” (“**Cancellation Policy**”) (**Gabel Affidavit, Exhibit B3**). DIR2018-01 sets out possible cancellation timelines under the *Pest Control Products Act* (“**PCPA**” or “**Act**”), some of which are a three-year phase-out similar to that used for the chlorpyrifos cancellation: one year of sale by registrant, followed by one year of sale by retailer, followed by one year of use. According to DIR2018-01,

⁵ Registration numbers 23621, 23704, 32694, 32768.

this timeline is only appropriate where “risks of concern are not considered imminent or serious” (**Gabel Affidavit, Exhibit B3**, p. 4).

15. The events surrounding the application of the Cancellation Policy for the May 13, 2021 Phase-out Decision is set out in the First MacDonald Affidavit at paras 115-133, and related **CTR Docs 211-215** and **431-433** reproduced in Exhibit D to that affidavit.

C. Post-decision concessions of the PMRA

16. I am advised by counsel and believe it to be true that on October 22, 2021, counsel for the respondents wrote to counsel for the applicants. This letter is attached to my affidavit as **Exhibit “D”**. The letter states:

I have confirmed that we have received instructions to consent to set aside the cancellation decision on the basis that, in the absence of any reasons for the phase-out period selected by the PMRA, that decision is unreasonable. In order to avoid a regulatory gap, PMRA will be asking for a stay of the set aside decision for 45 days to permit it to reconsider the issue.

17. On November 1, 2021, counsel for the respondents wrote to the Federal Court. This letter is attached to my affidavit as **Exhibit “E”**. The letter further describes the respondents’ position:

As noted in the Letter, we advised the Applicants on October 22, 2021 of our instructions to consent to set aside the decision that is at issue in the application bearing court file no. T-956-21... The decision at issue is that of the Pest Management Regulatory Agency (“PMRA”) made May 13, 2021 to cancel the registration of pest control products containing the active ingredient chlorpyrifos, which cancellation was made subject to a three-year phase-out period (the “Phase-out Decision”). As the Phase-out Decision did not give reasons for directing the three-year phase-out period, the Respondents acknowledge that the Phase-out Decision is unreasonable and must be set aside....

18. I am advised by counsel and believe it to be true that on November 25, 2021, the respondents served and filed written representations in response to a consolidation motion brought by the applicants. I attach an excerpt from these

written representations as **Exhibit “F”**. The written representations stated that “[g]iven that the Chlorpyrifos Update [the Phase-out Decision] does not include any reasons for the phase-out period selected, the Respondents have conceded it is unreasonable” (para 3).

19. In another part of the written submissions, the respondents elaborated on the basis for the concession:

The Chlorpyrifos Update does not indicate which [Pest Control Products] were subject to this cancellation, does not reference the Policy, and does not indicate why the three-year phase out period was selected. The Respondents have conceded the decision contains insufficient reasons such that it is unreasonable.

(**Exhibit F**, para 21)

20. The respondents also submitted that no evidence from the CTR served in November 2021 for Court File No. T-956-21 would be relevant given the respondents’ concession and that a new decision would render the judicial review application moot, which in their view could be determined without a record:

As PMRA is currently reconsidering its prior Chlorpyrifos Update in light of this concession, mootness may very well be an issue at or before the hearing of the Phase-out JR....

...the issues in the Phase-Out JR are limited to the appropriate remedy and, quite possibly, mootness. While the applicants seek a declaration from this Court that PMRA either lacked a factual basis for the phase-out period selected or lacked a rationale for the phase-out period selected, the former declaration (no factual basis) asks the Court to step into the shoes of the decision-maker whereas the latter (no rationale) is subsumed within the Respondents’ concession. In the absence of an articulation of the reasons for the phase-out period selected in the Chlorpyrifos Update, the Court cannot know the rationale for the PMRA’s decision. This legal issue can be argued in the absence of evidence.

(**Exhibit F**, paras 3 and 30)

D. The Amended Decision

21. In light of the respondents' November 15 submissions stating that the Minister intended to make a new decision, I am advised by counsel and believe it to be true that counsel for the applicants requested that the respondents advise them of the nature of and proposed timing of the new decision, and whether the PMRA would be conducting consultations on the proposed decision. Attached as **Exhibit "G"** is a December 8, 2021 letter from counsel for the applicants to counsel for the respondents, serving affidavits in Court File Nos. T-956-21 and T-1412-21 and asking for information about a new decision. The letter contains a link to download the First MacDonald Affidavit; this link has been redacted to protect confidential information.
22. On or about December 21, 2021, the PMRA published a new decision (the "**Amended Decision**"), purporting to cancel the chlorpyrifos registrations for four products, explaining the context for the decision, and imposing two reporting conditions. The Amended Decision imposes an identical phase-out period to the May 13, 2021 Phase-out Decision. The Amended Decision is included as Supplementary CTR Doc 24 and is attached to this affidavit as **Exhibit "H"**.
23. In contrast to the May 13, 2021 Phase-out Decision, the Amended Decision specifies the section of the Act the PMRA is relying on and the specific products subject to the decision. Unlike the first decision, the Amended Decision highlights only four specific registrations and implies that it does not apply to all 24 registrations that were listed as active registrations on the public registry until November 2021.⁶ The details of the 24 registrations are discussed at section L of the First MacDonald Affidavit, paragraphs 134-139, and are summarized in Exhibit L to that affidavit.

⁶ Registration numbers 23621, 23704, 32694, and 32768: **Exhibit H**, p. 2.

24. As noted earlier a number of these registrations appeared to have been covered by the May 13, 2021 Phase-out Decision as they still had uses that were permitted and not cancelled after the completion of the environmental risk assessment such as canola and garlic uses, or mountain pine beetle. For example, there are two registrations for Adama (23705 and 33113) which still had pine beetle, canola and garlic uses allowed beyond December 2023 (**CTR Doc 433**, attachment 1, Table 1; **CTR Doc 425** reproduced at **First MacDonald Affidavit, Exhibit D**). These registrations are not highlighted in the Amended Decision.
25. I am advised by counsel and believe it to be true that counsel for the respondents did not advise the applicants of the existence of the Amended Decision until January 14, 2022, six days before the limitation period ended. Attached as **Exhibit “I”** is a copy of an email from Andrew Law, counsel for the respondents in this application, dated January 14, 2022. There was no public consultation on the Amended Decision.

E. Cancellation policy update

26. On the same date as the Amended Decision was published, on December 21, 2021, the PMRA published an Information Note: “Update on implementation of post-market decisions” (“**Cancellation Policy Update**”), attached to this affidavit as **Exhibit “J”**.
27. The Cancellation Policy Update indicated that “[s]ince the adoption of the Cancellation Policy, Health Canada has received numerous questions and requests for clarifications on its implementation. While work to update the policy is beginning, Health Canada has identified an area that would benefit from greater clarity around the status of cancelled products.”
28. The Cancellation Policy Update states that “as of 21 December 2021, Health Canada will immediately cancel pest control product registrations on the date of a decision made under paragraph 20(1)(a) ...” It states that “[i]f there are no serious and imminent risks to human health or the environment, Health

Canada will allow for a phase-out period consistent with the Cancellation Policy and will impose any conditions necessary for carrying out the purposes of the *Pest Control Products Act* under the authority of paragraph 21(5)(a) of the *Pest Control Products Act*.”

29. The Cancellation Policy Update also clarifies that when this is done, there will be no further import or manufacture of the product. However, continued possession, handling, storage distribution and use will be permitted under subsection 21(5)(a) of the Act.
30. It is unclear from the Cancellation Policy Update whether this interpretation of DIR2018-01 applied at the time of the May 13, 2021 Phase-out Decision. The decision did not specify whether the PMRA relied on subsection 21(5)(a) of the Act, nor was there any guidance regarding manufacture or import in the decision or cancellation policy. Accordingly, it is not clear if registrants continued to manufacture or import during the remainder of 2021. (**Gabel Affidavit, Exhibit A11**)
31. No mention is made in the Amended Decision or the Cancellation Policy Update about the status of label conditions post-cancellation. Users are required to comply with the labels under subsection 6(5)(b) of the Act, but that section specifies that it applies to registered products. The PMRA does not mention whether it is a condition of phase-out that labels must be complied with in the Amended Decision or in the Cancellation Policy Update. (**Supplementary CTR Doc 24, Exhibit H**). Notably the PMRA relied extensively on label conditions for human health in its 2003 re-evaluation of chlorpyrifos, PACR2003-03 (see for example **Gabel Affidavit, Exhibit A6**, pp. 16, 18 and 21). PACR2003-03 is discussed further in paragraphs 26-29 of the First MacDonald Affidavit.

F. Updates to the public registry since May 13, 2021

32. I reviewed the public registry on March 4, 2022 with specific attention to the four registrations listed in the Amended Decision. Pest control products

containing chlorpyrifos as an active ingredient are still not listed as cancelled on the public registry, as requested by the applicants in T-956-21, but instead are now listed as “phase out”. The specific conditions on import and manufacture are not included in the public registry. It is unclear if the Cancellation Policy Update is intended to notify importers or manufacturers of the restrictions on import or manufacture placed on any specific product. The Cancellation Policy Update states that “Health Canada will be publishing further instructions on how to find information [in the public registry] on cancelled products that are being phased-out” (**Exhibit J**).

33. A further update was posted on the PMRA website on February 7, 2022. A copy of this update is attached as **Exhibit “K”**. The stated purpose of the update is to “explain how to find information from Health Canada’s Pesticide Product Information Database (PPID) on cancelled products that are currently being phased out.”
34. The update states that “[i]f there are no serious and imminent risks to human health or the environment, Health Canada will allow for a phase-out period consistent with the Cancellation Policy and will impose any conditions necessary for carrying out the purposes of the *Pest Control Products Act*...” This update explains that “phase-out” is listed as the registration status for these products, and that the products are not listed as “cancelled”, and also that the detailed registration page lists the last sale by registrant, retail and an “expiry date” (**Exhibit K**, pp. 1-3).
35. I have also used this tool in the public registry for chlorpyrifos and confirm that the chlorpyrifos products subject to a phase-out, including the four products listed in the Amended Decision, are not listed as cancelled in the public registry. The public registry does indicate the last date of sale and retail sale. The public registry for the four products listed in the Amended Decision do not include any other information on the conditions imposed on the cancellation such as use, label requirements or reporting requirements. The Amended Decision in REV2021-04 is not posted as a published document

associated with these products in the registry, so a member of the public is not notified when they view each product whether there are any conditions imposed on the phase-out or what the context or reason for the phase-out is.

36. Each product is also listed under “historical applications” as if it were “discontinued”, not cancelled, due to lack of data (**First MacDonald Affidavit, Exhibit L**). The four products listed in the Amended Decision are listed as having discontinuation applications dated April 12, 2021 (application numbers 2021-1514, 2021-1513, 2021-1502, and 2021-1511). All other products also have listings for discontinuation applications.

G. Additional information that was before the PMRA after the Phase-out Decision

37. An earlier version of the First MacDonald Affidavit was affirmed on November 24, 2021, and served upon the PMRA on December 8, 2021 along with the affidavit of Margaret Sears (affirmed November 2, 2021), the affidavit of Mary Lou McDonald (November 3, 2021), the affidavit of Elizabeth Gabel (November 17, 2021), and the affidavit of Charlotte Ireland (December 7, 2021). **Exhibit G** above contains the service letter for these affidavits with a redaction of the link to the confidential version of the documents.
38. The November 24, 2021 version of my affidavit is identical to the January 19, 2022 version now included in these applications, with one exception. The January 19, 2022 version removed one sentence of confidential information that was previously contained in the quote from CTR Doc 467 in paragraph 152 of my affidavit under the heading “higher potential residues”. This confidential information is highlighted in the January 14, 2022 email from PMRA counsel attached above as **Exhibit I** to this affidavit. I am advised by counsel and believe it to be true that this sentence was removed from my affidavit on consent of the parties to allow the entire affidavit to be public. The public version of my affidavit was re-commissioned and re-served on January 19, 2022.

39. Accordingly, the information and summaries of information contained in the First MacDonald Affidavit were before the PMRA when it made the Amended Decision on December 21, 2021. This includes:
- paragraph 164 and Exhibit O: regarding media indicating that Canadian farmers may have been stockpiling products containing chlorpyrifos ahead of the December 2023 end date for lawful use of the products;
 - paragraphs 76-89 (section D and E): regarding the PMRA’s drinking water assessment indicating exceedances of the acute reference dose for aggregate diet and drinking water exposures in Canada; and
 - paragraphs 90-93 (section F): describing the data deficiencies for occupational exposures arising from mosquito and greenhouse uses.
40. I am advised by counsel, and believe it to be true, that the applicants’ questions on December 8, 2021, about the nature of the proposed new decision, when it would be made and whether the PMRA would conduct public consultations, were not responded to prior to the decision. (see **Exhibit E, Exhibit G**).

H. PMRA ignored the Cancellation Policy requirement to consider the potential magnitude of harm

41. As set out in the First MacDonald Affidavit in paragraphs 36-47 and associated exhibits, the primary human health concern for chlorpyrifos is developmental neurotoxicity in infants and children. As discussed below, the potential for these effects, due to combined exposures from food and drinking water, were modelled by the PMRA’s scientists who predicted that the drinking water levels of comparison (“**DWLOCs**”) would be exceeded for “certain populations” due to high rates of application for certain crops.
42. The developmental neurotoxicity impacts of chlorpyrifos are potentially serious. In 2014, the EPA released a revised human health risk assessment for chlorpyrifos. This assessment concluded that the epidemiological evidence consistently identified adverse neurodevelopmental outcomes in children after

chlorpyrifos exposure, including evidence of “delays in mental development in infants (24-36 months), attention problems and pervasive developmental disorder in early childhood, and intelligence decrements in school age children” (**Gabel Affidavit, Exhibit C11**, 2014 EPA Human Health Risk Assessment, p. 42).

43. The 2014 EPA risk assessment also noted the uncertainty around effects on the developing brain meant that “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” (**Gabel Affidavit, Exhibit C11**, p. 50). The European Union summarized the situation as follows: “[t]he available regulatory studies and scientific literature, including epidemiological data, provide evidence of developmental neurotoxicity, leading to adverse neurological outcomes in children.” (**Affidavit of Charlotte Ireland, Exhibit B**, p. 11, **Supplementary CTR Doc 05**, p. 9).
44. The PMRA’s Cancellation Policy (**Gabel Affidavit, Exhibit B3**, p. 3) states that the health and environmental considerations for determining cancellation and amendment timelines include the “potential magnitude of harm, i.e., seriousness of the effect of concern, including irreversibility.” None of these potential effects are acknowledged or mentioned in the Amended Decision or in the associated December 2021 Briefing Note (**Supplementary CTR Docs 17 and 24**).

I. Lack of consideration of occupational risks

45. As described in the First MacDonald Affidavit in paragraphs 90-93 (section F) and associated CTR documents, the PMRA never received sufficient occupational risk information to characterize the risks from greenhouse and mosquito uses. This information was first requested in the 2000s and again in 2019 and 2021. A chart showing when the data requests were made is included in the First MacDonald Affidavit at Exhibit C. These uses were allowed to continue after the environmental risk assessment in 2020. The PMRA found it had insufficient information on these risks.

46. These uses, and occupational exposures and risks more generally are not mentioned in the Amended Decision or the associated Briefing Note (**Supplementary CTR Docs 17 and 24**). The PMRA makes no finding that these pose a low risk. These uses were permitted for the registration numbers listed as impacted by the Amended Decision (23621, 23704, 32694, 32768). The permitted label uses for these are summarized in Exhibit L of the First MacDonald Affidavit.
47. The full label for the pest control product Pyrate 480 EC (23704) as it was posted in June 2021 is contained in the First MacDonald Affidavit as Exhibit P and permits use on pests of ornamentals in greenhouses, and mosquito uses as well as other uses. I downloaded the label for Sharphos Insecticide (32768) from the PMRA database. This label has been updated some time after June 8, 2021, and indicates that this product is currently allowed to be used on onions, garlic and greenhouse ornamentals as well as other uses. This label is attached to this affidavit as **Exhibit “L”**.

J. Inconsistent treatment of food alone dietary risk information

48. The applicable policies explaining how the PMRA conducts dietary risk assessments are described at paragraphs 22-25 of the First MacDonald Affidavit, and are contained in the **Gabel Affidavit, Exhibit A6**, p. 7, **Exhibit B10**, pp. 7-9, **Exhibit B11**, p. 4, and **Exhibit B12**, pp. 2 - 5 and 6.
- a. PMRA reliance on the 2020 EPA Registration Decision*
49. The Amended Decision relies on the American assessment of dietary risks:

The decision of the United States to revoke all tolerances (in other words, MRLs) acknowledged that there were no risks of concern around chlorpyrifos residues on food based on their scientific assessment.

[The 2020] USEPA assessment took into consideration the more recent health information available since Health Canada’s assessment, as well as the more extensive use pattern that exists in the United States than in Canada. In other words, as acute and chronic dietary risks for all American populations exposed to food treated with

chlorpyrifos were shown to be acceptable, this would be the same for Canadians.

50. The EPA risk assessments and their analysis of dietary risk is described in paragraphs 45-47 of the First MacDonald Affidavit. The EPA's 2016 assessment, which concluded that the residues of chlorpyrifos on most individual food crops exceeded the reasonable certainty of no harm standard, is contained in the **Gabel Affidavit, Exhibit C13, p. 81050**. The EPA proposed to revoke all food tolerances due to these adverse safety findings in 2015, 2016 and again in 2021 (**Gabel Affidavit, Exhibits C8, C13, and C14**). The revocation took effect in February of 2022.
51. The EPA 2020 registration decision, relied on by the PMRA for the Amended Decision, is included as Supplementary CTR Doc 10. The EPA considered the 2020 risk assessment in the wake of a decision by the United States Court of Appeals for the Ninth Circuit (the "**9th Circuit Court**") (attached to the **First MacDonald Affidavit** as **Exhibit F**). The 9th Circuit Court indicated that if, based on the 2020 risk assessment and scientific advisory panel, the EPA could conclude that modified tolerances or registrations would be safe with reasonable certainty, then they could be maintained. This was not the outcome of the EPA's review. Instead, in the final rule in 2021, the EPA revoked all food tolerances based on the combined aggregate food, drinking water and residential exposures.
52. As noted at paragraphs 161-162 of the First MacDonald Affidavit, the EPA published an analysis and reasons for its final 2021 rule revoking all tolerances for chlorpyrifos (food residues, known in Canada as "maximum residue limits" or "**MRLs**"), thereby effectively banning all agricultural uses of chlorpyrifos in the United States on February 28, 2022. The EPA's 2021 final rule is included as **Supplementary CTR Doc 15** and in the **Gabel Affidavit, Exhibit C14**.
53. Based on the Amended Decision, it appears that the PMRA relies on EPA's 2020 dietary risk assessments, without comment on whether this analysis

considers the difference between Canadian and US reference doses. Elsewhere in the Amended Decision, the PMRA notes that Canadian reference doses are in some cases “more conservative (in other words more protective)” than those used by the US EPA (**Exhibit H**, Amended Decision, p. 6).

54. For example, the chart prepared by health experts at the PMRA for the May 2015 Briefing Note and supported in the October 2000 dietary risk assessment indicates that the acute food reference doses for infants, children and youth up to age 12 in Canada is 0.75 µg/L while the reference dose in the United States ranged from 12-15 µg/L (October 2000 dietary risk assessment, **First MacDonald Affidavit, Exhibit D, CTR Doc 375**, p. 22, Table 2; **CTR Doc 026**, attachment, p. 12, Table 1). It is not clear whether the PMRA compared predicted food-only exposure values from the US to Canadian reference doses.
55. The full 2020 EPA human health risk assessment containing those values is not included in the Supplementary CTR. I downloaded the EPA assessment from <https://www.regulations.gov/document/EPA-HQ-OPP-2008-0850-0944>, this document is attached to this affidavit as **Exhibit “M”**. The most recent dietary risk assessment for food alone in Canada found that the exposure attributable to food alone was a high percentage of the acute reference dose. The potential daily intake accounted for 71% of the acute reference dose for children 1-6 years and 74% of the acute reference dose in females 13-50 years (**Gabel Affidavit Exhibit A6**, p. 8; **First MacDonald Affidavit, Exhibit D, CTR Doc 375**).

b. Inconsistent treatment of food residues

56. The Amended Decision also states that “[n]o health risks from chlorpyrifos food residues alone were identified in Health Canada’s previous assessment” (**Supplementary CTR Doc 24**, p. 4). This likely reflects the fact that the acute reference dose was not exceeded for food alone in the October 2000 assessment, as described above.

57. As explained in paragraph 28 of the First MacDonald Affidavit, the previous dietary risk assessment was completed in October 2000 in support of the 2003 risk assessment (**Gabel Affidavit Exhibit A6**, section 4.3; **First MacDonald Affidavit, Exhibit D, CTR Doc 375**). At that time, there was no attempt to determine aggregate risks from food and drinking water due to a lack of data. (**Gabel Affidavit, Exhibit A6**, section 4.3.1). The PMRA also noted in 2003 that there were “significant data gaps in the field residue data” and that the MRLs relied on to determine food residues for the 2000 dietary risk assessment “do not meet the modern Residue Chemistry Guidelines and may not reflect current rates and methods of application.” The assessment therefore had limitations even when it was done in 2000. (**Gabel Affidavit, Exhibit A6, p. 9**)
58. Since that time, PMRA scientists have further questioned the reliability of the previous dietary risk assessment calling it “outdated” on several different grounds, including higher potential residues, higher percent crop treated, use expansions, new MRLs and newer consumption data (**First MacDonald Affidavit, Exhibit D, CTR Doc 467**, pp. 2-3, also see draft of this document at **CTR Doc 209 (attachment 2, p.4)**). None of these limitations are mentioned in the Amended Decision.

c. Inconsistent treatment of CFIA data, without explanation

59. In the Amended Decision, the PMRA also relies on a low frequency of detection on food, citing the 2013-2017 Canadian Food Inspection Agency (“**CFIA**”) food residue data and US Pesticide Data Program data (Amended Decision, **Supplementary CTR Doc 24**, p. 4). The PMRA also compares the level of residues detected in Canada and the United States and compares these residue values to the MRLs. Issues associated with reliability of detection, such as whether the limits of detection are low enough to reliably detect Canadian MRL exceedances, are not mentioned in the Amended Decision or Supplementary CTR. Further information related to this is contained at First MacDonald Affidavit, Exhibit D, CTR Docs 197 and 026, attachment, p.8.

60. The Amended Decision does not mention that in April 2021, PMRA scientific staff identified the same CFIA data as suggestive of higher potential risks, noting “[the monitoring data] showed residues of chlorpyrifos in various commodities were significantly higher than those used in the 2000 DEA. This suggests higher dietary exposure is possible, especially acute exposure” (**First MacDonald Affidavit, Exhibit D, CTR Doc 467**, p. 2).
61. These seemingly inconsistent conclusions in the record about the relevance of the CFIA residue data and whether the information points to higher or lower risks from food are not explained in the Amended Decision or in the Supplementary CTR. The Supplementary CTR and Amended Decision do not disclose whether the PMRA considered the potentially higher risks of higher residues on food detected in Canada that its own scientists emphasized in past analyses, or if so, how this was considered.
62. The Amended Decision also does not address how a focus on food alone, without consideration of aggregate risk, is in compliance with subsection 19(2) or the purposes of the PCPA.

K. PMRA ignored its own drinking water policies, modelling and data, and improperly relied on draft guideline revocation

a. PMRA policy on drinking water exposure assessments

63. In July 2003, the PMRA published a Science Policy Note entitled “General principles for performing aggregate exposure and risk assessments” (**Gabel Affidavit, Exhibit B15**). This policy explains the approach that the PMRA takes when performing aggregate exposure and risk assessments of food, residential and drinking water exposures, and explains how modelling is used to estimate combined exposure. For example, this document states:

If a pesticide has any potential to contaminate water resources based on use patterns, the PMRA uses water exposure models to estimate the concentration of the pesticide that could run off into surface water or leach into shallow groundwater. The concentration estimates generated from the models are considered to be upper bounds on pesticide concentrations in drinking water obtained from surface and groundwater sources. The

PMRA then calculates a drinking water level of comparison (DWLOC), which is the highest concentration of a pesticide in drinking water that would be acceptable (i.e., produce total exposure equal to the reference dose), considering the estimated exposure to that pesticide from other sources (i.e., food and residential uses). Upper-bound estimates (over-estimates) of water consumption are used for infants, children and adults. Separate DWLOCs are calculated for different exposure durations and age groups where warranted, e.g., for acute (one-day), or for chronic (long-term) exposures.

The PMRA compares the model-generated concentration estimates for a pesticide in ground- and surface water to the DWLOC. If the model-estimated concentrations in ground- and surface waters are less than the DWLOC, the PMRA concludes with reasonable certainty that residues of the pesticide in drinking water from present uses do not contribute towards an aggregate level of exposure (food and water) that exceeds a risk level of concern. If the model estimates are greater than the PMRA's levels of comparison for drinking water (DWLOC), the PMRA refines its model estimates using more realistic information/assumptions and compares the refined estimates to levels of comparison for drinking water again (USEPA, 2000a). If the model-estimated water concentrations still exceed the PMRA's levels of comparison (DWLOC) for the pesticide in drinking water, the PMRA may require water quality monitoring data for the pesticide, and conduct an in-depth review of the data to determine if they are acceptable and reliable for use in quantitative drinking water exposure and risk assessment. For products under re-evaluation, the PMRA considers all available monitoring data in conjunction with the modelling data to come up with potential exposures (Health Canada, 2003).

(emphasis added, **Gabel Affidavit, Exhibit B15**, pp. 8-9)

b. PMRA drinking water modelling

64. As explained in the First MacDonald Affidavit at paragraphs 51-59, 63-69, 72-85 and associated CTR documents, after the 2014 EPA risk assessment the PMRA identified chlorpyrifos oxon as a transformation product of concern and noted the absence of an aggregate food and drinking water assessment for chlorpyrifos. In 2016 and 2017, the PMRA conducted initial and refined modelling of drinking water exposures, using available drinking water monitoring data and the pre-oxon DWLOCs established in 2003. The result of both the initial and refined assessment was exceedances of the DWLOCs for

the use pattern that will be allowed under the phase-out until the end of December 2023. The modelling occurred as follows:

- In January 2016, the Environmental Assessment Directorate was to provide estimated environmental concentrations (“EECs”) to Health Evaluation Directorate for comparison to DWLOC previously published in PACR2003-03. The outcome would inform whether additional work would be needed for the health component. (January 26, 2016 minutes, **First MacDonald Affidavit, Exhibit D, CTR Doc 390**)
- When compared with the 2003 DWLOCs (acute 2.9 - 690 µg/L, chronic 7.4 - 700 µg/L), these revised EECs still exceeded the DWLOCs for certain populations. (May 31, 2016 Briefing Note, **First MacDonald Affidavit, Exhibit D, CTR Doc 391**)
- In a May 2016 directors general meeting, the Health Evaluation Directorate identified the need for refined level 2 EECs for chlorpyrifos and relevant transformation products. Environmental Assessment Directorate was to provide this to Health Evaluation Directorate by January 2017 (**First MacDonald Affidavit, Exhibit D, CTR Doc 394**)
- Environmental Assessment Directorate provided the drinking water review that assessed available environmental fate data of chlorpyrifos and its transformation products, as well as water monitoring information of chlorpyrifos from Canada and the United States in May 30, 2017. The revised EECs for chlorpyrifos alone exceeded the 2003 DWLOCs for acute risk for certain populations. The DWLOCs for acute risk ranged from 2.9 to 690 µg/L, and the water monitoring EEC value was 4µg/L (**First MacDonald Affidavit, Exhibit D, CTR Docs 045, 400, 451, 454**).

65. The technical memorandum describing the methods used in the 2017 drinking water model prepared by the Environmental Assessment Directorate scientists indicates that water monitoring data was considered. For example, the memorandum notes that the maximum concentration detected in Canadian

groundwater was 0.09µg/L, from a well in Quebec in 2005 (**First MacDonald Affidavit, Exhibit D, CTR Doc 454**, p. 7).

66. In the discussion of the methods to be used for the drinking water modelling, PMRA staff indicated that “all available relevant water monitoring data were considered” (**First MacDonald Affidavit, Exhibit D, CTR Doc 085, attachment**, p. 5).
67. The technical memorandum on drinking water modeling stated that limits of detection for samples were sometimes well above the DWLOCs. For example, the limits of detection ranged from 0.003-30 µg/L for treated and bottled water. (**First MacDonald Affidavit, Exhibit D, CTR Doc 454**, p. 7). My understanding of the relevance of this is that some exceedances may not have been detected, due to lab constraints.
68. The technical memorandum notes also that the maximum detection was 44 µg/L in Quebec in May 2011, although from a location unlikely to serve as a drinking water source (**First MacDonald Affidavit, Exhibit D, CTR Doc 454**, p. 10). The second highest detection, of 4 µg/L, was from a river that was considered to be a potential drinking water source. (**CTR Doc 454**, p. 11). The memorandum explains that maximum levels detected in Canadian surface water (44 µg/L; 4 µg/L) are within the range of those predicted through acute surface water modelling from onion and garlic uses (**CTR Doc 454**, pp. 7 and 10-12).
69. In other words, my understanding from the conclusions in the CTR from PMRA’s own scientists is that the exceedances of DWLOCs measured from actual drinking water monitoring were found to be consistent with what the model predicted would be found in drinking water as a result of applications on those crops.
70. Based on this the PMRA scientists’ memo concludes that “[t]he highest maximum detection in potential drinking water monitoring data (4µg/L) is an appropriate value to use in the acute dietary risk assessment of chlorpyrifos”

(emphasis added, **First MacDonald Affidavit, Exhibit D, CTR Doc 454**, p. 13). This conclusion seems to directly contradict the Amended Decision, but there is no supporting technical memorandum or analysis for the conclusion in the Amended Decision, nor is any such information contained in the Supplementary CTR.

71. In July 2018 the estimated environmental concentrations were modelled using a reduced use pattern. This proposed reduced use pattern is far more limited than what is currently in place until December 2023. Under the reduced use pattern, the DWLOCs for acute risk for chlorpyrifos alone were still exceeded even when *minimum* application rates were used and were much higher when maximum application rates were used or when chlorpyrifos and the transformation product TCP were included (**First MacDonald Affidavit, Exhibit D, CTR Doc 66** and attachment). That assessment included a variety of agricultural uses such as cereals, canola and lentil. A further assessment was then conducted with an even more reduced use pattern (see **CTR Doc 466**, included in **Exhibit A**). That assessment was limited to greenhouse, structural and mosquito uses and did not assess the full uses that would be permitted during the three-year phase out.
72. The PMRA never disclosed the drinking water modelling or provided it to the public. The PMRA also deleted a statement from the 2019-2020 re-evaluation documents recommended by the re-evaluation coordinator for chlorpyrifos, Mei Qi, that stated that drinking water exposures were found to be potentially unacceptable. The statement was as follows:

Regarding the health risk assessment from drinking water exposure, chlorpyrifos concentrations from the most recent water monitoring data, which would reflect the currently registered uses of chlorpyrifos, indicate potential unacceptable risk for some population groups.
(**CTR Doc 086**, attachment, pp. 2 and 30)
73. The context for this statement, and the rationale for deleting it as irrelevant to the environmental risk assessment, is explained in paragraphs 94-99 of the First MacDonald Affidavit (section G).

74. The PMRA documents in the CTR also identified various limitations of the drinking water assessment:
- The PMRA was using the DWLOCs from the 2003 risk assessment. Those were based on dietary exposure estimates (using the use patterns, dietary consumption information, and residue information that the PMRA had at that time) from October 2000. (**Gabel Affidavit, Exhibit A6**, section 4.3; **First MacDonald Affidavit, Exhibit D, CTR Doc 375**) These endpoints had been questioned by PMRA scientists and did not include endpoints for chlorpyrifos oxon. This is discussed in more detail in the First MacDonald Affidavit at paragraphs 14, 37-41, 44-50, 59, 61-65 and 67.
 - For the purpose of all of these assessments, it appears from the documents in the CTR that chlorpyrifos oxon was treated as being included in the chlorpyrifos assessment as if it had the same toxicity as chlorpyrifos (**First MacDonald Affidavit, Exhibit D, CTR Doc 045**). In the US EPA assessments, chlorpyrifos oxon was assessed as having far higher toxicity than chlorpyrifos alone. (see paragraphs 14 and 58-59, 67 and 69 of the **First MacDonald Affidavit and Exhibit D, CTR Doc 034**, attachment, **CTR Doc 038**, pp. 2-3 and first attachment, **CTR Doc 139**, p. 2; **Gabel Affidavit, Exhibit C8**).
 - The PMRA does not and did not have any reference doses or associated DWLOCs for chlorpyrifos oxon (**First MacDonald Affidavit** at paragraph 67, **CTR Doc 026**, attachment, pp. 12-14, **CTR Doc 034**, attachment, **CTR Doc 139**, p. 2). I was unable to find anything in the CTR explaining why chlorpyrifos oxon was assessed as having lower toxicity in Canada than in the US or if such an assessment occurred.
 - The CTR documents are clear that these analyses also did not consider the transformation product DES, a metabolite of concern of chlorpyrifos (**First MacDonald Affidavit, Exhibit D, CTR Doc 400**).

75. Apart from the limitations described above, the drinking water modelling up to early 2018 appears to follow the PMRA's publicly available policies for assessing drinking water risks and appears to account for aggregate risk from diet and drinking water.
- c. PMRA ignores its own modelling for the use pattern permitted in the phase out*
76. There is no reference to the PMRA's modelling or the conclusions reached from this modelling in the Amended Decision or Supplementary CTR.
77. Instead, the decision emphasizes only drinking water monitoring. This appears to be the same monitoring that was used for the modelling discussed in the First MacDonald Affidavit in paragraphs 76-85 and above. There is no analysis from scientific staff questioning the 2016-2018 modelling or incorporating newer monitoring data. The recommended use of the maximum detected levels in potential drinking water for the risk assessment, or its application to the currently allowed use pattern under the phase-out in the Supplementary CTR.
78. It is therefore difficult to understand the comments in the Amended Decision that suggest that because there were additional risk assessment measures in 2007, the monitored 2005 exceedance of the DWLOC can be discounted. This appears to be the same value that the PMRA decided should be used as the basis of the dietary risk assessment in 2016-2017 because it was consistent with modelling. The environmental assessment directorate found that the monitored exceedance was consistent with what they modelled for onion and garlic uses (**First MacDonald Affidavit, Exhibit D, CTR Doc 454**, p.11).
79. Onion and garlic uses were not cancelled in 2007, and the 2017 model is for onion and garlic, which are part of the use pattern permitted under the phase-out. There is no updated memorandum from the environmental assessment directorate in the Supplementary CTR rejecting the approach in the 2017 memo or concluding that the 4µg/L value they selected was not appropriate for use in dietary risk assessment. This entire analysis is simply not

mentioned. A member of the public without access to the CTR would not know that the PMRA had ever modelled drinking water exposures.

80. The Amended Decision also states that:

There is also a low level of concern for chlorpyrifos breakdown products including chlorpyrifos oxon, a byproduct of chlorine treatment. As chlorpyrifos is not often detected and unlikely to be found in Canadian drinking water sources at levels that may pose a risk to human health, the formation of oxon at a level of concern is not expected, if treated with chlorine.

(Supplementary CTR Doc 24, p. 5)

81. This reference to “the formation of oxon at a level of concern” is difficult to understand. There is nothing in the CTR or Supplementary CTR that I could locate comprising a toxicological assessment or a reference dose for chlorpyrifos oxon in Canada. It is not clear from the record whether there are any reference doses, drinking water levels of comparison, or scientific analysis at all regarding the toxicity of chlorpyrifos oxon. As noted above, the CTR documents state that the PMRA was using DWLOCs for chlorpyrifos alone that were developed in 2003 or earlier, prior to the 2014 EPA assessments that identified chlorpyrifos oxon as a drinking water metabolite of concern, and identified it as more toxic than chlorpyrifos.

82. As described in the First MacDonald Affidavit, PMRA staff scientists expressed specific concerns about chlorpyrifos oxon following the EPA’s 2014 risk assessment (see **First MacDonald Affidavit** at paragraphs 14 and 58-69, **CTR Doc 034**, attachment, **CTR Doc 038**, pp. 2-3 and 1st attachment, **CTR Doc 139**, p.2; and **Gabel Affidavit, Exhibit C8**). PMRA scientists recommended developing a reference dose for chlorpyrifos oxon (**CTR Doc 026**, attachment pp.4-9; **CTR Doc 038**).

83. The Amended Decision also states that “chlorpyrifos is not often detected and unlikely to be found in Canadian drinking water sources...” It is not clear what this conclusion is based on. There is no reference in the Amended Decision to drinking water modelling of the use pattern allowed during the

phase-out, or new estimates of environmental concentrations following the December 2023 phase-out. The reliability of monitoring information discussed in the environmental risk assessment is not addressed. There is also no scientific analysis or update to the drinking water assessment from PMRA staff in the Supplementary CTR, and no indication of whether there exists any scientific analysis from PMRA scientists that supports this conclusion.

84. As noted above, the 2017-2018 water modelling concluded that chlorpyrifos would be detected in levels above the DWLOCs in Canadian drinking water. It also concluded that the monitored exceedance was an appropriate value to use in the dietary risk assessment. The Amended Decision simply does not mention this or explain how it reaches the opposite conclusion.
85. I am not aware of any PMRA policies that support the use of water monitoring data alone, without any modelling or comparison of modelling with DWLOCs, to conclude that there is a low risk to human health from drinking water. This is explicitly cautioned against in the PMRA policies where there are limitations on drinking water monitoring data such as the ones the PMRA identified. It is also not clear how predictions about exposures following the end of the phase-out are relevant to whether the risks posed by the uses permitted in the phase-out is sound from a risk assessment point of view. Nevertheless, this appears to be the approach taken in the Amended Decision.
86. PMRA scientists have repeatedly emphasized that the available water monitoring data has limitations. For example, in the proposed environmental risk assessment, the PMRA indicated that there were uncertainties in the water monitoring. This document explains how the frequency of detection is influenced by the limit of detection (“**LOD**”), the lowest concentration that could be detected in a particular lab, as well as other limitations in water monitoring data:

Monitoring data likely underestimates short-term exposure to chlorpyrifos, as most sampling regimes are unlikely to capture peak

concentrations. Sampling protocols differ across the country, with some watersheds being sampled only a few times during the growing season, resulting in uncertainty as to the duration of exposure. There is variation in the analytical methods used. In some cases, such as with data from British Columbia, a very low LOD was achieved resulting in a high detection frequency, where as in other regions (such as Saskatchewan), the LOD is much higher, making the interpretation of detection frequency and analysis of non-detections challenging. The usefulness of the BC monitoring data was hampered by the paucity of samples that were taken during the growing season when chlorpyrifos would be expected to be used.

The lack of ancillary information (use of chlorpyrifos in the watershed, crops grown) further complicates the interpretation of non-detections, which could be related to chlorpyrifos not being transported from the site of application or be a result of chlorpyrifos not being used in the watershed.

In areas where chlorpyrifos is used, but monitoring data are lacking or sporadic, there is no reason to believe that detection patterns would differ compared to those observed in areas where robust water monitoring data are available. With the lack of ancillary information available for almost all sampling sites, it is generally impossible to relate chlorpyrifos concentrations at a particular site to use on a specific crop.

(**Gabel Affidavit, Exhibit A9**, pp. 24-25)

87. Further discussion of the deficiencies in water monitoring data is contained in RVD2020-14, the PMRA's final environmental risk assessment re-evaluation decision (**Gabel Affidavit, Exhibit A10**). This document explains that "[t]he vast majority of the composite dataset of available water monitoring data was deficient on a spatial and temporal basis and is not suitable for use in refinement of the risk assessment." (emphasis added, **Gabel Affidavit, Exhibit A10**, p. 7).
88. It goes on to explain that the "water monitoring data was deficient" because of a lack of sampling frequency that would capture peak concentrations, frequent sampling at the same location is required, a lack of sampling during growing seasons when chlorpyrifos is needed to capture peak concentrations, reliance on older data when the use patterns have changed, and issues with the limit of detection used in different sampling sources (**Gabel Affidavit, Exhibit A10**,

p. 7). This document also explains that where robust water monitoring data was lacking, Health Canada relied on extensive water modelling to determine estimate environmental concentrations (**Gabel Affidavit, Exhibit A10**, p. 7).

89. Nothing in the Supplementary CTR or Amended Decision indicates that the PMRA considered these uncertainties, deficiencies, or limitations which the PMRA’s scientists had previously identified, when concluding that, (based on water monitoring alone), drinking water exposure posed a low risk to human health.

d. Request to withdraw Canadian Water Quality Guideline for chlorpyrifos

90. The Amended Decision and attached Briefing Note rely on a request by Health Canada to revoke the guideline for chlorpyrifos to support the conclusion that drinking water is unlikely to be detected. The Supplementary CTR includes a public consultation document regarding this proposal for a consultation period ending on April 24, 2020 (**Supplementary CTR Doc 07**). The document states that it “may be revised following the evaluation of comments received ... [and] should be considered a draft for comment only.” The document also states that a change in registration status to pesticides may be a consideration for withdrawing a guideline.
91. There is no substantive information in the Supplementary CTR indicating what considerations went into the recommendation for chlorpyrifos. For example, we do not know if this request took into account the PMRA’s 2016-2017 modelling for current use patterns, which will continue until December 2023. Given the timing, it is unclear if the 2019 proposed decision to cancel most uses of chlorpyrifos in the environmental risk assessment (and related analyses set out at section E of the First MacDonald Affidavit, paragraphs 86-89) formed the basis for the proposal. It is not clear whether this recommendation takes into account the continuation of all uses to December 2023 through the phase-out or associated modelling.

92. The Amended Decision does not explain how this request is relevant to the acute risks that would be posed by drinking water exposure until December 2023. There is also no document that explains this in the Supplementary CTR.
93. As of the date of the Amended Decision in December 2021, the Federal-Provincial-Territorial Committee on Drinking Water had not actually revoked the guideline for chlorpyrifos, nor has it to date. Attached to this affidavit as **Exhibit “N”** is a copy of the existing drinking water guideline for chlorpyrifos which was downloaded from the Canada.ca website.
94. There is also a guideline for chlorpyrifos for the protection of aquatic life issued by the Canadian Council of Ministers for the Environment; this document was downloaded from ccme.ca and is attached to this affidavit as **Exhibit “O”**.
95. Ontario also regulates chlorpyrifos in drinking water. For example, Ontario Regulation 373/15 under the *Safe Drinking Water Act, 2002* provides a chemical standard for chlorpyrifos in drinking water in Ontario.

L. PMRA backtracked on the seriousness of the human health incident reports

96. In a November 21, 2018 briefing note to the Science Operation Committee, sponsored by Margherita Conti and presented by Mei Qui, the human health incident reports for chlorpyrifos were described as including 14 “serious” incidents in the US and 24 “moderate or minor” incidents (**CTR Doc 404**). Eighteen incidents involving 41 people in Canada were considered to be at least possibly related to chlorpyrifos exposure. One “minor” incident in Canada involved 23 people (**CTR Doc 372**).
97. The actual incident reports are contained in the CTR as Documents 355-373, and are reproduced in **Exhibit A** to this affidavit. The incident reports included symptoms such as arrhythmia, spots in visual field, malaise, ataxia and hallucination, chronic neurological dysfunction, decreased pulmonary function, respiratory irritation and tingling skin lasting for greater than six

months (**CTR Doc 355**). Two incidents culminated in death (**CTR Docs 356, 365**).

98. Another incident lasting greater than six months included cardiac difficulties, acute cardiac symptoms, atrial fibrillation, heart failure, myasthenia gravis, loss of vision, diarrhea, weakness in the left leg, abnormal gait, difficulty getting up, loss of coordination, muscle weakness, cellulitis of the legs, sensorimotor peripheral polyneuropathy, stiffness, infertility, difficulty breathing and acute respiratory symptoms (**CTR Doc 357**).
99. Canadian incidents included heart pounding (palpitations), pupil dilation, salivating excessively, sleepiness, disorientation, kidney pain, liver pain and tingling skin associated with an elm bark application near a residence in 2008 (**CTR Doc 360**).
100. Many of the incident reports conclude that there is uncertainty about the circumstances of exposure and most incident reports were labelled as having insufficient information. The details are provided in each of the incident reports in the CTR.
101. In the Cancellation Policy, the PMRA describes the level of harm required to expedite a phase-out or issuing a recall as requiring “a significant likelihood of serious effects occurring, for example, adverse effects reported in incident reports submitted to the PMRA involving death or serious bodily harm” (**Gabel Affidavit, Exhibit B3**, p. 3).
102. In the Amended Decision these same incident reports are described, and the conclusion was that “there were no deaths or other serious human incidents reported in Canada” (emphasis added, **Supplementary CTR Doc 24**, p. 6). The Amended Decision does not comment on whether it is reasonably certain that no harm occurred to the health of any of the individuals involved in the reported incidents due to chlorpyrifos uses allowed until December 2023. It is not clear why only Canadian incidents only are emphasized, as incidents in

the United States are required to be reported under the *Pest Control Products Incident Reporting Regulations* SOR 2006-260, s. 8.

103. The PMRA points out in the Amended Decision and Briefing Note that in some of the reported incidents, the label was not followed or unapproved uses were involved (**Supplementary CTR Doc 17**, and **Supplementary CTR Doc 24**, p. 6). However, it is not clear from the Amended Decision or the Supplementary CTR whether the PMRA considered the enforceability of labels or use restrictions post-cancellation when assessing the risk of serious human health incidents during the phase-out period.
104. The incident reports in the CTR are generally acute poisonings associated with pesticide application. For example, a bystander exposed to spray drift, or a worker who is exposed while applying a pesticide. Further, it is common in the incident reports that there is insufficient information about exposure to confirm whether chlorpyrifos was the cause. It is not clear from the CTR whether the PMRA ever sought clarification about the circumstances of exposure to better identify whether chlorpyrifos was the cause.
105. It is not intuitive that incident reports based on discrete exposure events would be relevant to the aggregate drinking water and dietary effects of concern for chlorpyrifos. Neurodevelopmental effects associated with aggregate effects of food and drinking water is an effect that is generally identified with an epidemiological study of these exposures. Epidemiological studies are not required to be reported as incidents unless they are sponsored by the registrant (*Pest Control Products Incident Reporting Regulations* SOR 2006-260, s. 2(h)). Although epidemiological studies do exist, to my knowledge the PMRA has never incorporated them into its risk assessment because of the lack of response to the calls for data.

M. The PMRA did not conduct a cumulative risk assessment for chlorpyrifos with other organophosphates

106. Subsection 19(2)(b)(i) of the *Pest Control Products Act* requires the PMRA to consider available information on cumulative effects of the pest control product and other pest control products that have a common mechanism of toxicity when evaluating the health and environmental risks of a pest control product and in determining whether those risks are acceptable.
107. As discussed at paragraph 133 and elaborated on in Exhibit K of the First MacDonald Affidavit, although the PMRA acknowledges that organophosphates such as chlorpyrifos share common mechanisms of toxicity, the PMRA decided not to conduct cumulative effects assessments for any organophosphates until after the post-market reviews (i.e. re-evaluations or special reviews) were complete for all organophosphates. This is stated in the 2003 re-evaluation update (**Gabel Affidavit, Exhibit A6**, pp. 2, 16), and in SPN2018-02, a 2018 Science Policy Note, attached to this affidavit as **Exhibit “P”**.
108. The cumulative risks potentially posed by other organophosphates that are still on the market or still being phased out do not appear to have been considered by the PMRA in the Amended Decision. The Amended Decision and Supplementary CTR contain no information indicating that the PMRA considered cumulative effects in assessing whether the objectives of the Act were met by the phase-out.

N. Failure to consider whether chlorpyrifos is persistent and bioaccumulative under the Toxic Substances Management Policy

109. Canada has a Toxic Substances Management Policy under the *Canadian Environmental Protection Act*. As part of each of its evaluations, the PMRA implements that policy and it does so relying on specific directives. One such directive is DIR99-03, “The Pest Management Regulatory Agency’s Strategy for Implementing the Toxic Substances Management Policy”, a copy of which is attached to this affidavit as **Exhibit “Q”**. DIR99-03 indicates that the

PMRA engages in a “systematic screening of registered active ingredients using the [Toxic Substances Management Policy] criteria for persistence and bioaccumulation” (**Exhibit P**, p. 6).

110. Subsection 19(3) of the *Pest Control Products Act* states that “in evaluating the health and environmental risks and value of a pest control product, the Minister shall give effect to government policy.” Government policy is defined in subsection 2(1) as meaning the Toxic Substances Management Policy.
111. While the PMRA has previously concluded that chlorpyrifos may be persistent it has not determined that it may be bioaccumulative. The last time the PMRA appears to have considered persistence and bioaccumulation issues related to the Toxic Substance Management Policy under the *Canadian Environmental Protection Act* in respect of chlorpyrifos was in 2003 (**PACR2003-03, Gabel Affidavit A6**, pp. 14-15). The PMRA did not mention whether it evaluated persistence or bioaccumulation of chlorpyrifos in RVD2020-14, its final environmental risk re-evaluation decision dated December 10, 2020 (**Gabel Affidavit, Exhibit A11**).
112. Canada is a signatory to the Stockholm Convention on Persistent Organic Pollutants (the “**Stockholm Convention**”). The Stockholm Convention obligates party states to prohibit and/or take legal and administrative measures to eliminate the production and import of persistent organic pollutants listed in the convention as well as a variety of other measures to eliminate releases from stockpiles and wastes. Canada ratified the convention in May 2001; it has been in-force since May 2004. Canada implements the Stockholm Convention through the Toxic Substances Management Policy. In this section I have downloaded exhibits from the website of the Stockholm Convention at <http://www.pops.int>. Attached to this affidavit as **Exhibit “R”** is a copy of the Stockholm Convention downloaded from that website.
113. Canada “actively participates on” the Stockholm Convention Persistent Organic Pollutants Review Committee (“**POPRC**”). A copy of the

Government of Canada website stating that Canada actively participates on POPRC and explaining how Canada implements the Convention is attached as **Exhibit “S”**. The POPRC reviews proposals submitted by parties for listing new chemicals in accordance with Article 8 of the Stockholm Convention.

114. In early 2021, the European Union forwarded a request to the Secretariat of the Stockholm Convention to add chlorpyrifos to the list of persistent organic pollutants under the Stockholm Convention.

115. The Secretariat of the Stockholm Convention prepared a note for POPRC dated June 3, 2021. The note from the Secretariat sets out the information relevant to the screening criteria. This note is attached to my affidavit as **Exhibit “T”**.

116. The Secretariat note concludes at paragraph 173:

Based on the persistence, potential for bioaccumulation, toxicity to aquatic organisms and terrestrial animals (including humans) and the widespread occurrence in environmental compartments including remote regions, it is concluded that **the use of chlorpyrifos is likely to lead to significant adverse human health and environmental effects such that global action is warranted.**

(emphasis added, Exhibit T, p. 26)

117. The Secretariat document also mentions potential adverse impacts in the Arctic, at paragraph 169:

Monitoring data from the Arctic and Antarctic demonstrate that chlorpyrifos can be transported over long distances to remote regions. Since degradation of chlorpyrifos is temperature dependent, it is expected to persist in these regions for a considerable length of time. Frequent findings of chlorpyrifos in all media in the Arctic support this. In addition, chlorpyrifos is found in dated sediment cores in Arctic and sub-Arctic lakes (Landers, 2008). Thus, it can be concluded that chlorpyrifos is sufficiently persistent to justify its consideration within the Convention.

(Exhibit T, p. 26)

118. There is a brief reference to monitoring of chlorpyrifos in the Arctic in the final environmental risk re-evaluation decision, RVD2020-14 (**Gabel**

Affidavit, Exhibit A10, p. 24). The last time the PMRA evaluated persistence and bioaccumulation was in the proposed environmental risk assessment (**Gabel Affidavit, Exhibit A9**, p.5-6,).

119. The Amended Decision and Supplementary CTR make no mention of whether chlorpyrifos is persistent or bio-accumulative, and accordingly does not mention whether the PMRA evaluated any longer-term impacts or long distance (i.e. arctic) exposures from the three year phase-out.
120. I am advised by counsel and believe it to be true that on February 15, 2022 counsel for the applicants wrote to counsel for the respondents inquiring whether there was any additional documentation such as science memos that should have been provided in the CTR.⁷ This is attached as **Exhibit “U”**. Counsel for the respondents responded on February 18, 2022 indicating that there was no further documentation. This response is attached as **Exhibit “V”**.
121. I make this affidavit for the applications for judicial review in Court File Nos. T-956-21, and T-121-22 and for no improper purpose.

AFFIRMED REMOTELY by Dr. Elaine MacDonald stated as being located at the City of Toronto, in the Province of Ontario, before me at the City of Toronto, in the Province of Ontario on March 7, 2022, in accordance with O. Reg 431/20, Administering Oath or Declaration Remotely.



Commissioner for Taking Affidavits
(or as may be)

Charlotte Ireland, LSO # P10772



DR. ELAINE MACDONALD

⁷ This letter was incorrectly dated February 15, 2021.

This is **Exhibit “A”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

PLEASE SEE **EXHIBIT “A”** FOLDER
CONTAINING NOVEMBER 15 CTR EXCERPTS

This is **Exhibit “B”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

Document No.	Application No.	Document ID	Description	Title
3051357	2019-5985	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3046845	2019-5987		0.8 CORRESPONDENCE- APPLICANT - GENERAL	-
3051359	2019-5987	E_Disc_Never_Sold	Discontinuation Letter Never Sold	-
3051360	2019-5987	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3156786	2020-4532	0.1.6000	6000 - APPLICATION FOR REGISTRATION RENEWAL	-
3180073	2020-4532	Renewal_Letter_E	Renewal Letter English	-
3180074	2020-4532	Signed_Renewal_Certificate	Signed Renewal Certificate	-
3180554	2020-5846		0.8 CORRESPONDENCE- APPLICANT - GENERAL	Notice of Intent to Discontinue Sales_IPCO Citadel_ 27479
3180555	2020-5846	0.1.6000	6000 - APPLICATION FOR REGISTRATION RENEWAL	6000_Discontinuation_IPCO Citadel_ 27479
3185270	2020-5846	E_Disc_Old_Last_Sale_Date	Discontinuation Letter Old Last Sale Date	-
3185271	2020-5846	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185283	2020-5907	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185285	2020-5907	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185287	2020-5908	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185291	2020-5908	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185293	2020-5909	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185295	2020-5909	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185297	2020-5910	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185299	2020-5910	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185312	2020-5918	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185314	2020-5918	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185316	2020-5919	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185318	2020-5919	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3185320	2020-5920	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3185322	2020-5920	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192236	2021-0233		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter, Chlopyrifos EP discontinuations
3192237	2021-0233	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form,210120 CL, Chlopyrifos EP discontinuations
3201521	2021-0233	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201522	2021-0233	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192238	2021-0234		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter, CL, Chlopyrifos EP discontinuations
3192239	2021-0234	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form, Discontinuation, Dursban HF 20320
3201529	2021-0234	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201530	2021-0234	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192243	2021-0235		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter,Chlopyrifos EP discontinuations
3192245	2021-0235	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form, Chlopyrifos EP discontinuations
3201534	2021-0235	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201535	2021-0235	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192246	2021-0236		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter, Chlopyrifos EP discontinuations
3192247	2021-0236	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form, Discontinuation, Dursban Water Sol 21997
3201537	2021-0236	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201539	2021-0236	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192279	2021-0237		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter,Chlopyrifos EP discontinuations
3192280	2021-0237	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form, Discontinuation, Lorsban NT 29650
3201541	2021-0237	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201542	2021-0237	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192286	2021-0238		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter, Chlopyrifos EP discontinuations
3192287	2021-0238	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form, Discontinuation, Lorsban 50W 20944
3201545	2021-0238	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201548	2021-0238	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3192290	2021-0239		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter, Chlopyrifos EP discontinuations
3192291	2021-0239	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form,Discontinuation, Lorsban 4E 14879
3201550	2021-0239	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201551	2021-0239	Signed_Certificate	Signed Letter and Revised Registration Certificate	-

Document No.	Application No.	Document ID	Description	Title
3192293	2021-0240		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DAS letter, Discontinuation, Lorsban 15G, 16458
3192294	2021-0240	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	Application form,Chlopyrifos EP discontinuations
3201553	2021-0240	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3201554	2021-0240	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3194520	2021-0368	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	6005 - Application for New or Amended Product - Pyrate 20210125-Completed
3194522	2021-0368		0.8 CORRESPONDENCE- APPLICANT - GENERAL	Pyrate 480 formulation update LOI 20210125
3195110	2021-0368		0.8 CORRESPONDENCE- APPLICANT - GENERAL	2021-0368 SPSF revision LOI 20210128
3196540	2021-0476	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	32694 Application Form
3219888	2021-0476	Email_Message_(MSG)	DUB cancellation	-
3219898	2021-0476	Signed_Letter	Category C - Withdrawal Letter	-
3219899	2021-0476	Withdrawal_Letter	Category C - Withdrawal Letter	-
3196541	2021-0476		0.8 CORRESPONDENCE- APPLICANT - GENERAL	32694 Cover Letter
3198735	2021-0571	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	32768 Application Form
3219900	2021-0571	Email_Message_(MSG)	DUB cancellation	-
3219901	2021-0571	Signed_Letter	Category C - Withdrawal Letter	-
3219902	2021-0571	Withdrawal_Letter	Category C - Withdrawal Letter	-
3198738	2021-0571		0.8 CORRESPONDENCE- APPLICANT - GENERAL	32768 Cover Letter Label Amendment for Sharphos Insecticide (Reg. No. 32768) in Response to the Re-evaluation Decision for Chlorpyrifos, Reference Number 2019-3275
3207506	2021-0946	0.1.6000	6000 - APPLICATION FOR REGISTRATION RENEWAL	33113 Pyrinex 450 LV EC Discontinuation - 20210302
3207507	2021-0946		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DUB Re-evaluation Decision Letter Environment ADAMA 10DEC2020
3207508	2021-0946		0.8 CORRESPONDENCE- APPLICANT - GENERAL	Pyrinex 450 RVD Discont LOI 20210303
3210466	2021-0946	E_D_7_2_DISC_REVAL	D_7_2_Discontinuation_Reevaluation_Negotiated	-
3210469	2021-0946	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3207511	2021-0947	0.1.6000	6000 - APPLICATION FOR REGISTRATION RENEWAL	23705 Pyrinex Discontinuation - 20210302
3207512	2021-0947		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DUB Re-evaluation Decision Letter Environment ADAMA 10DEC2020
3207513	2021-0947		0.8 CORRESPONDENCE- APPLICANT - GENERAL	Pyrinex 480 RVD Label Update LOI 20210302
3210473	2021-0947	E_D_7_2_DISC_REVAL	D_7_2_Discontinuation_Reevaluation_Negotiated	-
3210479	2021-0947	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3207551	2021-0959	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	6005 - Application for New or Amended Product - Chlorpyrifos label amendment
3219906	2021-0959	Email_Message_(MSG)	DUB cancellation	-
3219907	2021-0959	Signed_Letter	Category C - Withdrawal Letter	-
3219908	2021-0959	Withdrawal_Letter	Category C - Withdrawal Letter	-
3207553	2021-0959		0.8 CORRESPONDENCE- APPLICANT - GENERAL	Pyrate 480 RVD Label Update LOI 20210302
3207554	2021-0959		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DUB Re-evaluation Decision Letter Environment ADAMA 10DEC2020
3207570	2021-0973	0.1.6005	6005- APPLICATION FOR NEW OR AMENDED REGISTRATION	6005 - Application for New or Amended Product - Chlorpyrifos label amendment
3219903	2021-0973	Email_Message_(MSG)	DUB cancellation	-
3219904	2021-0973	Signed_Letter	Category C - Withdrawal Letter	-
3219905	2021-0973	Withdrawal_Letter	Category C - Withdrawal Letter	-
3207572	2021-0973		0.8 CORRESPONDENCE- APPLICANT - GENERAL	Pyrinex Technical Chlorpyrifos Insecticide RVD Label Update LOI
3207573	2021-0973		0.8 CORRESPONDENCE- APPLICANT - GENERAL	DUB Re-evaluation Decision Letter Environment ADAMA 10DEC2020
3218904	2021-1502	0.1.6000	6000 - APPLICATION FOR REGISTRATION RENEWAL	-
3219708	2021-1502	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3221311	2021-1502	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3218906	2021-1511	0.1.6000	6000 - APPLICATION FOR REGISTRATION RENEWAL	-
3219711	2021-1511	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3221301	2021-1511	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3218913	2021-1513		0.8 6000 - APPLICATION FOR REGISTRATION RENEWAL	-
3219723	2021-1513	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3219725	2021-1513	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3219728	2021-1514	E_Disc_Re-eval	Discontinuation Letter Re-Evaluation	-
3219730	2021-1514	Signed_Certificate	Signed Letter and Revised Registration Certificate	-
3219740	2021-1514		0.8 CORRESPONDENCE- APPLICANT - GENERAL	-

This is **Exhibit “C”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Health Santé
Canada Canada

Access to Information and Privacy Division
7th Floor, Suite 700, Holland Cross - Tower B
1600 Scott Street, (Mail Stop: 3107A)
Ottawa, Ontario K1A 0K9

EPOST

Our file: A-2021-000964 / UM

October 21, 2021

Charlotte Ireland
EcoJustice
1910 - 777 Bay Street
Post Office Box: 106
Toronto, Ontario
M5G 2C8

Dear Charlotte Ireland:

This is further to your request made under the *Access to Information Act* (the Act) for the following information:

This request is a follow up to request # A-2021-000382, which provided a summary document listing regarding copies of all registrations, renewal, amendment or discontinuance applications and Pest Management Regulatory Agency (PMRA) response for registered Chlorpyrifos products from the years 2006 to 2021. Based on the summary document that was released, we are seeking the documents listed in the attached PDF table.

Pursuant to paragraph 9(1)(a) and (b) of the Act, an extension of up to 260 days is required as your request involves a large number of records and/or necessitates a search through a large number of records and we will need to conduct consultations outside the department.

In accordance with section 27 of the Act, we are also required to notify the third parties concerned of our intention to release the requested records. In order to carry out this notification, an extension of the time limit for completion of this request is required pursuant to paragraph 9(1)(c) of the Act. Please note that it is important to us to complete the processing of your request in a timely manner.

Your request is important to us and we will continue to make reasonable efforts to respond to your request in accordance with our operational realities. Thank you in advance for your patience and understanding during this period as we all navigate these unprecedented challenges.

Should you have any questions or concerns about the processing of your request, please do not hesitate to contact Uroosa Malik, the analyst responsible for this file, either by

phone at 613-410-8554, by email at uroosa.malik@hc-sc.gc.ca, with reference to our file number cited above.

Please be advised that you are entitled to complain to the Office of the Information Commissioner of Canada concerning the processing of your request within 60 days of the receipt of this notice. In the event you decide to avail yourself of this right, your notice of complaint can be made online at: <https://www.oic-ci.gc.ca/en/submitting-complaint> or by mail to:

Office of the Information Commissioner of Canada
30 Victoria Street
Gatineau, Quebec K1A 1H3

Yours sincerely,



Digitally signed by Janet Sewell McPherson
DN: C=CA, OU=HC - ATIP, O=Health
Canada, CN=Janet Sewell McPherson,
E=janet.sewellmcperson@canada.ca
Reason: I am approving this document with
my legally binding signature
Location: your signing location here
Date: 2021.10.21 10:49:43-0400'
Foxit PDF Editor Version: 11.0.1

Janet Sewell McPherson
Manager, Access to Information and Privacy

c.c.: Office of the Information Commissioner of Canada

This is **Exhibit “D”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



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Via Email

Our File Number: LEX-500016917

October 22, 2021

Laura Bowman and Daniel Cheater
Ecojustice
1910 – 777 Bay Street, PO Box 106
Toronto, ON M5G 2C8
Fax: 416-363-2746
Tel: 416-368-7533 ext 522

Dear Ms. Bowman and Mr. Cheater:

Re: Safe Food Matters et al v AGC et al (T-1412-21)

I write to provide an update on the Attorney General of Canada's ("AGC") position in respect of the judicial review application in Court File T-956-21 ("Cancellation JR") and further to your letter of October 19, 2021 in which you set out your understanding of our prior without prejudice conversations.

First, I can confirm that we have received instructions to consent to set aside the cancellation decision on the basis that, in the absence of any reasons for the phase-out period selected by PMRA, that decision is unreasonable. In order to avoid a regulatory gap, PMRA will be asking for a stay of the set aside decision for 45 days to permit it to reconsider the issue. In the event it would be useful to discuss this issue further in advance of the case management conference, we are available to do so.

This position renders any further consolidation moot. However, to the extent that any issues we discussed in relation to consolidation may still be relevant, I will briefly re-state the AGC's position.

You correctly indicate in your correspondence that your clients elected to issue the above Notice of Application because the AGC did not consent to amendments to the Notice of Application in the Cancellation JR that would add a challenge to PMRA's decision in relation to MRLs for chlorpyrifos in advance of the time limit that your client takes the position applies to that decision (namely, 30 days from receipt of the CTR). However, you fail to recall that the precise reason I indicated that the AGC would not be in a position to confirm our consent to the proposed amendments related to our concerns that the amendments sought to challenge a separate decision in relation to MRLs, such that that challenge could not be simply rolled into the first application. The AGC has never taken any position that suggests the MRL decision is not distinct from the cancellation decision.

Similarly, in respect of the CTR, the AGC does not take the position that the CTR in the Cancellation JR is the same CTR as would exist for the decision in respect of MRLs. The Applicants did not request the CTR in respect of the MRL decision, and instead noted in their application that they would rely on the material provided in response to the CTR request in the Cancellation JR. The AGC has confirmed that the CTR filed in the Cancellation JR included, but was not limited to, the documents relevant to the MRL decision. The AGC also agreed that the parties could make any necessary amendments to the Confidentiality Agreement to permit the Applicants to rely on documents from the CTR in the Cancellation JR that the Applicants may seek to put forward in the MRL application. This position was without prejudice to the AGC's ability to assert that any particular document from that CTR was not relevant to the MRL decision.

In our conversations concerning consolidation, we believe we were clear that the MRL decision is distinct from the cancellation decision. That position remains unchanged.

Sincerely,



Andrea Bourke
Senior Counsel
Litigation, Extradition and Advisory Division

This is **Exhibit “E”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



**Department of Justice
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Email: Andrea.bourke@justice.gc.ca

Our File:
Notre dossier:

Your File:
Votre dossier:

November 1, 2021

VIA E-FILING

Federal Court Registry

Federal Court of Canada
180 Queen Street West, Suite 200
Toronto, Ontario
M5V 3L6
Fax: (416) 954-5068

Dear Registrar:

Re: **SAFE FOOD MATTERS INC et al v ATTORNEY GENERAL OF CANADA et al**
Court File No.: T-956-21 / T-1412-21

We represent the Respondents (“AGC”) in these matters and kindly request that you bring this letter to the attention of Prothonotary Horne, the Case Management Judge assigned to these proceedings.

We write with respect to the case management conference scheduled for 1:00 pm tomorrow, November 2, 2021. Specifically, we write in response to the letter from counsel for the Applicants dated October 29, 2021 (the “Letter”) that we received this morning and that Applicants’ counsel directed to the Court without giving the parties prior notice or seeking their consent.

Status of Application T-956-21

As noted in the Letter, we advised the Applicants on October 22, 2021 of our instructions to consent to set aside the decision that is at issue in the application bearing court file no. T-956-21, which the Letter refers to as the “Phase-out Application”. The decision at issue is that of the Pest Management Regulatory Agency (“PMRA”) made May 13, 2021 to cancel the registration of pest control products containing the active ingredient chlorpyrifos, which cancellation was made subject to a three-year phase-out period (the “Phase-out Decision”).

As the Phase-out Decision did not give reasons for directing the three-year phase-out period, the Respondents acknowledge that the Phase-out Decision is unreasonable and must be set aside. In order to avoid a regulatory gap, the AGC proposed a stay of any decision setting aside PMRA’s Phase-out Decision for 45 days to permit PMRA to issue a new decision. Notwithstanding this concession, the Applicants now take the position that their application for judicial review should continue with the Respondents’ concession being a matter to be taken in to account by the judge hearing the merits of that application. The Letter was the first that we heard of the Applicants’ position on our clients’ concession. We will therefore need to seek instructions on how to address the AGC’s concession.

Canada

Applicants' Consolidation Motion

The Letter correctly identifies as a preliminary matter for determination by the Court the Applicants' request for a consolidation of the Phase-out Application and the MRL Application. However, the Letter goes on – improperly, in our view – to address substantive issues relevant to the consolidation request. The matter of consolidation will be appropriately addressed in the course of the Applicants' motion to consolidate the proceedings. The Respondents will set out and particularize their position in that forum. For present purposes, we simply note that the applications arise from two separate decisions and will involve evidence that, from the AGC's perspective, is neither inter-changeable nor wholly relevant to both proceedings.

The parties have discussed and agreed to the following timetable for the Applicants' consolidation motion:

1. The Applicants to deliver their motion record by November 5, 2021;
2. The Respondents to deliver their responding motion record by November 22, 2021;
3. The Applicants to deliver their reply by November 29, 2021.

In our view, the timing for the delivery of evidence ought not to be determined until the consolidation motion is decided.

Confidentiality Issues

The parties entered into a confidentiality agreement that permitted the AGC to deliver both a confidential and a public version of the Certified Tribunal Record ("CTR") to the Applicants. The AGC delivered a copy of the public CTR to counsel for the Proposed Intervenor on October 27, 2021. The parties initially contemplated proposing that the AGC would bring a confidentiality motion following the close of cross-examinations, at which point all confidential documents would be known. This process was intended to avoid the potential for multiple motions.

However, given the addition of a proposed Intervenor, the AGC (or any interested third parties) could bring a motion to address the confidentiality of the CTR and a subsequent motion following the close of cross-examinations to address any additional confidential material. If this approach is preferable, the AGC would propose that any motions regarding the confidentiality of documents in the CTR be brought in writing, by December 15, 2021. The AGC would also ask for a Direction that the motion record could be delivered under seal, so that the confidentiality of the documents at issue would be preserved pending the determination of the motion.

Sincerely,



Andrea Bourke
Counsel for the Respondents

Cc: Laura Bowman, Daniel Cheater, Counsel for the Applicants at lbowman@ecojustice.ca
and dcheater@ecojustice.ca

Martin Masse, Jenna Anne De Jong, Jean-Simon Schoenholz, Counsel for Crop Life at
martin.masse@nortonrosefulbright.com; jennaanne.dejong@nortonrosefulbright.com;
jean-simon.schoenholz@nortonrosefulbright.com;

This is **Exhibit “F”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

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PART I - OVERVIEW AND STATEMENT OF FACTS

A. OVERVIEW

1. The Applicants, Safe Food Matters Inc. and Prevent Cancer Now, seek to consolidate two judicial review proceedings (Court file numbers T-956-21 and T-1412-21) that challenge two distinct administrative decisions made at different times by the Pest Management Regulatory Agency (“PMRA”). The Applicants have not met their onus of establishing that consolidation of these two applications will promote the most expeditious and inexpensive determination of the proceedings, nor have they demonstrated that the relief sought will not prejudice the Respondents. Accordingly, this motion should be dismissed.

2. First, the legal issues in the two applications are entirely distinct. No efficiency is served by tying them together and no multiplicity of proceedings results from having them heard in the ordinary course.

3. In Court File T-956-21 (“Phase-Out JR”), the Applicants challenge PMRA’s *Update on the Re-evaluation of Chlorpyrifos* (“Chlorpyrifos Update”). In the Chlorpyrifos Update, PMRA indicated that all remaining registrations of chlorpyrifos products were cancelled, subject to a three-year phase out period, following registrants’ failures to satisfy data requirements under the *Pest Control Products Act* (“Act”). Given that the Chlorpyrifos Update does not include any reasons for the phase-out period selected, the Respondents have conceded it is unreasonable. Accordingly, the only live issue in the Phase-Out JR is the appropriate remedy. As PMRA is currently reconsidering its prior Chlorpyrifos Update in light of this concession, mootness may very well be an issue at or before the hearing of the Phase-Out JR. As the Applicants note, the Respondents have delivered a voluminous certified tribunal record (“CTR”) in the Phase-Out JR. Aside from an administrative affidavit attaching any new decision that PMRA may issue, the Respondents do not anticipate any additional responding evidence will be needed for this Court to determine the narrow issues in the Phase-Out JR.

4. In Court File T-1412, the Applicants seek to challenge PMRA’s decision (“MRL Decision”) not to revoke all maximum residue levels (“MRLs”) in

2) Phase-Out JR

i. Relevant Legal Framework for the Phase-Out JR

15. PMRA, acting on behalf of the Minister, is responsible for the regulation of all PCPs in Canada in accordance with the Act and regulations thereunder. The Act prohibits the manufacture, possession, handling, storage, transport, import, distribution or use of a PCP unless the product is registered *or otherwise authorized*.¹⁸ Contravention of the Act is an offence that may be punishable on summary conviction or indictment.¹⁹

16. An applicant seeking to register a new PCP or amend an existing registration must submit an application.²⁰ Once a PCP is registered, there are several mechanisms for a review of that registration in the Act. For example, pursuant to section 16 of the Act, PMRA must initiate a re-evaluation of every registered PCP no later than 16 years from the most recent major decision affecting that product's registration.²¹ In addition, PMRA may initiate a re-evaluation at any time where it determines that there has been a change in the information required or the procedure used for assessing the risk.²² Where PMRA has reasonable grounds to believe the risks of a PCP, or its value, is unacceptable, PMRA must initiate a special review.²³

17. During the course of a re-evaluation or special review, PMRA may require registrants to provide additional information that PMRA considers necessary to complete the evaluation.²⁴ If the registrant fails to provide the requested information, PMRA may cancel the registration for that product on that basis.²⁵

¹⁸ Act, [s 6\(1\)](#), RBA, Tab 1

¹⁹ Act, [s 6\(9\)](#), RBA, Tab 1

²⁰ Act, [s 7](#), RBA, Tab 1

²¹ Act, [s 16\(2\)](#), RBA, Tab 1

²² Act, [s 16\(1\)](#), RBA, Tab 1

²³ Act, [s 17\(1\)](#), RBA, Tab 1

²⁴ Act, [s 19\(1\)](#), RBA, Tab 1

²⁵ Act, [s 20\(1\)\(a\)](#), RBA, Tab 1

18. When PMRA cancels the registration of a PCP, PMRA may allow for the continued possession, handling, storage, distribution, and use of stocks of the product in Canada at the time of cancellation subject to any conditions that PMRA considers necessary for carrying out the purposes of the Act.²⁶

19. In addition to cancellations initiated by PMRA, a registrant may discontinue a PCP at any time by delivering a Notice of Discontinuance to PMRA.²⁷ Upon receipt of the Notice, PMRA must cancel the PCP.²⁸ When cancelling a PCP following receipt of a Notice of Discontinuance, PMRA may determine the effective date of the cancellation and may impose any conditions it considers necessary for carrying out the purpose of the Act.²⁹

20. The *Policy* sets out general “phase out” timelines that PMRA considers appropriate when cancelling a PCP’s registration at the conclusion of a special review or re-evaluation, or in instances where a registrant fails to provide information requested by PMRA.³⁰ The purpose of the *Policy* is to enhance transparency and facilitate effective implementation of re-evaluations and special reviews by providing a general framework.³¹ The *Policy* provides that, where there are no serious and imminent risks to human health or the environment, cancelled PCPs will be phased-out over a three-year period as follows: one year of sale by the registrant; one additional year of sale by the retailer; and one additional year of permitted use.³² The *Policy* does not apply to discontinued uses.

²⁶ Act, [s 21\(5\)](#), **RBA, Tab 1**

²⁷ Act, [s 22\(1\)](#), **RBA, Tab 1**

²⁸ Act, [s 22\(3\)](#), **RBA, Tab 1**

²⁹ Act, [s 22\(3\)](#), **RBA, Tab 1**

³⁰ *Policy*, pp 1-4, Ex E to Minarovich Affidavit, **RMR, Tab 1E**. The *Policy* also applies to amendments to PCPs’ uses, which are not at issue in this proceeding.

³¹ *Policy*, p 1, Ex E to Minarovich Affidavit, **RMR, Tab 1E**

³² *Policy*, p 4, Ex E to Minarovich Affidavit, **RMR, Tab 1E**

ii. Chlorpyrifos Update

21. On May 13, 2021, PMRA published the Chlorpyrifos Update. In that decision, PMRA noted that Health Canada had published a re-evaluation decision in respect of chlorpyrifos concerning the environmental risks in December 2020. As a result of that decision, PMRA noted that most agricultural uses of chlorpyrifos were cancelled and would be phased out by December 10, 2023. The Chlorpyrifos Update also noted that the environmental re-evaluation decision had indicated that PMRA would be updating the human health aspect of chlorpyrifos and that PMRA issued a data call-in notice to carry out this assessment. As the remaining registrants failed to satisfy the data call-in notice, the Chlorpyrifos Update indicated that the remaining registrations of chlorpyrifos products were cancelled and that the last date of sale would be December 10, 2023. The Chlorpyrifos Update does not indicate which PCPs were subject to this cancellation, does not reference the *Policy*, and does not indicate why the three-year phase out period was selected. The Respondents have conceded the decision contains insufficient reasons such that it is unreasonable.

3) MRL JR

i. Relevant Legislative Framework

22. The MRL is the maximum amount of a specific pesticide residue legally permitted to remain in or on food that is sold in Canada. This includes both residues on food products created in Canada as well as residues that may be on food products imported into Canada from other countries. MRLs are set for every crop or crop group for which a pesticide is registered.³³

23. Pursuant to section 9 of the Act, when PMRA is making a decision regarding the registration of a PCP, the Minister shall, *if necessary*, specify any MRLs for the product or for its components or derivatives that the Minister considers appropriate in the circumstances.³⁴ Section 10 of the Act permits PMRA to set MRLs

³³ [Maximum Residue Levels for Pesticides](#), Exhibit D to Minarovich Affidavit, **RMR, Tab 1D**

³⁴ Act, [s 9](#), **RBA, Tab 1**

party also bears the “heavy onus” of establishing that proceeding with the matters separately would cause prejudice, not simply inconvenience, to the moving party.⁴⁴

B. Consolidation is not the most expeditious way forward

1) Legal Issues are Distinct

29. While both the Phase-Out JR and the MRL JR involve the same parties and concern challenges to decisions under the Act, there are significant differences between the legal issues in the proceedings, such that no efficiency is served by tying them together and, conversely, no multiplicity of proceedings would arise in hearing each application in the ordinary course.

30. In particular, the issues in the Phase-Out JR are limited to the appropriate remedy and, quite possibly, mootness. While the Applicants seek a declaration from this Court that PMRA either lacked a factual basis for the phase-out period selected or lacked a rationale for the phase-out period selected, the former declaration (no factual basis) asks the Court to step into the shoes of the decision-maker, whereas the latter (no rationale) is subsumed within the Respondents’ concession. In the absence of an articulation of the reasons for the phase-out period selected in the Chlorpyrifos Update, the Court cannot know the rationale for PMRA’s decision. This legal issue can be argued in the absence of evidence. Indeed, affidavit evidence going to the substantive merits of the decision would be impermissible.

31. The legal and factual issues in the MRL JR are more complex. The Applicants seek an order revoking all MRLs in relation to chlorpyrifos and a declaration that PMRA’s decision not to revoke the MRLs was unreasonable and unlawful.

32. Pursuant to section 9 of the Act, MRLs must be set, *when necessary*, when PMRA makes a decision concerning the registration of a PCP. Pursuant to section 10, MRLs *may* be set for unregistered PCPs.⁴⁵ As a result of the various recent

⁴⁴ *Sanofi* at paras [11-14](#), [25](#), **ABA, Tab 1**

⁴⁵ Act, s [9-10](#), **RBA, Tab 1**

This is **Exhibit “G”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Laura Bowman

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File No.: 2062

December 8, 2021

Andrea Bourke
Karen Lovell
Elizabeth Koudys
Andrew Law
Department of Justice Canada
Ontario Regional Office
sent by email: andrea.bourke@justice.gc.ca et al.

Dear Counsel:

Re: *Safe Food Matters et al v AGC et al* (Court File Nos. T-956-21 and T-1412-21)

This letter is in regards to the service of the applicants' affidavits in the above two matters. We note that the attorney general has previously consented to our clients filing joint evidence and the enclosed affidavits are the same for both matters and incorporate the court file numbers for both matters.

[REDACTED]

We note that the affidavit of Elaine MacDonald describes the record and that this affidavit has been marked confidential out of an abundance of caution. We have reviewed the affidavit and we do not believe it contains any confidential information, as it relies on the November 15, 2021 public version of the certified tribunal record. However, before removing the designation we are providing the respondents with an opportunity to review it. If you could please provide your clients position on whether any portions of it need to maintain a confidentiality designation this would be appreciated.

We note that in the recent response to the consolidation motion, the Minister of Health indicated that he would likely make a new decision in respect of the cancellation and/or phase-out of chlorpyrifos registrations raised in T-956-21. Although the respondents take the position that this new decision, whatever it is, would render the judicial review in T-956-21 moot, the respondents in T-956-21 have not provided any other information such as the timing or nature of this anticipated new decision. In the event that a new decision is made by the Minister, we note

that our clients may well need to revisit their affidavit evidence served upon you today as well as other aspects of this litigation.

In light of this we would like more information about when the Minister intends to make his decision, the nature of that decision and whether the public would be consulted on the decision in order that our clients can be advised of the impact of this, if any, on the litigation and so that any adjustments to the timetable in the above two matters may be proposed to the case management judge in a timely way.

It is most unfortunate that several months into this litigation, and after our clients' affidavits are completed the Minister is only now proposing to make a new decision and without providing these crucial details to the opposing parties.

Sincerely,

A handwritten signature in black ink, appearing to read 'LB', with a long horizontal flourish extending to the right.

Laura Bowman
Counsel

cc: Daniel Cheater (co-counsel)
Martin Masse, Jean-Simon Schoenholz, and Jenna Anne de Jong, counsel for the proposed intervenors,
CropLife Canada

This is **Exhibit “H”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Health
Canada

Santé
Canada

Your health and
safety... our priority.

Votre santé et votre
sécurité... notre priorité.

Re-evaluation Note

REV2021-04

Cancellation of remaining chlorpyrifos registrations under paragraph 20(1)(a) of the *Pest Control Products Act*

(publié aussi en français)

21 December 2021

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This decision replaces Re-evaluation Note ([REV2021-02](#)¹), which informed the public that the registrations of the remaining pest control products containing chlorpyrifos were being cancelled due to failure to fulfill the mandatory data requirements under the *Pest Control Products Act*. Re-evaluation Note REV2021-02 of 13 May 2021 did not contain reasons for the phase-out period selected by Health Canada. This decision (REV2021-04) immediately cancels the registrations of the remaining chlorpyrifos products subject to the mandatory data call-in under the *Pest Control Products Act* and provides reasons for the phase-out period.

Background

The re-evaluation for chlorpyrifos proceeded in several phases: the first phases in 2000, 2003 and 2007 assessed the health risks and some environmental risks, with the full environmental assessment completed in 2020. The final phase of re-evaluation was intended to update the current health risk assessment. The chlorpyrifos re-evaluation decision related to environmental risk (PRVD2019-05² and RVD2020-14³) resulted in the cancellation of a number of registrations of pest control products. Health Canada also identified additional data needed for the re-evaluation to update the current health risk assessment for the remaining registered products.

On 10 February 2021, Health Canada sent a notice to the two registrants of the remaining products containing chlorpyrifos requiring various data in order to complete the update to the health risk assessment. By that time, only products from these two registrants remained subject to the ongoing re-evaluation with respect to the health risk assessment because all other products containing chlorpyrifos were already in the course of being phased-out following prior cancellation decisions or following voluntary discontinuations. See Appendix I for the complete list of all products containing chlorpyrifos subject to a phase-out period.

As the registrants of chlorpyrifos products were unable to fulfill these data requirements, Health Canada cancelled the registrations of the remaining pest control products containing chlorpyrifos, according to the phase-out timeline below. This timeline was the same as that which was imposed on product registrations cancelled as a result of the environmental risk assessment (RVD2020-14), with the exception of uses on canola and garlic, which were originally extended until 2024 in RVD2020-14, but were then aligned with the same phase-out timeframe as all of the other cancelled uses.

Phase-out Timeline:

- Last date of sale by registrant: 10 December 2021
- Last date of sale by retailers: 10 December 2022
- Last date of use for all chlorpyrifos uses/products including canola (for alfalfa looper) and garlic (for darksided and redbacked cutworm): 10 December 2023

¹ REV2021-02, *Update on the re-evaluation of chlorpyrifos*

² PRVD2019-05, *Chlorpyrifos and Its Associated End-use Products: Updated Environmental Risk Assessment*

³ RVD2020-14, *Chlorpyrifos and Its Associated End-use Products (Environment)*

On 13 May 2021, Health Canada published a Re-evaluation Note (REV2021-02) informing the public that the registrations of the remaining pest control products containing chlorpyrifos were being cancelled with a phase-out period due to failure to fulfill the mandatory data requirements. In the Re-evaluation Note, Health Canada did not explain its reasons for applying the phase-out period.

This decision (REV2021-04) confirms the cancellation of the registrations of the remaining products/uses of chlorpyrifos and sets out Health Canada's determination that, in accordance with the *Pest Control Products Act* and [Regulatory Directive DIR2018-01, Policy on Cancellations and Amendments Following Re-evaluation and Special Review](#),⁴ the risks are not imminent and serious during the phase-out period.

Final determination with respect to chlorpyrifos

The remaining products containing chlorpyrifos are now cancelled, effective as the date of this publication, in accordance with Information Note: *Update on implementation of post-market decisions* published 21 December 2021. No manufacturing within Canada or importation into Canada is allowed. The remaining products whose registrations are immediately cancelled are:

- Pyrinex Technical Chlorpyrifos Insecticide (Registration Number 23621)
- Pyrate 480 EC Insecticide (Registration Number 23704)
- Sharda Chlorpyrifos Technical Insecticide (Registration Number 32694)
- Sharphos Insecticide (Registration Number 32768)

Paragraph 21(5)(a) of the *Pest Control Products Act* permits Health Canada to allow existing stocks of cancelled products in Canada to remain authorized for continued possession, handling, storage, distribution and use over a phase-out period, subject to any conditions that are necessary for carrying out the purposes of the *Pest Control Products Act*.

The following conditions apply to the products subject to this decision:

- There shall be no further distribution and sale by registrants of any products containing chlorpyrifos;
- Retailers and other distributors are permitted to distribute and sell their existing stock until 10 December 2022;
- The last date of permitted use will be 10 December 2023;
- Registrants are required to comply with incident reporting obligations during the phase-out period; and
- Registrants are required to comply with sales reporting obligations until all reports relevant to the 2021 calendar year have been submitted.

⁴ Regulatory Directive 2018-01, *Policy on Cancellations and Amendments Following Re-evaluation and Special Review*

This allows existing stocks of chlorpyrifos products in Canada to be exhausted in an orderly manner, to minimize potential risks associated with disposing of existing product all at once, and to minimize potential confusion for the users.

i) Overview of Policy on Cancellations and Amendments Following Re-evaluation and Special Review

The [Policy on Cancellations and Amendments Following Re-evaluation and Special Review](#), provides a framework for the cancellation of pesticide products or amendments to pesticide product uses, labels, or other conditions of registration following a re-evaluation or special review decision, or the failure to meet mandatory data requirements. The policy also outlines the process, the associated timelines as well as how the timelines for cancellation or amendment of pesticide products are established.

This policy is intended to enhance transparency of the process and associated timelines when regulatory action is required to remove products from the market, change approved uses, or introduce amendments to labels. It is also intended to facilitate efficient and effective implementation of re-evaluation and special review decisions, including by ensuring an orderly transition in order to minimize the potential for non-compliance. Standardized timelines aim to clarify expectations, obligations and communications around the implementation of regulatory decisions.

The primary consideration for the implementation timelines for cancellation and amendment is based on the risks to human health or the environment, in other words, whether risks are considered imminent and serious, taking into account the following factors:

- Potential magnitude of harm, in other words, seriousness of the effect of concern, including reversibility;
- Likelihood of the effect occurring, in other words, whether an effect of concern is likely to happen based on how the product is being used;
- The population exposed to the product, for example, trained pesticide applicators, the general public, or bystanders; and
- Information from post-market surveillance considered as part of the re-evaluation or special review, for example, incident reports, poison control centre data, or monitoring data.

In cases where no imminent and serious risks to human health or the environment are identified, the implementation timelines outlined in DIR2018-01⁵ are applied to products or uses subject to the re-evaluation or special review decision.

Implementation is expedited when risks of concern are considered to be imminent and serious. Such circumstances involve a significant likelihood of serious effects occurring, for example, adverse effects reported in incident reports submitted to Health Canada involving death or serious bodily harm.

⁵ DIR2018-01, *Policy on cancellation and amendments following re-evaluation and special review*.

In these circumstances, other appropriate measures may also be required, such as requiring the registrant to over-sticker labels on existing stocks with risk mitigation statements, or issuing an immediate product recall in accordance with the *Pest Control Products Act* (p. 21(5)(b)).

ii) No imminent and serious risks during ongoing phase-out

Health Canada has determined that the risks for current chlorpyrifos uses are not imminent and serious during the period of the phase-out described above, taking into account the following considerations:

- **No residential uses by homeowners in Canada:** In 2000, Health Canada stopped allowing all uses by homeowners and chlorpyrifos labels were updated accordingly (with the exception of containerized low concentration ant baits/bait stations that were discontinued in 2017). Thus, there has been virtually no exposure to chlorpyrifos products from use by the general public in residential settings for over 20 years.
- **Mitigation in place for workers:** Health Canada implemented mitigation measures in 2007 (REV2007-01, *Update on the Re-evaluation of Chlorpyrifos*) to further protect human health, following an assessment of agricultural and forestry uses. Mitigation measures included discontinuation of certain uses and specific types of application equipment, implementation of engineering controls and additional personal protective equipment for workers, and the establishment of restricted intervals for postapplication workers.
- **Seldom detected in food:** Potential dietary exposure and risks from chlorpyrifos have also been considered based on **current** Canadian registered uses, including recent food residue surveillance data representative of the national food supply from the Canadian Food Inspection Agency's (CFIA) National Chemical Residue Monitoring Program and the United States Department of Agriculture's (USDA) Pesticide Data Program (PDP). Food monitoring programs show a very low frequency of chlorpyrifos detections in both Canada and the United States. In Canada, the frequency of detection was 0.62% from domestically grown crops; and 2.7% overall in samples from domestic and imported foods from 34 114 samples tested in Canada between 2013–2017. This low detection frequency is consistent with that noted in PACR2003-03⁶, which reported detections in less than 1% (0.3%) of domestic and 1.9% of imported commodities in 44 397 shipments. Furthermore, chlorpyrifos residues, when detected, were also generally lower in Canada than the United States, and were also **in compliance** with established maximum residue limits (MRLs).
- **Low health concern from food:** No health risks from chlorpyrifos food residues alone were identified in Health Canada's previous assessment. Similarly, the **recent** proposed United States Environmental Protection Agency (USEPA) assessment for chlorpyrifos

⁶ PACR2003-03, *Phase 2 of the Re-evaluation of Chlorpyrifos*

(proposed interim decision, [December 2020](#)⁷), had the same conclusion. Furthermore, the USEPA assessment took into consideration the more recent health information available since Health Canada's assessment, as well as the more extensive use pattern that exists in the United States than in Canada. In other words, as acute and chronic dietary risks for all American populations exposed to food treated with chlorpyrifos were shown to be acceptable, this would be the same for Canadians.

- **Low health concern from drinking water:** While a fully updated assessment for drinking water has not been completed in Canada, Health Canada's analysis of Canadian water monitoring data collected over many years showed that only a fraction of samples had detectable levels of chlorpyrifos. Moreover, these levels were below the Health Canada's drinking water level of concern that had been determined in the 2003 assessment, with the exception of one sample⁸ collected in 2005. Several mitigation measures were then implemented in 2007, including buffer zones and a reduced use pattern, and no samples exceeded the level of concern since that time. A total of 166 816 potential drinking water samples (from 1972–2016)⁹ were analyzed for chlorpyrifos (groundwater, ambient surface water, and treated drinking water) from Canada and the United States, with a detection frequency of 8%. Moreover, in February 2020,¹⁰ Health Canada, in collaboration with the Federal-Provincial-Territorial Committee on Drinking Water, proposed to withdraw the existing Guidelines for Canadian Drinking Water Quality for several pesticides, including chlorpyrifos, as it was determined that these are unlikely to be found in Canadian drinking water at levels that may pose a risk to human health. Therefore, the Guidelines are no longer required. There is also a low level of concern for chlorpyrifos breakdown products including chlorpyrifos oxon, a byproduct of chlorine treatment. As chlorpyrifos is not often detected and unlikely to be found in Canadian drinking water sources at levels that may pose a risk to human health, the formation of oxon at a level of concern is not expected, if treated with chlorine.
- **Health Canada's assessment continues to be protective of the Canadian population:** As previously noted, Health Canada's most recent human health mitigation measures were published in 2007 ([REV2007-01](#)). At the time the cancellation notice for Canadian registrations of chlorpyrifos ([REV2021-02](#)) was published in May 2021 (now superseded by this current decision), the most recent (2019)¹¹ international, risk-based **decision** on chlorpyrifos had been issued by the Australian Pesticide and Veterinary Medicine

⁷ Chlorpyrifos Proposed Interim Registration Review Decision Case Number 0100 December 2020

⁸ The maximum detection of 4 µg chlorpyrifos/L from Canadian monitoring data was from one sample in Québec, in 2005. All other samples were below the drinking water level of concern (DWLOC).

⁹ Further characterization of risks concentrated on a 2000-2016 subset of 15,080 samples from the available data.

¹⁰ Withdrawal of Select Guidelines for Canadian Drinking Water Quality

¹¹ APVMA Reconsideration of chlorpyrifos: Residential exposure and public space use exposure assessment and risk characterisation update. https://apvma.gov.au/sites/default/files/publication/50121-chlorpyrifos_2019_residential_exposure_assessment_and_risk_characterisation_report.pdf

Authority (APVMA). In addition, as noted above, the USEPA posted a more recent assessment in [December 2020](#) (which was a **proposed** decision). Both the APVMA and USEPA assessments took into consideration the more recent health information including epidemiology data and published scientific literature, on which they based updated human health reference values (that is, acceptable human exposure levels) for use in their risk assessments. While Health Canada has not updated the human health reference values in consideration of this additional information prior to the cancellation of all uses in Canada, it is important to note that Health Canada's reference values established in 2000 continue to be either aligned with those of APVMA and USEPA for sensitive subpopulations including women of child-bearing age, or more conservative (in other words, more protective) in the case of infants and children. Thus, this indicated that Health Canada's existing assessment would still be protective of the Canadian population, or even more protective in the case of infants and children.

- **Declining sales in Canada:** With the cancellation of all registrations of pest control products containing chlorpyrifos, the use of, and therefore, exposure to chlorpyrifos is expected to continuously decrease over the phase-out period as products are depleted. To date, there has been an overall trend in declining sales of chlorpyrifos in Canada. More specifically, sales in 2016, for example, were approximately 30% lower than those of 2008. Since 2016, decreasing trends have continued, with the most recent data from 2020 (not yet published) indicating sales to be approximately 83% lower than those reported for 2008. This supports the assumption that dietary exposure from existing Canadian products has been decreasing, and will continue to decrease during the phase-out period on an ongoing basis.
- **Decreasing use internationally:** Cancellation actions have also occurred in other jurisdictions, such as the European Union.¹² This further decreases dietary exposure to imported food treated with chlorpyrifos, which will continue to decline on an ongoing basis. Health Canada will continue to monitor the regulatory status of chlorpyrifos in other countries, as well as the degree of potential exposure in imported and domestically produced foods.
- **No serious Canadian incident reports:** Between 2007 and 2021, Health Canada received 56 human and domestic animal incidents reports in relation to chlorpyrifos. Of these, 11 were classified as human major, all of which occurred in the United States. Of the six American incidents with a causal relationship of possible (3), or probable (3), five involved occupational exposure to multiple pesticides, with some reporting improper use or lack of personal protective equipment. (The remainder were unlikely or had insufficient information). There were no deaths or other serious human incidents reported in Canada.

¹² July 31, 2019 statement by the European Food Safety Authority (EFSA): <https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2019.5809>

iii) International status and Canadian comparison

European Union

In 2020, the European Commission (EC) prohibited all uses of chlorpyrifos based on human health concerns resulting from data uncertainties. Following a preliminary analysis of the 2020 EC decision concerning the non-renewal of plant protection products containing chlorpyrifos, Health Canada identified the following aspects of concern:

- Genotoxic potential of chlorpyrifos,
- Developmental neurotoxicity of chlorpyrifos, and
- Reproductive toxicity of chlorpyrifos.

The basis of the European decision was articulated in the 31 July 2019 statement by the European Food Safety Authority (EFSA¹³), which noted that no toxicology reference values were established and a risk assessment was not conducted. Thus, the EC decision was based on potential hazard (any possible adverse or toxic effect), rather than risk (likelihood of an adverse effect based on the amount of exposure). It is important to note that a hazard classification is not a health risk assessment. A hazard describes any possible adverse or toxic effect that may be attributed to a substance at various dose or exposure levels, whereas an assessment of risk focusses on the likelihood of an adverse effect occurring with a given amount of exposure. Thus, the levels of human exposure, which determine the actual risk, were not taken into account in the EC decision. In Canada, pesticides undergo a health and environmental risk assessment to establish the level of exposure to Canadians and the environment that does not result in harmful effects. The level of acceptable exposure that is established by Health Canada and used for health risk assessment also incorporates additional safety factors, providing a further degree of protection.

On 10 February 2021, a notice was issued by Health Canada (Reference No. 2019-3275) that a new special review of chlorpyrifos relating to a 2020 EC decision to cancel all uses would not be initiated under subsection 17(2) of the *Pest Control Products Act*. This was because the identified aspects of concern would be assessed with the ongoing re-evaluation of chlorpyrifos at that time, specifically in relation to updating the human health risk assessment, as per subsection 17(7) of the *Pest Control Products Act*. Because the remaining product registrations were cancelled in the now superseded May 2021 decision, and that has not changed with this new decision, a health risk assessment will not be conducted. However, for the reasons described above, Health Canada has determined that there are no imminent and serious health risks that would warrant a shorter phase-out period.

¹³ July 31, 2019 statement by the European Food Safety Authority (EFSA):
<https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2019.5809>

Australia

As noted previously, the most recent final risk-based decision, which took into consideration the additional health information, was published in [2019](#) by the Australian Pesticide and Veterinary Medicine Authority (APVMA). Health Canada's human health reference values continue to be either aligned with those of APVMA for sensitive subpopulations including women of child-bearing age, or more conservative (in other words, more protective) in the case of infants and children.

United States

In the United States, the USEPA registration review of chlorpyrifos is ongoing, and a final decision regarding the registration status of chlorpyrifos is not scheduled until 2022. A December 2020 proposed interim decision proposed retaining 11 critical uses (alfalfa, apple, cherries (tart), asparagus, citrus, cotton, peach, soybean, strawberry, sugar beet, wheat), which were found to have acceptable health risk with mitigation measures. However, a recent (August 2021) USEPA Final Rule¹⁴ made in response to an order from the United States Court of Appeals for the Ninth Circuit has since resulted in the phase-out of all food uses of chlorpyrifos, including revocation of all Maximum Residue Limits, (referred to as tolerances in the United States). The decision of the United States to revoke all tolerances (in other words, MRLs) acknowledged that there were no risks of concern around chlorpyrifos residues on food based on their scientific assessment. However, the American tolerances were revoked based on different factors. First, there were concerns involving drinking water in the United States that are not applicable to the Canadian situation, given how rarely chlorpyrifos has been detected in Canadian drinking water, and when detected, falls below the level of concern. Second, a United States court order required an all or nothing conclusion on acceptable risk from the combined exposure to chlorpyrifos residues from drinking water, plus all current uses (food, commercial turf (for example, golf courses), etc.). Conversely, Canada has cancelled all uses and is applying the above-noted schedule, and overall the Canadian use pattern is smaller and more restrictive than that of the United States, having comparatively lower application rates and shorter seasonal uses.

Thus, it is important to keep in mind that this action in the United States is separate and distinct from the USEPA registration review process. Uses in non-food settings remain registered in the United States until completion of the re-evaluation.

Canada

As noted in Section (ii), Health Canada's current human health reference values (acceptable levels of exposure) continue to be either aligned with those of the APVMA and USEPA for sensitive subpopulations including women of child-bearing age, or more conservative (in other words, more protective) in the case of infants and children.

¹⁴ USEPA, Chlorpyrifos Tolerance Final Rule Docket

Thus, given dietary risks were acceptable in Health Canada's original assessment using health reference values that are either aligned with or more conservative than the more recently updated human health reference values of other jurisdictions, Health Canada's assessment would still be protective of the Canadian population, including infants and children.

Conclusion

As noted above, Health Canada has implemented several risk reduction measures for chlorpyrifos over the years. In 2000, Health Canada stopped allowing almost¹⁵ all uses by homeowners¹⁶ and updated chlorpyrifos labels to reflect this. In addition, Health Canada implemented mitigation measures in 2007 ([REV2007-01, Update on the Re-evaluation of Chlorpyrifos](#)) to further protect human health and the environment, following an assessment on agricultural and forestry uses. In December 2020, Health Canada published a re-evaluation decision (RVD2020-14, *Chlorpyrifos and Its Associated End-use Products (Environment)*) based on an updated environmental risk assessment (PRVD2019-05, *Chlorpyrifos and Its Associated End-use Products: Updated Environmental Risk Assessment*). In this decision, Health Canada cancelled almost all agricultural uses due to environmental risks of concern, while a few uses were acceptable from the environmental perspective. In this current decision (REV2021-04), all remaining registrations of pest control products containing chlorpyrifos are cancelled **immediately** due to failure to fulfill the mandatory data requirements to update the human health risk assessment for the final phase of the re-evaluation. Health Canada has determined that the current chlorpyrifos uses will not pose imminent and serious risks during the period of the phase-out described under the section entitled: **Final Determination with Respect to Chlorpyrifos**, taking into account the considerations outlined under section (ii).

¹⁵ Containerized low concentration ant baits/bait stations were discontinued in 2017

¹⁶ Re-evaluation Note REV2000-05 *Chlorpyrifos*, 28 September 2000

Appendix I – Products containing chlorpyrifos subject to a phase-out period

Table 1 Products containing chlorpyrifos subject to a phase-out period¹⁷

Registration number	Product name	Registrant name	Status*
14879	Lorsban 4E Insecticide	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
16458	Lorsban 15G Insecticide	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
19656	Dursban FM Insecticidal Chemical	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
20320	Dursban HF Insecticidal Concentrate	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
20407	Dursban W Insecticidal Concentrate	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
20944	Lorsban 50W Insecticide	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
21997	Dursban Water Soluble Insecticide	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
23621	Pyrinex Technical Chlorpyrifos Insecticide	Adama Agricultural Solutions Canada Ltd.	Phase-Out Ending 2023-12-10
23704	Pyrate 480 EC Insecticide	Adama Agricultural Solutions Canada Ltd.	Phase-Out Ending 2023-12-10
23705	Pyrinex 480EC For Food Crops	Adama Agricultural Solutions Canada Ltd.	Phase-Out Ending 2023-12-10
24648	Pyrifos 15G Insecticide	Loveland Products Canada Inc.	Phase-Out Ending 2023-12-10
25823	Chlorpyrifos Technical	FMC of Canada Limited	Phase-Out Ending 2022-12-31
25831	Nufos 4E Insecticide	FMC of Canada Limited	Phase-Out Ending 2023-12-10
27479	Citadel 480EC Insecticide	Interprovincial Cooperative Limited	Phase-Out Ending 2022-12-10
29650	Lorsban NT Insecticide	Corteva Agriscience Canada Company	Phase-Out Ending 2023-12-09
29984	Warhawk 480 EC Insecticide	Loveland Products, Inc.	Phase-Out Ending 2023-12-10

¹⁷ Source: Pesticide Product Information Database [<https://pesticide-registry.canada.ca/en/index.html>]

Registration number	Product name	Registrant name	Status*
30985	Mpower Krypton	NewAgco Inc.	Phase-Out Ending 2023-12-10
31417	Chlorpyrifos Agrogill Technical Grade Active Ingredient	Agrogill Chemicals Pty Ltd	Phase-Out Ending 2023-12-10
32694	Sharda Chlorpyrifos Technical Insecticide	Sharda Cropchem Limited	Phase-Out Ending 2023-12-10
32768	Sharphos Insecticide	Sharda Cropchem Limited	Phase-Out Ending 2023-12-10
33113	Pyrinex 450 LV EC	Adama Agricultural Solutions Canada Ltd.	Phase-Out Ending 2023-12-10
33295	Newagco Chlorpyrifos Technical	NewAgco Inc.	Phase-Out Ending 2023-12-10
33356	Mpower Chlorpyrifos Insecticide	NewAgco Inc.	Phase-Out Ending 2023-12-10

* For details, consult the Pesticide Product Information Database

This is **Exhibit "I"** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

Laura Bowman

From: Law, Andrew <Andrew.Law@justice.gc.ca>
Sent: Friday, January 14, 2022 3:55 PM
To: Laura Bowman; Daniel Cheater
Cc: Bourke, Andrea; Lovell, Karen; Koudys, Elizabeth
Subject: RE: Safe Food Matters et al v AGC (T-956-21) and (T-1412-21) - Service of affidavits and confidentiality [ECO-ACTIVE.FID37043]

Follow Up Flag: Follow up
Flag Status: Flagged

Hi Laura and Dan,

In response to your letter, please note that the excerpted text at para.152 of the MacDonald affidavit contains confidential material under the sub-heading "Higher Potential Residues". The redactions made to this information as reflected in document #467 in the public CTR are not reflected in para.152 of the affidavit. Otherwise, we have no concerns regarding confidentiality.

Lastly, I imagine that you are aware that the PMRA has issued a decision replacing Re-evaluation Note (REV2021-02), which can be found at the following link: <https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/decisions-updates/reevaluation-note/2021/cancellation-remaining-chlorpyrifos-registrations.html>.

Best regards,

Andrew Law (he/il)
Counsel | Avocat
National Litigation Sector | Secteur national du contentieux
Department of Justice | Ministère de la Justice
Ontario Regional Office | Bureau régional de l'Ontario
120 Adelaide Street West, Suite #400
Toronto, ON M5H 1T1
Tel. | tél.: (647) 967-8104
Government of Canada | Gouvernement du Canada

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From: Laura Bowman <lbowman@ecojustice.ca>
Sent: Wednesday, January 5, 2022 9:14 AM
To: Bourke, Andrea <Andrea.Bourke@justice.gc.ca>; Lovell, Karen <Karen.Lovell@justice.gc.ca>; Law, Andrew <Andrew.Law@justice.gc.ca>; Koudys, Elizabeth <Elizabeth.Koudys@justice.gc.ca>
Cc: Daniel Cheater <dcheater@ecojustice.ca>

Subject: Safe Food Matters et al v AGC (T-956-21) and (T-1412-21) - Service of affidavits and confidentiality [ECO-ACTIVE.FID37043]

Dear counsel,

Please find attached correspondence in the above matter.

Laura Bowman (she/her)
Staff Lawyer | [Ecojustice](#)
1910-777 Bay Street, PO Box 106, Toronto, ON M5G 2C8
T: 416-368-7533, ext. 522 | 1-800-926-7744, ext. 522

[Ecojustice is Canada's largest environmental law charity. Help us build the case for a better earth.](#)

I am grateful to be a guest on the traditional territories of several First Nations including the Huron-Wendat, the Anishnaabeg, Haudenosaunee, Chippewas and the Mississaugas of the Credit First Nation. I am committed to protecting the cultural and natural heritage of Indigenous peoples in accordance with Indigenous law. I strive to respect the principles of sharing and sustainability embodied by the Dish with One Spoon Covenant and to end discriminatory and colonial practices that create barriers for Indigenous peoples.

This message may contain confidential and/or privileged information. If you are not the addressee or authorized to receive this for the addressee, you must not use, copy, disclose or take any action based on this message or any information herein. If you have received this message in error, please advise the sender immediately by reply e-mail and delete this message. Thank you.

This is **Exhibit “J”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



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of Canada

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- > [Reports and Publications – Consumer Product Safety](#)
- > [Pesticides and pest management reports and publications](#)
- > [Fact Sheets and Other Resources](#)

Information Note: Update on implementation of post-market decisions

Pest Management Regulatory Agency

21 December 2021

Introduction

Health Canada is providing an update on the implementation of post-market review decisions and how phase-out measures following the cancellation of pest control product registrations will be imposed under subsection 21(5) of the *Pest Control Products Act*.

Background

In 2018, Health Canada published *Regulatory Directive DIR2018-01, Policy on Cancellations and Amendments Following Re-evaluation and Special Review* (“Cancellation Policy”), which outlined the framework for the cancellation and amendment of pest control products.

Since the adoption of the Cancellation Policy, Health Canada has received

numerous questions and requests for clarifications on its implementation. While work to update the policy is beginning, Health Canada has identified an area that would benefit from greater clarity around the status of cancelled products.

Registration status during the phase-out period

As of 21 December 2021, Health Canada will **immediately** cancel pest control product registrations on the date of a decision made under paragraph 20(1)(a), where a registrant fails to provide the required data pursuant to a notice, and on the date of a re-evaluation or special review decision made under paragraph 21(2)(b) of the *Pest Control Products Act*, unless the effective date is delayed under subsection 21(3) of the *Pest Control Products Act*. If there are no serious and imminent risks to human health or the environment, Health Canada will allow for a phase-out period consistent with the Cancellation Policy and will impose any **conditions** necessary for carrying out the purposes of the *Pest Control Products Act* under the authority of paragraph 21(5)(a) of the *Pest Control Products Act*.

Consistent with prior cancellation decisions that imposed a phase-out period, there can be:

- no further import of the cancelled pest control product into Canada, and
- no manufacture of the cancelled product within Canada.

While the pest control product registration is cancelled immediately, the product continues to be authorized under the *Pest Control Products Act* so that registrants, retailers and users **may continue to possess, handle,**

store, distribute or use existing stocks of the product in Canada, as the case may be, in accordance with the conditions imposed under paragraph 21(5)(a) of the *Pest Control Products Act*.

Registrants, retailers/distributors and users will be required to meet any other conditions that may be imposed. These conditions may include disposal requirements, or continuing to report incidents or sales.

When risks of concern are considered to be imminent and serious, Health Canada may require the registrant to recall and dispose of the product in a manner specified by the Minister or may seize and dispose of the product in accordance with paragraph 21(5)(b) or 21(5)(c) of the *Pest Control Products Act*.

Impact on Registrant / Retailers / Users

During the phase-out period, cancelled products will be authorized under the *Pest Control Products Act*, and existing stocks in Canada will continue to be available for sale and use as per the periods described in the Cancellation Policy. Impact on registrants, retailers/distributors or users is considered minimal. Registrants, retailers/distributors and users will continue to be required to meet any conditions imposed by Health Canada in order to meet the purposes of the *Pest Control Products Act*.

Improved transparency

Health Canada's Pest Management Regulatory Agency (PMRA) recently updated its [Public Registry](#) to communicate to the public that a cancelled product is being phased-out. These products will no longer appear as "Registered" and will be listed as "Phase-out". For improved

transparency and to minimize confusion among users and other stakeholders, Health Canada will be publishing further instructions on how to find information in the [Pesticide Product Information Database \(PPID\)](#) on cancelled products that are being phased-out.

Next Steps

Health Canada will be reviewing the policy on cancellations and amendments following re-evaluation and special review.

Date modified:

2021-12-21

This is **Exhibit “K”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
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> [Protecting Your Health and the Environment](#) > [Public Registry](#)

Finding information on cancelled pesticide products during the phase-out period

The purpose of this document is to explain how to find information from Health Canada's Pesticide Product Information Database (PPID) on cancelled products that are currently being phased out. When a product registration is cancelled with a phase-out period, its registration status in the [Pesticide Product Information Database](#) will show as "Phase-out" until the phase-out period is complete. Once the phase-out period is complete, the registration status will be changed to "Cancelled". This facilitates Health Canada and provincial regulatory authorities in monitoring for regulatory compliance during the phase-out period. Additionally, information on the phase-out period of a cancelled product (in other words, last date of sale by registrant, last date of sale by retailers/distributors, and the last date of use or expiry date) is available by searching the PPID.

Registrations of pesticide products may be cancelled due to various reasons, including the following:

- if a registrant fails to provide information required under the *Pest Control Products Act*,
- if product cancellation is required as a result of re-evaluation or

special review or

- if a registrant submits a notice to discontinue the registration of the product.

When a product is cancelled, a phase-out period may be established to allow for an orderly depletion of existing stock in Canada. In 2018, Health Canada published *DIR2018-01: Policy on Cancellations and Amendments Following Re-evaluation and Special Reviews* ([Health Canada's Cancellation Policy](#)). In accordance with the Cancellation Policy, Health Canada considers the level of risk and may impose a phase-out period. This would allow existing stocks in Canada of the cancelled product to be exhausted in an orderly manner, to minimize potential risks associated with disposing of existing product all at once.

If there are no serious and imminent risks to human health or the environment, Health Canada will allow for a phase-out period consistent with the Cancellation Policy and will impose any conditions necessary for carrying out the purposes of the *Pest Control Product Act* under the authority of paragraph 21(5)(a) of the Act ([Information Note: Update on implementation of post-market decisions](#), published on 21 December 2021).

No one is allowed to import or manufacture a cancelled product during the phase-out period.

As outlined in the Information Note, the cancelled product continues to be authorized under the *Pest Control Product Act* during the phase-out period. Registrants, retailers and users may continue to possess, handle, store, distribute or use existing stocks of the product in Canada, as the case may be, in accordance with the conditions imposed by Health Canada under paragraph 21(5)(a) of the *Pest Control Product Act*.

Information on the phase-out periods of cancelled products (in other words, last date of sale by registrant, last date of sale by retail, and product expiry date after which time it is no longer authorized) are available in the PPID. The following steps in the PPID illustrate how to find this information.

Searching the PPID

The Home Page

When you reach the Pesticide Products Information Database (PPID), you will be presented with different search modules. Note that the PPID only contains information about decisions that were made under the current *Pest Control Products Act* that came into force 2006.

To search for products that are cancelled, but undergoing a phase-out period, you need to query the product database. Click on the "Product Search" module.

Pesticide Product Information Database

Welcome to the new and improved version of the Pesticide Product Information Database. This upgraded version allows you to search, sort and filter information on application, product, active ingredient, and incident reports.

If you have any questions, please contact the [PMRA Information Service](#)

Search specific areas

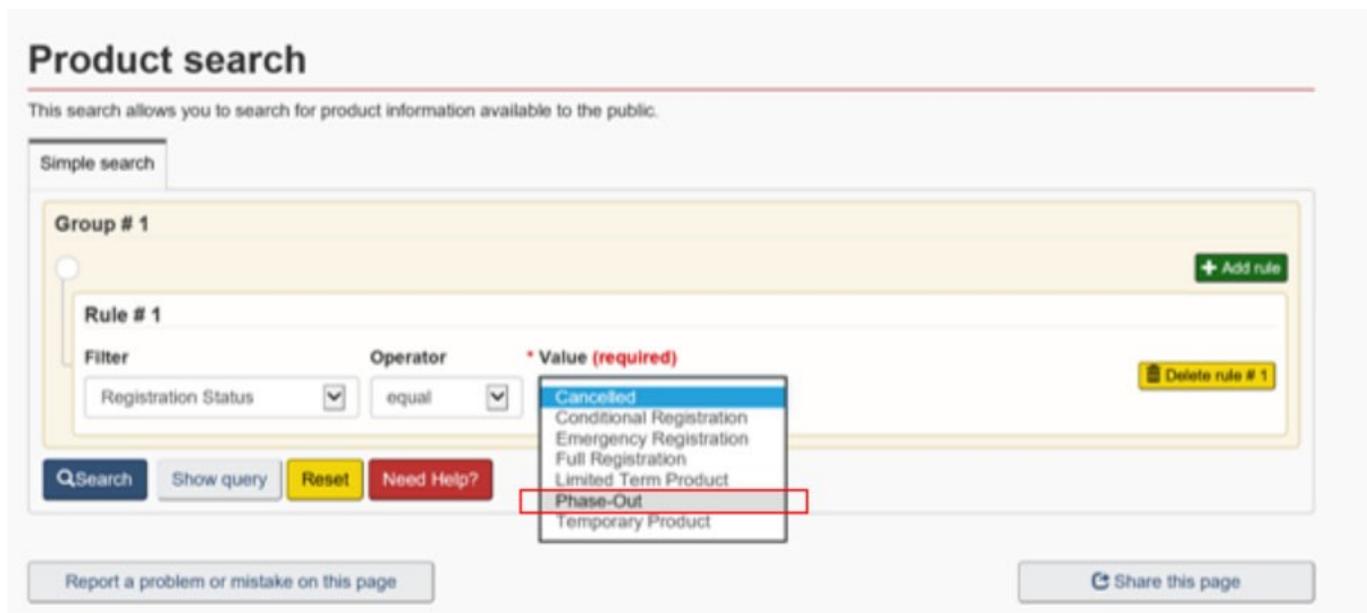
Select an area below to perform a search against a specific part of the Public Registry's database.

Application	Product	Active ingredient	Incident report
Applications to register or amend pest control product are submitted from external parties to the PMRA for review. This search will allow you to search for open and completed applications.	This search allows you to search for product information available to the public.	This search allows you to search for active ingredient information available to the public.	The search allows you to search within the incident reporting database. This database houses all incident reports for Canadian marketed pesticides that have been submitted to Health Canada.
Application search	Product search	Active ingredient search	Incident report search

[Report a problem or mistake on this page](#) [Share this page](#)

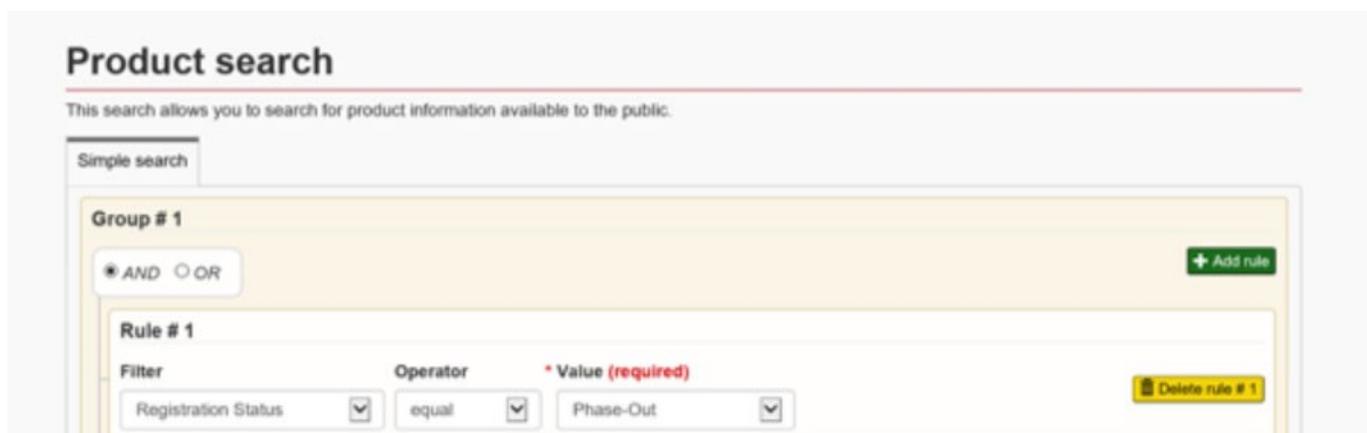
The Query

After selecting "Product Search", you will be presented with a module that allows you to filter through the product database. In order to filter for products that are undergoing a phase-out, select the Filter "Registration Status", the operator "equal", and select "Phase-Out" from the value dropdown list.



Click "Search" to run the query

If you wish to confirm a phase-out period for a specific active ingredient, click "Add rule". Under the new rule, select the filter "Active Ingredient-English", select the operator "Contains", and in the value write the name of the active ingredient, or part of the name of the active ingredient.



Rule # 2

Filter: Active Ingredient - English Operator: contains * Value (required): dichlorv

[Delete rule # 2](#)

[Search](#) [Show query](#) [Reset](#) [Need Help?](#)

[Report a problem or mistake on this page](#) [Share this page](#)

Click "Search" to run the query

The Search Results

The search results will appear underneath the search query.

Product search

This search allows you to search for product information available to the public.

Simple search

Group # 1 [+ Add rule](#)

AND OR

Rule # 1

Filter: Registration Status Operator: equal * Value (required): Phase-Out [Delete rule # 1](#)

Rule # 2

Filter: Active Ingredient - English Operator: contains * Value (required): dichlorv [Delete rule # 2](#)

[Search](#) [Show Query](#) [Reset](#) [Need Help?](#)

Search results

[Print List](#)
[Download CSV](#)

(May need to scroll to see all columns)

Filter items: Showing 1 to 5 of 5 entries | Show 10 entries

Registration number	Product name - English	Active ingredients - English	Registrant	Product types	Marketing type	Registration status	Status expiry date	Date first registered	Est d
11819	GARDEX VAPONA INSECTICIDE INDUSTRIAL FOGGING SOLUTION	<ul style="list-style-type: none"> • DICHLORVOS • PLUS RELATED ACTIVE COMPOUNDS 	GARDEX CHEMICALS LTD.*	INSECTICIDE	COMMERCIAL	Phase-Out	2023-08-20	1973-07-01	11 0'
16476	GARDEX VAPONA-20 ULV CONCENTRATE	<ul style="list-style-type: none"> • DICHLORVOS • PLUS RELATED ACTIVE COMPOUNDS 	GARDEX CHEMICALS LTD.*	INSECTICIDE	COMMERCIAL	Phase-Out	2023-08-20	1980-06-04	11 0'
21824	DICHLORVOS PLUS #1 READY TO USE INSECTICIDE	<ul style="list-style-type: none"> • DICHLORVOS • PLUS RELATED ACTIVE COMPOUNDS 	PLUS (0021-7993 QUEBEC INC)*	INSECTICIDE	COMMERCIAL	Phase-Out	2023-08-20	1991-03-07	11 0'
22027	ORTHO HOME DEFENSE MAX	<ul style="list-style-type: none"> • DICHLORVOS • PLUS RELATED 	SCOTTS CANADA LTD.*	INSECTICIDE	DOMESTIC	Phase-Out	2023-08-20	1994-08-03	11 0'

Clicking the Registration Number of any single record will navigate to the details page for that product. For example, if you click on "11819", it will bring you to the details page for "Gardex Vapona Insecticide Industrial Fogging Solution"

Product details for: GARDEX VAPONA INSECTICIDE INDUSTRIAL FOGGING SOLUTION

[Print details](#)

Registration number	11819
Product name - English	GARDEX VAPONA INSECTICIDE INDUSTRIAL FOGGING SOLUTION
Product name - French	SOLUTION INSECTICIDE VAPONA BRUMISANTE POUR USAGE INDUSTRIEL GARDEX
Registrant	GARDEX CHEMICALS LTD.*
Count of active ingredients	1
Product types	INSECTICIDE
Registration status	Phase-Out
Marketing type	COMMERCIAL
Date first registered	1973-07-01
Exclusive period start date	1928-07-01
Last sale by registrant	2021-08-20
Last sale by retail	2022-08-20
Expiry date	2023-08-20
Re-evaluation status	NO
Count of historical applications	6
Use Site Category	5-GREENHOUSE FOOD CROPS, 25-HUMAN HABITAT AND RECREATIONAL AREAS, 20-STRUCTURAL
Current/Historical	Current

- [Historical applications](#)
- [Active ingredients](#)
- [Published documents](#)
- [Labels](#)

Products that are cancelled will have a date entered in the "Last sale by registrant" and "Last sale by retail" and "Expiry date" rows. The Expiry date is the last date of use and the last day on which the product is authorized.

Date modified:

2022-02-07

This is **Exhibit “L”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

This product has been cancelled effective as of December 21, 2021, but is authorized under paragraph 21(5)(a) of the Pest Control Products Act. Manufacturing and importing of the product are no longer permitted. The existing stocks in Canada are to be depleted according to the phase-out schedule, as listed in the Pesticide Product Information Database (<https://pesticide-registry.canada.ca>).

GROUP	1B	INSECTICIDE
-------	-----------	-------------

<Container label>

SHARPHOS INSECTICIDE

AGRICULTURAL

Emulsifiable Concentrate, Contains Chlorpyrifos

This product is not to be used in and around homes or other residential areas such as parks, school grounds, playing fields. It is not for use by homeowners or other uncertified users.

DANGER



POISON

EYE AND SKIN IRRITANT
POTENTIAL SKIN SENSITIZER

READ THE LABEL AND BROCHURE BEFORE USING

KEEP OUT OF REACH OF CHILDREN

ACTIVE INGREDIENT:
Chlorpyrifos 480 g/L

REGISTRATION NUMBER 32768 PEST CONTROL PRODUCTS ACT

NET CONTENTS: 1 - 500 L

Sharda Cropchem Limited
2nd Floor, Prime Business Park
Dashrathlal Joshi Road,
Vile Parle (West)
Mumbai 400056
India

Canadian Agent:
Sharda Cropchem Limited
63 Kingsview Blvd
Etobicoke, Ontario, CA
M9R1V1
1-844-810-5720
1-416-840-5639

PRECAUTIONS

KEEP OUT OF REACH OF CHILDREN

Fatal if swallowed. May be harmful if inhaled or absorbed through skin. Causes eye and skin irritation. Do not get in eyes, on skin, or on clothing. Potential skin sensitizer. Do not inhale vapours or spray mist. Handle chemical in a ventilated area. Wear protective clothing and rubber gloves when handling. Wash thoroughly with soap and water after handling and before eating, drinking, or smoking. Remove contaminated clothing and laundry separately before reuse. Do not wear contaminated shoes or boots. Keep away from food, feedstuffs, and water supplies.

FIRST AID

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control centre or doctor for treatment advice.

IF SWALLOWED, call a poison control centre or doctor immediately for treatment advice. Do not induce vomiting unless told to do so by a poison control centre or doctor. Do not give any liquid to the person. Do not give anything by mouth to an unconscious person.

IF ON SKIN OR CLOTHING, take off contaminated clothing. Rinse skin immediately with plenty of water for 15– 20 minutes. Call a poison control centre or doctor for treatment advice.

IF INHALED, move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. Call a poison control centre or doctor for further treatment advice.

Take container label or product name and Pest Control Product Registration Number with you when seeking medical attention.

TOXICOLOGICAL INFORMATION

Chlorpyrifos is an organophosphate that is a cholinesterase inhibitor affecting the central and peripheral nervous systems and producing respiratory and cardiac depression. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation, runny nose and eyes. This may progress to muscle twitching, weakness and tremor in coordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). **ANTIDOTE:** Atropine, only by injection, is the preferable antidote. Administer atropine sulphate in large doses; TWO or FOUR mg intravenously or intramuscularly as soon as cyanosis is overcome. Repeat at 5 to 10 minute intervals until signs of atropinization appear. Oximes, such as pralidoxime chloride, may be therapeutic if used early; however, use only in conjunction with atropine. **DO NOT GIVE MORPHINE OR**

TRANQUILIZERS. In cases of severe acute poisoning, use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician. At first sign of pulmonary edema, the patient should be given supplemental oxygen and treated symptomatically. Continued absorption of chlorpyrifos may occur and relapse may occur after initial improvement. **VERY CLOSE SUPERVISION OF THE PATIENT IS INDICATED FOR AT LEAST 48 HOURS.**

NOTE: Product contains a petroleum distillate solvent. Vomiting may cause aspiration pneumonia.

STORAGE

Keep away from food, drinks, and animal feedstuffs. Keep only in the original container, tightly closed. Do not store near heat or open flame.

Do not contaminate water, food or feed by storage. Store only in original container in secure, dry storage area. Prevent cross-contamination with other pesticides and fertilizers. Do not store above 38°C (100°F) for extended periods of time. If container is damaged or spill occurs, use product immediately or dispose of product and damaged container as indicated below.

DISPOSAL

Recyclable Containers:

Do not reuse this container for any purpose. This is a recyclable container, and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.
2. Make the empty, rinsed container unsuitable for further use.

If there is no container collection site in your area, dispose of the container in accordance with provincial requirements.

Returnable Containers:

Do not reuse this container for any purpose. For disposal, this empty container may be returned to the point of purchase (distributor/dealer).

For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

Returnable-Refillable Containers:

For disposal, this container may be returned to the point of purchase (distributor/dealer). It must be refilled by the distributor/dealer with the same product. Do not reuse this container for any other purpose. For information on the disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the

manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

NOTICE TO USER: This pest control product is to be used only in accordance with the directions on the label. It is an offence under the *Pest Control Products Act* to use this product in a way that is inconsistent with the directions on the label. The user assumes the risk to persons or property that arises from any such use of this product.

<Detachable pamphlet>

GROUP

1B

INSECTICIDE

SHARPHOS INSECTICIDE

Emulsifiable Concentrate, Contains Chlorpyrifos

This product is not to be used in and around homes or other residential areas such as parks, school grounds, playing fields. It is not for use by homeowners or other uncertified users.

DANGER



POISON

EYE AND SKIN IRRITANT
POTENTIAL SKIN SENSITIZER

READ THE LABEL AND BROCHURE BEFORE USING

KEEP OUT OF REACH OF CHILDREN

ACTIVE INGREDIENT: Chlorpyrifos 480 g/L

REGISTRATION NUMBER 32768 PEST CONTROL PRODUCTS ACT

NET CONTENTS: 1 - 500 L

Sharda Cropchem Limited
2nd Floor, Prime Business Park
Dashrathlal Joshi Road,
Vile Parle (West)
Mumbai 400056
India

Canadian Agent:
Sharda Cropchem Limited
63 Kingsview Blvd
Etobicoke, Ontario, CA
M9R1V1
1-844-810-5720
1-416-840-5639

PRECAUTIONS

KEEP OUT OF REACH OF CHILDREN

Fatal if swallowed. May be harmful if inhaled or absorbed through skin. Causes eye and skin irritation. Do not get in eyes, on skin, or on clothing. Potential skin sensitizer. Do not inhale vapours or spray mist. Handle chemical in a ventilated area. Wear protective clothing and rubber gloves when handling. Wash thoroughly with soap and water after handling and before eating, drinking, or smoking. Remove contaminated clothing and launder separately before reuse. Do not wear contaminated shoes or boots. Keep away from food, feedstuffs, and water supplies.

FIRST AID

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control centre or doctor for treatment advice.

IF SWALLOWED, call a poison control centre or doctor immediately for treatment advice. Do not induce vomiting unless told to do so by a poison control centre or doctor. Do not give any liquid to the person. Do not give anything by mouth to an unconscious person.

IF ON SKIN OR CLOTHING, take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control centre or doctor for treatment advice.

IF INHALED, move person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably by mouth-to-mouth, if possible. Call a poison control centre or doctor for further treatment advice.

Take the container label or product name and Pest Control Product Registration Number with you when seeking medical attention.

TOXICOLOGICAL INFORMATION

Chlorpyrifos is an organophosphate that is a cholinesterase inhibitor affecting the central and peripheral nervous systems and producing respiratory and cardiac depression. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation, runny nose and eyes. This may progress to muscle twitching, weakness and tremor in coordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). **ANTIDOTE:** Atropine, only by injection, is the preferable antidote. Administer atropine sulphate in large doses; **TWO** or **FOUR** mg intravenously or intramuscularly as soon as cyanosis is overcome. Repeat at 5 to 10 minute intervals until signs of atropinization appear. Oximes, such as pralidoxime chloride, may be therapeutic if used early; however, use only in conjunction with atropine. **DO NOT GIVE MORPHINE OR TRANQUILIZERS.** In cases of severe acute poisoning, use antidotes immediately after

establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician. At first sign of pulmonary edema, the patient should be given supplemental oxygen and treated symptomatically. Continued absorption of chlorpyrifos may occur and relapse may occur after initial improvement. **VERY CLOSE SUPERVISION OF THE PATIENT IS INDICATED FOR AT LEAST 48 HOURS.**

NOTE: Product contains a petroleum distillate solvent. Vomiting may cause aspiration pneumonia.

STORAGE

Keep away from food, drinks, and animal feedstuffs. Keep only in the original container, tightly closed. Do not store near heat or open flame.

Do not contaminate water, food or feed by storage. Store only in original container in secure, dry storage area. Prevent cross-contamination with other pesticides and fertilizers. Do not store above 38°C (100°F) for extended periods of time. If container is damaged or spill occurs, use product immediately or dispose of product and damaged container as indicated below.

DISPOSAL

Recyclable Containers:

Do not reuse this container for any purpose. This is a recyclable container, and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.
2. Make the empty, rinsed container unsuitable for further use.

If there is no container collection site in your area, dispose of the container in accordance with provincial requirements.

Returnable Containers:

Do not reuse this container for any purpose. For disposal, this empty container may be returned to the point of purchase (distributor/dealer).

For information on disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

Returnable-Refillable Containers:

For disposal, this container may be returned to the point of purchase (distributor/dealer). It must be refilled by the distributor/dealer with the same product. Do not reuse this container for any other purpose. For information on the disposal of unused, unwanted product, contact the manufacturer or the provincial regulatory agency. Contact the manufacturer and the provincial regulatory agency in case of a spill, and for clean-up of spills.

ENVIRONMENTAL AND USE PRECAUTIONS

This pesticide contains a petroleum distillate and is extremely toxic to fish and aquatic organisms, toxic to birds and wild mammals. This pesticide is TOXIC to bees exposed to direct treatment, drift, or residues on blooming plants. Do not use on flowering crops or weeds. DO NOT apply this product or allow it to drift to flowering crops or weeds if bees are visiting the treatment area. Applicators should inform local bee keepers prior to application if hives are in adjacent fields. Minimize spray drift to reduce harmful effects on bees in habitats close to the application site. TOXIC to certain beneficial insects. Minimize spray drift to reduce harmful effects on beneficial insects in habitats next to the application site such as hedgerows and woodland. Avoid contamination of aquatic systems such as lakes, streams, ponds, estuaries, oceans, or other waters during application. Do not contaminate these systems through direct application, disposal of waste, or cleaning of equipment. Drift and runoff from treated areas may be hazardous to aquatic organisms in adjacent aquatic sites. Spilled material should be soaked up with absorbent material and disposed of in an approved manner. To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g., soils that are compacted or fine textured such as clay). Avoid application of this product when heavy rain is forecast. Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip (buffer zone) between the treated area and the edge of the water body. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance, contact the provincial regulatory authority or the manufacturer.

RESISTANCE-MANAGEMENT RECOMMENDATIONS

For resistance management, please note that SHARPHOS INSECTICIDE contains a Group 1B insecticide. Any insect/mite population may contain individuals naturally resistant to SHARPHOS INSECTICIDE and other Group 1B insecticides. The resistant individuals may dominate the insect population if this group of insecticides is used repeatedly in the same fields. Other resistance mechanisms that are not linked to site of action but are specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance-management strategies should be followed.

To delay insecticide resistance:

- Where possible, rotate the use of SHARPHOS INSECTICIDE or other Group 1B insecticides with different groups that control the same pests.
- Use tank mixtures with insecticides from a different group when such use is permitted.
- Insecticide use should be based on an IPM program that includes scouting and record keeping, and considers cultural, biological and other chemical control practices.
- Monitor treated pest populations for resistance development.
- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance management and/or IPM recommendations for the specific site and pest problems in your area.

- For further information or to report suspected resistance contact Sharda Cropchem Limited at 1-844-810-5720.

NOTICE TO USER:

This pest control product is to be used only in accordance with the directions on the label. It is an offence under the Pest Control Products Act to use this product in a way that is inconsistent with the directions on the label. The user assumes the risk to persons or property that arises from any such use of this product.

GENERAL INFORMATION

SHARPHOS INSECTICIDE is active against various insect pests by contact and ingestion. It is not systemic in the plant. Treatment of plants that are under extreme drought stress may result in some crop damage. The active ingredient in this product is decomposed by sunlight.

PRECAUTIONS FOR USE

Do not spray under windy conditions or from spraying equipment which could be expected to cause spray drift onto nearby crops or pastures. Do not mix with other pesticides when used on vegetables. Compatible with most commonly used pesticides except those that are alkaline. Do not add any additional adjuvants, surfactants, or spreader-stickers.

PRECAUTIONS FOR MIXERS/LOADERS

Formulations packaged in containers more than 10 L

Mixers/loaders must use a closed mechanical transfer loading system. Mixers/loaders must wear:

- coveralls over a long-sleeved shirt and long pants
- chemical-resistant gloves
- a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides socks and shoes

Formulations packaged in containers holding 10 L or less

Mixers/loaders must wear:

- coveralls over a long-sleeved shirt and long pants
- chemical-resistant gloves
- a chemical-resistant apron
- chemical-resistant footwear plus socks
- goggles or face shield

a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides

PRECAUTIONS FOR APPLICATORS

Do not apply with a mechanically pressurized handgun'.

Applicators using airblast equipment with a closed cab must wear:

- a long-sleeved shirt and long pants

- socks and shoes
- chemical-resistant gloves when leaving cab for clean-up and repair (gloves must be removed and left outside when re-entering the cab)

Applicators using airblast equipment with an open cab must wear:

- a long-sleeved shirt and long pants
- chemical-resistant coveralls and head protection
- socks and shoes
- chemical-resistant gloves
- goggles or face shield

a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides'

Applicators using ground application equipment with a closed cab must wear:

- a long-sleeved shirt and long pants
- chemical-resistant gloves when leaving cab for clean up and repair (gloves must be removed when re-entering the cab)
- socks and shoes

Applicators using ground application equipment with an open cab must wear:

- coveralls over a long-sleeved shirt and long pants
- chemical-resistant gloves
- socks and shoes

Applicators using aerial application equipment must use enclosed cockpits and must wear:

- a long-sleeved shirt and long pants
- socks and shoes

Applicators using handheld equipment must wear:

- a long-sleeved shirt and long pants
- chemical-resistant coveralls and head protection (if spray is upwardly directed)
- chemical-resistant footwear and socks
- chemical-resistant gloves

a respirator with a NIOSH-approved organic-vapour-removing cartridge with a prefilter approved for pesticides OR a NIOSH-approved canister approved for pesticides

DIRECTIOS FOR USE

MIXING:

To prepare the spray, add approximately 1/4 of the required amount of water to the clean spray tank, add required quantity of product and mix well. Complete filling the tank with the balance of the water needed.

Do not allow the pesticide to come into contact with the water intake pipe. Maintain sufficient agitation during both mixing and application to ensure uniformity of the spray mixture.

To avoid injury to the crop, mix only with pesticides listed on this label.

For all applications: DO NOT apply during periods of dead calm. Avoid application of this product when winds are gusty. Apply only when the potential for drift to areas of human habitation or areas of human activity (such as houses, cottages and recreational areas) is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

For aerial applications: DO NOT apply when wind speed is greater than 16 km/h at flying height at the site of application. The nozzle type is restricted to CP®, with the following set-up restriction:

Nozzle Type Restriction

CP® **DO NOT** use greater than 30° deflection

For airblast applications: Airblast applications are only permitted on filbert (hazelnut) trees. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

Buffer Zones

The buffer zones specified in the following tables are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands), estuarine habitats and marine habitats.

Aerial Applications

For all aerial applications, a buffer zone of 100 metres is required for the protection of aquatic habitats.

Field Sprayer Applications^{1,2}

Rate of Application (L/ha)	Buffer Zones (metres) Required for the Protection of Aquatic Habitats With Water Depths Of:		
	< 1 metre	1-3 metres	> 3 metres
Up to 1.2	50	40	30
Greater than 1.2, and less than or equal to 2.4	55	45	35
Greater than 2.4 and up to 4.8	60	50	40

¹For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy or ground, the labeled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy or ground, the labeled buffer zone can be reduced by 30%.

²Buffer zones are not required for treatments applied as a drench (i.e., drench applications for control of cabbage maggot, onion maggot and seedcorn maggot).

Airblast Applications

Rate of Application (L/ha)	Buffer Zones (metres) Required for the Protection of Aquatic Habitats With Water Depths Of:		
	< 1 metre	1–3 metre	> 3 metre
Up to 3.6	80	70	55

AERIAL APPLICATION

Directions for Use

Apply only by fixed-wing or rotary aircraft equipment which has been functionally and operationally calibrated for the atmospheric conditions of the area and the application rates and conditions of this label.

Label rates, conditions and precautions are product specific. Read and understand the entire label before opening this product. Apply only at the rate recommended for aerial application on this label. Where no rate for aerial application appears for the specific use, this product cannot be applied by any type of aerial equipment.

Ensure uniform application. To avoid streaked, uneven or overlapped application, use appropriate marking devices.

Use Precautions

Apply only when meteorological conditions at the treatment site allow for complete and even crop coverage. Apply only under conditions of good practice specific to aerial application as outlined in the National Aerial Pesticide Application Manual, developed by the Federal/Provincial/Territorial Committee on Pest Management and Pesticides.

Do not apply to any body of water. Avoid drifting of spray onto any body of water or other non-target areas. Specified buffer zones should be observed.

Coarse sprays are less likely to drift, therefore, avoid combinations of pressure and nozzle type that will result in fine particles (mist). Do not apply during periods of dead calm or when wind velocity and direction pose a risk of spray drift. Do not spray when the wind is blowing towards a nearby sensitive crop, garden, terrestrial habitat (such as shelter-belt) or aquatic habitat.

Operator Precautions

Do not allow the pilot to mix chemicals to be loaded onto the aircraft. Loading of premixed chemicals with a closed system is permitted.

It is desirable that the pilot have communication capabilities at each treatment site at the time of application.

The field crew and the mixer/loaders must wear chemical resistant gloves, coveralls and goggles or face shield during mixing/loading, cleanup and repair. Follow the more stringent label precautions in cases where the operator precautions exceed the generic label recommendations on the existing ground boom label.

All personnel on the job site must wash hands and face thoroughly before eating and drinking. Protective clothing, aircraft cockpit and vehicle cabs must be decontaminated regularly.

Product Specific Precautions

Read and understand the entire label before opening this product. If you have questions, call the manufacturer at 1-844-810-5720 or obtain technical advice from the distributor or your provincial agricultural representative. Application of this specific product must meet and/or conform to the following:

VOLUME: Apply the recommended rate in a minimum spray volume of 20 litres per hectare.

DO NOT apply this product directly to aquatic habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands), estuaries habitats or marine habitats.

DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

Application by aircraft is permitted only where specified in the directions for use.

A plantback interval of 30 days must be observed between application and planting of rotational crops, with the exception of radish, Chinese cabbage, pak choi and cole crops for which no plantback restriction is required.

TANK-MIX COMBINATIONS WITH HERBICIDES

SHARPHOS INSECTICIDE can be tank mixed with the herbicides listed for wheat, oats and barley. The mixture will control insect pests as well as broadleaved or grassy weeds as recommended on the labels of the products used. Read carefully and follow all use directions and use precautions on both the SHARPHOS INSECTICIDE label and the label of the herbicide to be used for tank mixing. The most stringent precautions of tank mix products must be followed. Failure to follow the rates of use and timing of application as recommended for each product will result in unsatisfactory control of the insect or weed target pest.

NOTE: If SHARPHOS INSECTICIDE is added first, it may settle out and cause plugging of lines or nozzles.

When tank-mixing with the following herbicides, always add herbicide to the partially water-filled spray tank, then add the SHARPHOS INSECTICIDE, then add the remaining water:

2,4-D Amine
2,4-D Ester
AVENGE 200-C
BANVEL
BUCTRIL M
GLEAN Herbicide Dry Flowable
MCPA Amine
MCPA Ester
TORDON 202 C Liquid Herbicide

Soil Applications

The higher rate of SHARPHOS INSECTICIDE should be used when the soil surface is extremely dry or the insect infestation is heavy. When preplant soil applications of SHARPHOS INSECTICIDE are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm.

Foliar Applications

Best results will be obtained when application is made during the early evening. Apply as a broadcast application in sufficient water to ensure thorough coverage of the foliage.

Restricted Entry Intervals

The workers' restricted-entry interval (REI) is 24 hours for all crops and activities, except for cauliflowers (10 days), filbert (4 days for scouting) and greenhouse ornamentals (2 days).

Sites and Pests	Rates and Directions
CANOLA	Do not apply more than once per season. Do not apply within 21 days of harvest. Application is permitted by ground application equipment or aircraft where specified. Do not enter treated fields until 1 day after application.
Bertha armyworm, alfalfa looper, armyworm	Apply 0.75-1 litres in 50-200 L/ha for ground application equipment, or in 10-30 L/ha for aircraft. Apply as a foliar spray. Use the higher rate of dilution when infestations are heavy and when the foliage is dense. Spray in the evening to reduce harm to pollinators.
Diamondback moth (larvae)	Apply 1-1.5 litres in 50-200 L/ha for ground application equipment, or in 40 L/ha for aircraft. Apply as a foliar spray. Use the higher rate of dilution when infestations are heavy and when the foliage is dense. Spray in the evening to reduce harm to pollinators.
Lygus bugs	Apply 0.5-1 litre in 50-200 L/ha for ground application equipment, or in 10-30 L/ha for aircraft. Apply as a foliar spray. Use the higher rate of dilution when infestations are heavy and when the foliage is dense. Spray in the evening to reduce harm to pollinators.
Army cutworm, darksided cutworm, pale western cutworm, redbacked cutworm, variegated cutworm	Apply 0.875-1.2 litres in 50-200 L/ha for ground application equipment, or in 10-30 L/ha for aircraft. Apply to the soil or foliage. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm.
Grasshoppers	Apply 0.58-0.875 litre in 50-200 L/ha for ground

	application equipment, or in 10-30 L/ha for aircraft. Apply as a foliar spray. Use the low rate for the control of juvenile grasshoppers and the high rate for the control of adult grasshoppers. Adjacent ungrazed and unoccupied areas such as roadsides, rights-of-way and fence lines should be treated at the first sign of infestation.
FILBERT (hazelnut)	Do not apply more than three times per season. Do not apply within 14 days of harvest. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 4 days after application to conduct scouting activities.
Filbert aphid	Apply 4.2 – 4.8 litres of product in 100 L/ha. Apply as a foliar spray with ground application only using an airblast sprayer. Direct nozzles of air blast sprayer into the orchard when spraying border rows.
FLAX	Do not apply more than once per season. Do not apply within 21 days of harvest. Application is permitted by ground application equipment or aircraft where specified. Do not enter treated fields until 1 day after application.
Bertha armyworm	Apply 0.75-1 litres in 50-200 L/ha for ground application equipment and 10-30 L/ha for aircraft. Apply as a foliar spray. Use the higher rate for larger larvae or when foliage is dense.
Army cutworm, darksided cutworm, pale western cutworm, redbacked cutworm, variegated cutworm, armyworm	Apply 0.875-1.2 litres in 50-200 L/ha for ground application equipment, or in 10-30 L/ha for aircraft. Apply to the soil or foliage.
LENTIL	Application is permitted by ground application equipment or aircraft where specified. Do not apply more than once per season. Do not apply within 21 days of harvest for applications up to 0.875 L/ha. For applications greater than 0.875 L/ha, do not apply within 60 days of harvest. Do not enter treated fields until 1 day after application.
Pale western cutworm	Apply once at seedling stage, when damage is first noticed. Use boom configurations that maximize spray coverage and penetration of the crop canopy. Apply 0.875 L – 1.2 L in 100–200 L of water/ha for ground application equipment, or in 20 L/ha for aircraft. Apply as a broadcast spray when damage first appears.
Grasshoppers	Use a boom and nozzle configuration which

	<p>provides optimum coverage.</p> <p>Foliar applications: Best results will be obtained when application is made during the early evening. Apply as a broadcast application in sufficient water to ensure thorough coverage of the foliage. Use the higher rate when infestations are heavy and when foliage is dense.</p> <p>Apply 0.58 L – 1.2 L in 50–200 L water/ha for ground application equipment, or in 10–30 L/ha for aircraft. Apply once per year at the flowering to early podding stage of crop. Uniform coverage of the crop and the crop canopy is essential. Use the low rate for the control of juvenile grasshoppers and the high rate for the control of adult grasshoppers. Adjacent ungrazed and unoccupied areas such as roadsides, right-of-ways and fence lines should be treated at the first sign of infestation.</p>
CORN (FIELD, SWEET) (Seedling treatment only)	Do not apply more than 1 application per season. Do not apply within 70 days of harvest. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 1 day after application.
Black cutworm, darksided cutworm, redbacked cutworm	<p>SOIL TREATMENT (PREPLANTING): Apply 2.4 litres in 200-400 L/ha. Apply once as a soil treatment 3-7 days before planting. Do not incorporate. Also apply to a 15 m strip into adjacent fence rows.</p> <p>SEEDLING TREATMENT: Apply 1.2-2.4 litres in 200-400 L/ha. Apply once as a broadcast spray at the 2- to 5-leaf stage of the crop.</p>
STRAWBERRY	Do not apply more than once per season. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply within 20 days of harvest. Do not enter treated fields until 1 day after application.
Strawberry cutworm (crown borer)	Apply 1.2 litres in 2000 L/ha. Apply once as a foliar spray between June 1 and June 15. Large volumes of water are desirable to ensure full wetting of the crown area of the plants.
CELERY, CUCUMBER, PEPPER (GREEN)	Do not apply more than once per season. Do not apply within 70 days of harvest for celery, 40 days of harvest for pepper, or 60 days of harvest for cucumber. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 1 day after application.

Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4 litres in 200-400 L/ha. Apply once as a soil treatment 3-7 days before planting or transplanting. Do not incorporate. Also apply to a 15 m strip into adjacent fence rows.														
	SEEDLING TREATMENT: Apply 1.2-2.4 litres in 200-400 L/ha. Apply once as a broadcast spray at the 2- to 5-leaf stage of the crop.														
PAK CHOI, BROCCOLI, BRUSSELS SPROUT, CABBAGE, CAULIFLOWER, CHINESE CABBAGE	Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 1 day after application for pak choi and Chinese cabbages. Do not enter treated fields until 10 days after application for cauliflower, 1 day after application for all other crops. [See also below.]														
	If no granular chlorpyrifos treatment has been used, do not apply more than twice per season to broccoli, cabbages, cauliflower, Chinese cabbages and pak choi, or three times per season to Brussels sprouts. If granular treatment has been used, do not apply more than once per season to broccoli, cabbages, cauliflower, Chinese cabbages and pak choi, or twice per season to Brussels sprouts. Do not apply within 32 days of harvest for broccoli, Brussels sprouts, cabbages, cauliflower or Chinese cabbages; or within 15 days of harvest for pak choi.														
Cabbage maggot	AT-PLANTING TREATMENT: Apply 210 mL/1000 m row. Apply one drench spray in 1000 L/ha spray solution, 10 cm on each side of the plant, 7-10 days after seeding or 3 days after transplanting.														
	POST PLANTING DRENCH: Mix 1.7 litres in enough water to make 1000 L of finished spray. Apply 12.5 L of this solution per 100 m of row on soil, 10 cm on each side of the plant. Do not apply to harvestable portions of the crop. <table data-bbox="727 1480 1015 1732"> <thead> <tr> <th>Row Spacing</th> <th>L/ha</th> </tr> </thead> <tbody> <tr> <td>30 cm</td> <td>7.0</td> </tr> <tr> <td>60 cm</td> <td>3.5</td> </tr> <tr> <td>75 cm</td> <td>2.8</td> </tr> <tr> <td>80 cm</td> <td>2.63</td> </tr> <tr> <td>90 cm</td> <td>2.33</td> </tr> <tr> <td>105 cm</td> <td>2.0</td> </tr> </tbody> </table> <p>If no granular treatment was used at seeding: For broccoli, Brussels sprouts, cabbages and cauliflower, apply a drench treatment within 3 days of transplanting (after plant recovery) or 7-10 days</p>	Row Spacing	L/ha	30 cm	7.0	60 cm	3.5	75 cm	2.8	80 cm	2.63	90 cm	2.33	105 cm	2.0
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	after seeding. Repeat 21 days after the transplanting drench or 28 days after the seeding drench.												
Black cutworm, darksided cutworm, redbacked cutworm (for BROCCOLI, BRUSSEL SPROUTS, CABBAGE, CAULIFLOWER, CHINESE CABBAGE)	SOIL TREATMENT: Apply 2.4 litres in 200-400 L/ha. Apply once, 3-7 days before transplanting. Do not incorporate. Also apply to a 15 m strip into adjacent fence rows.												
	SEEDLING TREATMENT: Apply 1.2-2.4 litres in 200-400 L/ha. Apply once as a broadcast spray at the 2- to 5-leaf stage of the crop.												
GARLIC	Do not apply more than twice per season. Do not apply within 50 days of harvest. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 1 day after application.												
Onion maggot	Apply 3.5 litres in 1000 L/ha. Apply as a drench to the soil over the seedling row.												
Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4 litres in 200-400 L/ha. Apply once, 3-7 days before transplanting. Do not incorporate. Also apply to a 15 m strip into adjacent fence rows.												
	SEEDLING TREATMENT: Apply 1.2-2.4 litres in 200-400 L/ha Apply once as a broadcast spray at the 2- to 5-leaf stage of the crop.												
RUTABAGA	Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 1 day after application. Do not apply within 30 days of harvest. If no granular chlorpyrifos treatment has been used, do not apply more than 4 times per season. If granular chlorpyrifos treatment has been used, do not apply more than 3 times per season.												
Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4 litres in 200-400 L/ha. Apply once, 3-7 days before transplanting. Do not incorporate. Also apply to a 15 m strip into adjacent fence rows.												
	SEEDLING TREATMENT: Apply 1.2-2.4 litres in 200-400 L/ha. Apply once as a broadcast spray at the 2- to 5-leaf stage of the crop.												
Cabbage maggot	Apply 210 mL in 125 L/1000 m row. Apply as a postplanting drench to soil, 10 cm on each side of the plant. Application rates for different row spacings are as follows: <table style="margin-left: 40px; border: none;"> <thead> <tr> <th style="text-align: left;">Row Spacing</th> <th style="text-align: left;">L/ha</th> </tr> </thead> <tbody> <tr> <td>30 cm</td> <td>7.0</td> </tr> <tr> <td>60 cm</td> <td>3.5</td> </tr> <tr> <td>75 cm</td> <td>2.8</td> </tr> <tr> <td>80 cm</td> <td>2.6</td> </tr> <tr> <td>90 cm</td> <td>2.3</td> </tr> </tbody> </table>	Row Spacing	L/ha	30 cm	7.0	60 cm	3.5	75 cm	2.8	80 cm	2.6	90 cm	2.3
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75 cm	2.8												
80 cm	2.6												
90 cm	2.3												

	105 cm 2.0 Do not apply to harvestable portions of the crop. If no granular treatment was used at seeding, apply drench treatments at 10, 28, 49 and 70 days after seeding. If granular treatment with a chlorpyrifos insecticide was used at seeding, apply drench treatments at 28, 49 and 70 days after seeding.
CARROT	Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply more than once per season. Do not apply within 60 days of harvest. Do not enter treated fields until 1 day after application.
Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4-4.8 litres in 200-400 L/ha. Apply once per season before planting or transplanting. May also be applied to a 15 m strip adjacent to fence rows. Use the low rate except under conditions of low soil moisture. Use the high rate if the top 1 cm of soil is dry. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm. SEEDLING TREATMENT: Apply 2.4-4.8 litres in 200-400 L/ha. Apply as a broadcast spray at the 2- to 5-leaf stage. Use the low rate except under conditions of low soil moisture. Use the high rate if the top 1 cm of soil is dry.
POTATO	Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply more than once per season. Do not apply within 7 days of harvest. Do not enter treated fields to conduct scouting, hand weeding or irrigation activities until 1 day after application. Potatoes cannot be harvested within 70 days of treatment for wireworm.
Wireworm	Apply in furrow at planting. Apply 21.6 mL in 5 L/100 m of row (equivalent to 2.4 L of product/ha, based on 90 cm row spacing).
Colorado potato beetle (larvae), potato flea beetle, tarnished plant bug	Apply 1 Litre in 400-800 L/ha as a foliar spray.
Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4 litres in 200-400 L/ha. Apply once as a broadcast spray 3-7 days before planting. Do not incorporate. Also apply to a 15 m strip into adjacent fence rows. SEEDLING TREATMENT: Apply 1.2-2.4 litres in 200-400 L/ha. Apply once as a broadcast spray when damage first appears.
SUNFLOWER	Application is permitted by ground application

	equipment or aircraft where specified. Do not apply more than once per season. Do not apply within 42 days of harvest. Do not enter treated fields until 1 day after application.
Army cutworm, pale western cutworm, redbacked cutworm	Ground application only (DO NOT APPLY BY AIRCRAFT). Apply 1.2 litres in 50-200 L/ha. Apply as a broadcast spray when damage first appears. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm.
Seed weevil	Ground or aerial application. Apply 1.2 litres in at least 20 L/ha. Apply in late July to early August when populations of weevils are observed in the sunflower heads. For aerial applications, apply 1.2 L/ha in a maximum of 40 L/ha spray solution using a boom configuration that maximizes spray coverage of the target.”
SUGARBEET	Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply more than once per season. Do not apply within 90 days of harvest. Do not enter treated fields until 1 day after application.
Pale western cutworm, redbacked cutworm	Apply 1.2-2.4 litres in 50-200 L/ha. Apply as a broadcast spray to crop seedlings when damage first appears. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm.
BARLEY, WHEAT, OATS	Do not apply more than once per season to barley or wheat. Do not apply within 60 days of harvest. Application is permitted by ground application equipment or aircraft where specified. Do not enter treated fields until 1 day after application.
Armyworm (including bertha armyworm), army cutworm, darksided cutworm, pale western cutworm, redbacked cutworm	Apply 0.875-1.2 litres in 50-200 L/ha for ground application equipment or in 10-30 L/ha for aircraft. Apply to soil or foliage. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm.
Grasshoppers	Apply 0.58-0.875 litres in 50-200 L/ha for ground application equipment, or in 10-30 L/ha for aircraft. Apply as a broadcast foliar spray. Use the low rate for juvenile grasshoppers and the high rate for adults. Treat adjacent ungrazed and unoccupied areas such as roadsides, rights-of-way and fence lines at the first sign of infestation.

Brown wheat mite	Apply 625 mL in 50-200 L/ha for ground application equipment or in 10-30 L/ha for aircraft. Apply as a foliar spray.
Russian wheat aphid	Apply 0.5 litres in a minimum of 100 L/ha for ground application equipment or in a minimum of 20 L/ha and maximum of 40 L/ha for aircraft. Apply as a foliar spray. Application can be made in spring or fall when aphids exceed the economic threshold. Use a boom configuration that will maximize spray coverage and penetration of the crop canopy.
Wheat midge (WHEAT only)	Apply 0.83-1 litre in 50-200 L/ha for ground application. Apply 1 litre in 10-30 L/ha for aerial application. Apply when adults reach the economic threshold and when 25% of the wheat heads have emerged from the boot, but preferably delay spraying until 30% of the crop is flowering. Timing is critical to ensure good control. Applications should be made in the late afternoon or early evening when temperatures exceed 15°C and wind speed is less than 10 km/h. Apply as a foliar spray. Use boom configurations that maximize spray coverage and penetration of crop canopy.
ONION (bulb)	Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply more than once per season. Do not enter treated fields until 1 day after application. Do not apply to bunching onions. [See also below.] Do not apply within 60 days of harvest.
Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4-4.8 litres in 200-400 L/ha. Apply once per season before planting or transplanting. Application is also permitted on a 15 m strip adjacent to fence rows. Use the low rate except under conditions of low soil moisture. Use the high rate if the top 1 cm of soil is dry. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm. SEEDLING TREATMENT: Apply 2.4-4.8 litres in 200-400 L/ha. Apply as a broadcast spray at the 2- to 5-leaf stage. Use the low rate except under conditions of low soil moisture. Use the high rate if the top 1 cm of soil is dry.
TOBACCO	Do not apply more than once per season. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not enter treated fields until 1 day after application.

Black cutworm, darksided cutworm, redbacked cutworm	SOIL TREATMENT: Apply 2.4-4.8 litres in 200-400 L/ha. Apply once, 3-7 days before planting or transplanting. If the top 1 cm or more of soil is dry, use the higher rate. When preplant soil applications are being made to muck soil, do not incorporate. Incorporation on mineral soils should be no deeper than 5 cm. Also apply to a 15 m strip into adjacent cover crop and to fence rows.
Darksided cutworm	COVER CROP TREATMENT: Apply 1.125-1.2 litres in 200-400 L/ha. Darksided cutworms may feed on the cover crop before spring plough-down. Apply to the area planted to tobacco and to a strip about 15 m into nearby cover crop and fence rows. Application should be made in mid to late April, 4 to 5 days before plough-down. When the rye cover crop is about 15 cm tall, the cutworm larvae will be at the right stage for the best control. Cereals grown for cover crop treated with this insecticide should not be used for human or animal consumption if treated within 60 days of harvest.
ASIAN RADISH (LO BOK, DAIKON)	Do not apply more than 3 times per season. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply within 32 days of harvest. Do not enter treated fields until 1 day after application.
Cabbage maggot	Apply 210 mL in 1000 L of water per 1000 m row. Apply as a drench over seeded rows at 7, 20 and 35 days after seeding.
RADISH	Do not apply more than once per season. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply within 21 days of harvest. Do not enter treated fields until 1 day after application.
Cabbage maggot	Apply 85 mL of product in 380 L of water per 1000 m row. Apply as a drench with seed at planting time.
CHINESE BROCCOLI	Do not apply more than once per season. Ground application only (DO NOT APPLY BY AIRCRAFT). Do not apply within 21 days of harvest. Do not enter treated fields until 1 day after application.
Cabbage maggot	Apply 150 mL of product in 800 L/1000 m row. Apply once per season banded over the row 5–7 days after seeding.

FORESTRY: Lodgepole Pine	RESTRICTED USE Ground application only (DO NOT APPLY BY AIRCRAFT). For use in Western Canada only.
Mountain pine beetle	<p>NATURE OF RESTRICTION: This product is to be used only in the manner authorized. Contact local pesticide regulatory authorities about appropriate use permits that may be required.</p> <p>To be applied only under the direct supervision of commercial applicator responsible for insect control programs.</p> <p>For ground use only to control small infestations of mountain pine beetle in lodgepole pine forest stands. Monitor stands from mid-June to mid-July to determine the trees that are infested. Treat infested trees within a few weeks of expected beetle emergence, usually early July, to kill the adult beetles. Avoid spraying when conditions favour drift from spray area.</p> <p>Prepare a spray solution of 41.66 litres of product/1000 L of water to make a spray containing 2% active ingredient by weight. Apply at a rate of 1 L spray /m² of bark prior to adult beetle emergence. Treat boles from ground level up to a height of at least 3 m or until a bole diameter of 12.5 cm is reached.</p>
ALWAYS REFER TO THE PRODUCT LABEL FOR FURTHER INFORMATION ON PESTS CONTROLLED, APPLICATION DIRECTIONS, AND OTHER USE PRECAUTIONS.	

PESTS OF ORNAMENTALS (COMMERCIAL PRODUCTION ONLY) - GREENHOUSES AND NURSERIES ONLY

Use SHARPHOS INSECTICIDE to treat flowers, shrubs, vines, shade and flowering trees and evergreens found to be infested with the pests listed in the following table. Dilute SHARPHOS INSECTICIDE with water according to directions given in the table and apply using suitable hand or power spray equipment in a manner to provide complete and uniform coverage. For best results apply a wetting spray to both upper and lower leaf surfaces and infested limb and trunk areas. Attempt to penetrate dense foliage but avoid overspraying to the point of excessive run-off. Treat when pests appear and repeat at 7 to 10 day intervals, if needed.

A re-entry interval of two days for workers conducting crop contact activities is required for use on Greenhouse Ornamentals.

NOTE: Environmental factors have significant effects on phytotoxic expression. SHARPHOS INSECTICIDE has been tested on numerous ornamental plants without causing serious phytotoxicity. However, do not use on azaleas, camellias, poinsettias, rose bushes or variegated ivy because of possible injury to these plants.

Pest	Amount of Product per 1000 L	Specific Host Plants
spittlebugs	88-150 mL	various ornamental plants
mealybugs	200 mL	various ornamental plants
aphids	375 mL	beech, birch, elm, hickory, linden, maple, oak, pine, flowering cherry, flowering plum, spruce, tulip tree, viburnum, willow, spirea, nasturtium
clover mite, European red mite, honeylocust spider mite, red oak mite, spruce spider mite, twospotted spider mite	375-500 mL	Arborvitae, juniper
borers such as ash and lilac borers	500 mL	locust, birch, mountain ash, willow, lilac
Eastern and forest tent caterpillars	500 mL	ash, birch
European pine sawfly, redheaded pine sawfly	500 mL	conifers, mountain ash
grasshoppers	500 mL	various ornamental plants
thrips	500 mL	various ornamental plants
whiteflies	500 mL	various ornamental plants
leafhoppers such as potato and six-spotted leafhoppers	1 L	various ornamental plants
scale insects such as lecanium, cottony maple, San Jose, oystershell	2 L	various ornamental plants

500 mL is equivalent to 240 g of chlorpyrifos per 1000 L

1 L is equivalent to 480 g of chlorpyrifos per 1000 L

2 L is equivalent to 960 g of chlorpyrifos per 1000 L

For Control of Japanese beetle (larvae)

Controls Japanese beetle (larvae) infesting soil in which outdoor ornamentals (including containerized nursery stock) are growing. Apply to the soil when grubs are young and actively feeding near the soil surface, usually during late July, August, September or as recommended by your local agricultural representative. Use at rates of 4.5 L/1000 L on various ornamental plants. Apply as a coarse, low pressure spray using suitable

application equipment. Immediately after spraying irrigate the treated area with 1 to 2 cm of water to wash the insecticide into the underlying soil. Spraying may also take place in April and May.

For container grown stock: Submerge the entire root ball or container in a solution of 45 mL SHARPHOS INSECTICIDE /10 L water (4.5 L/1000 L) until all bubbling stops. Remove plants from solution and allow to drain.

PESTS OF TURF (SOD FARMS ONLY)

Use SHARPHOS INSECTICIDE to control the pests listed in the following table by application at the recommended dosages and in accordance with the directions given below. Dilute SHARPHOS INSECTICIDE in enough water to obtain complete and uniform coverage of pest infested areas and apply as a coarse, low pressure spray using suitable application equipment. Do not use on ornamental plants including flowers, shrubs, vines, shade and flowering trees and evergreens.

Pest	Amount of Product per 100 m²	Specific Directions
ants, chinch bugs, cutworms	22.5 mL	Spray when pests first appear, repeat when needed.
crane fly larvae (leatherjackets)	20-25 mL	Apply as drenching spray in water in late fall after the flight of adult crane flies has ceased for the year.
sod webworms	22.5 mL	For sod webworms delay watering or mowing the treated area for 12-24 hours after treatment.
annual bluegrass weevil	22.5 mL	Spray suspected problem areas in mid-April and again in mid-May, or as recommended by your local agricultural representative.

22.5 mL/100 m² = 112.5 mL/500 m² = 225 mL/1000 m² or 2.25 L/ha

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Buctril M is a trademark of Bayer CropScience Inc.

Glean is a trademark of E.I. Dupont de Nemours and Company

This is **Exhibit “M”** referred to in the affidavit
of **Dr. Elaine MacDonald** affirmed remotely
before me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



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

**OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION**

MEMORANDUM

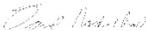
Date: September 21, 2020

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

PC Code: 059101
Decision No.: 559846
Petition No.: NA
Risk Assessment Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: NA

DP Barcode: D456427
Registration No.: NA
Regulatory Action: Registration Review
Case No.: NA
CAS No.: 2921-88-2
40 CFR: §180.342

FROM: Danette Drew, Chemist 
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THROUGH: Michael S. Metzger, Chief
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TO: Patricia Biggio, Chemical Review Manager
Risk Management and Implementation Branch I (RMIB I)

Pesticide Re-evaluation Division (PRD) (7508P)

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 European Food Safety 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 99.9th 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.

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.

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 2012³ 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 distances⁵ 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 2014⁷ following submission of two high-quality vapor phase nose-only inhalation toxicity studies for chlorpyrifos and chlorpyrifos oxon⁸. 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 ≥ 2.3 lb ai/A. In addition, the 2012 agreement requires buffer distances of ≥ 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 approach⁹ 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 ($\mu\text{g}/\text{cm}^2$) = [Chlorpyrifos DFR ($\mu\text{g}/\text{cm}^2$) * TAF] + [Chlorpyrifos DFR ($\mu\text{g}/\text{cm}^2$)]

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

Toxicology

None.

Residue Chemistry

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.

Occupational/Residential

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 harmonization with Codex, are presented in Tables 2.2.2.1 and 2.2.2.2.

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

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	

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.

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

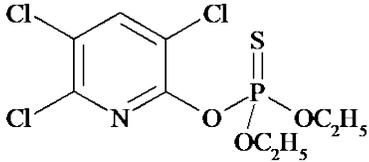
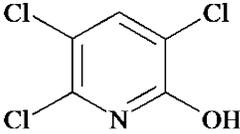
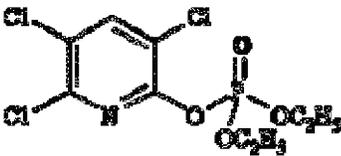
The Codex Alimentarius Commission and Canada Pesticide Management Regulatory Agency (PMRA) have established Maximum Residue Limits (MRLs) for chlorpyrifos. Mexico generally adopts U.S. tolerances and/or Codex MRLs for its export purposes. The residue definition for enforcement is harmonized for U.S. 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	<i>O,O</i> -diethyl <i>O</i> -3,5,6-trichloro-2-pyridyl phosphorothioate
CAS name	<i>O,O</i> -diethyl <i>O</i> -(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 <i>O,O</i> -diethyl. <i>O</i> -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 degrades 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 lifestyle; 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) Survey¹¹ 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>

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:1 1-16 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/day¹². For youths and female adults, they were assumed to consume water 4 times per day, with a total consumption volume of 1.71 L/day¹³.

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.

Parameter	Mean value	Standard Deviation	CV	Variability Reference
Total Blood Volume (L/kg body	0.08	0.0022	0.027	P ³ M; Price <i>et al.</i> , 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	P ³ M; Price <i>et al.</i> , 2003
RBC ChE Degradation Rate (l/hr)	0.01	0.0014	0.14	Chapman <i>et al.</i> , 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 <i>et al.</i> , 2001
Intestinal CYP Detoxification to TCPy (μmol/hr×kg tissue)	53	28	0.52	Obach <i>et al.</i> , 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	P ³ M; Price <i>et al.</i> , 2003
Hepatic Carboxyl Basal Activity Rate (l/hr/kg tissue)	1,270,000	460,000	0.36	Pope <i>et al.</i> , 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.			
<i>hepatic CYP450 activation of chlorpyrifos to chlorpyrifos oxon</i>	total blood volume	RBC ChE degradation rate	transfer rate of chlorpyrifos or oxon from the stomach to the intestine
<i>hepatic PON1 detoxification of chlorpyrifos oxon to TCPy</i>	hepatic blood flow	RBC ChE reactivation rate	volume of the liver
<i>PON1 detoxification of chlorpyrifos oxon to TCPy in plasma</i>	RBC AChE inhibition rate	intestinal CYP bioactivation to chlorpyrifos oxon	hepatic carboxyl basal activity rate
<i>hepatic PON1 detoxification of chlorpyrifos oxon to TCPy</i>	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 ED₁₀ to the infant ED₁₀ 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 5th 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 99th 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 99th 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 99th-ile, only 1% of infants will experience 10% or greater RBC AChE inhibition at the POD.

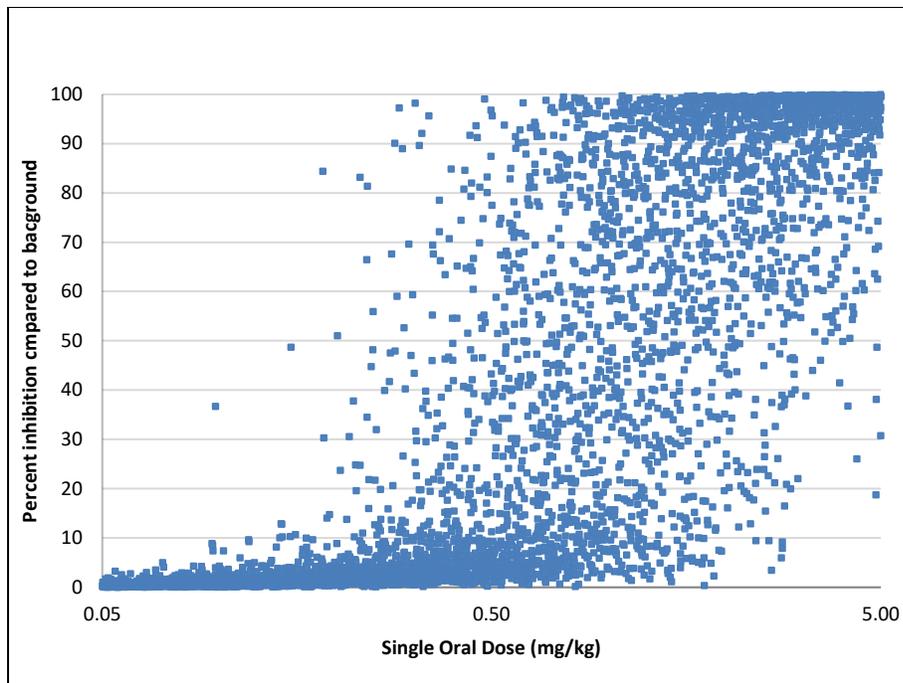


Figure 1a. Simulated population of 6 month olds for intra-species extrapolation DDEF derivation. Percent RBC AChE inhibition from exposure to single oral doses of chlorpyrifos ranging from 0.05 to 5.0 mg/kg/day (X and Y axes provided on the log scale).

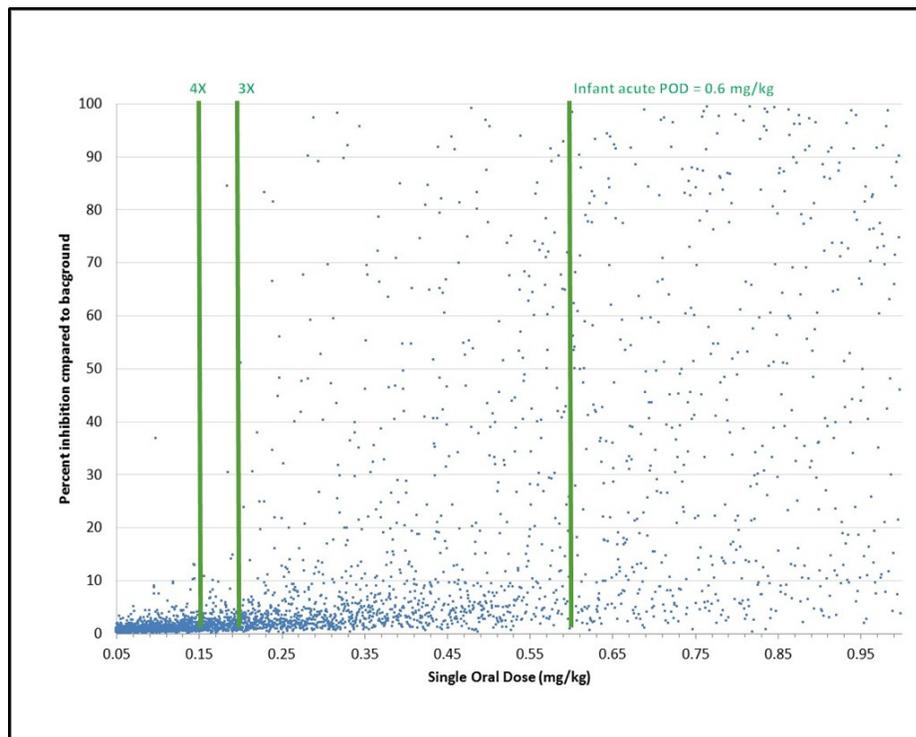


Figure 1b. Simulated population of 6 month olds for intra-species extrapolation DDEF derivation. Percent RBC AChE inhibition from exposure to single oral doses of chlorpyrifos ranging from 0.05 to 1.0 mg/kg/day. Green lines represent the infant acute POD for chlorpyrifos, the POD adjusted for the 3X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

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).¹⁶ 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.

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 Retained¹.															
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 ($\mu\text{g}/\text{kg}/\text{day}$)	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) = $\text{POD} \div \text{LOC}$ (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 1X¹.															
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 ($\mu\text{g}/\text{kg}/\text{day}$)	4	150	26	4	150	25	4	130	23	4	120	20	10	47	7.8

1. Population Adjusted Dose (PAD) = $\text{POD} \div \text{LOC}$ (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).

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.

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)

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.

³aPAD= 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.

⁴aPAD= 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.

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.

³ssPAD= 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.

⁴ssPAD= 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 chlorpyrifos 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 mound treatment was assessed qualitatively because post-application exposures to treated ant mounds 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 \geq 40 for children 6 to < 11 years old and youths 11 to < 16 years old and MOEs \geq 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 \geq 40 for children 1 to < 2 years old and MOEs \geq 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				
			1.0 (Granular)	IN	0.0082	2,800
				MS	0.014	1,600
				Mean	0.011	2,000
Adult (Females 13-49 years old)				CA	0.0088	1,400
Youths 11 to < 16 years old				CA	0.0088	1,600
Children 6 to < 11 years old				CA	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/m³) ÷ Dose (mg/m³). 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/m³) ÷ Dose (mg/m³). 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 (µg/cm ²)	Dermal Dose ³ (mg/kg/day)	MOE ⁴
1 mph Wind Speed Dv 0.5 = 60 µm	Adults	0.010	1.0	0.00038	0.0015	16,000
75 Foot Release Height	Children 1 to < 2 Years Old				0.0026	53,000
10 mph Wind Speed Dv 0.5 = 40 µm	Adults	0.010	0.086	0.000033	0.00013	180,000
300 Foot Release Height	Children 1 to < 2 Years Old				0.00022	610,000

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

- Ground fraction of mosquitocide application rate deposited on turf as determined using eight published studies on ground ULV application in which deposition was measured.
- $TTR_t (\mu\text{g}/\text{cm}^2) = [(\text{Day 0 Residue from MS TTR study } (\mu\text{g}/\text{cm}^2) \times \text{Application Rate (0.010 lb ai/A)}) \div \text{Application Rate of MS TTR Study (3.83 lb ai/A)}] \times \text{AgDISP Deposition Fraction}$
- $\text{Dermal Dose (mg/kg/day)} = [(TTR_t (\mu\text{g}/\text{cm}^2) \times \text{CF1 (0.001 mg}/\mu\text{g)}) \times \text{Transfer Coefficient (cm}^2/\text{hr - 180,000, adults; 49,000, children)} \times \text{ET (1.5 hrs)}] \div \text{BW (kg)}$
- $\text{MOE} = \text{POD (mg/kg/day)} \div \text{Dose (mg/kg/day)}$. 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 μ m					
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) \div 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	4.5x10 ⁻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) \div 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/m³)¹	MOE²	Combined Routes³	Combined MOEs⁴	
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	5.2x10 ⁻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	4.5x10 ⁻⁶	22,000			
	Ground Mosquitocide Application – WMB		Inhalation	0.0051	460	X	450
			Dermal	0.00022	610,000		
			Incidental Oral	4.54x10 ⁻⁶	22,000		

1. See Tables 6.2.3 – 6.2.7 for route-specific exposure inputs and risk estimates.
2. MOE = POD (mg/m³) ÷ Dose (mg/m³). See Table 4.2.2.1.2 for PODs.
3. X indicates the exposure scenarios included in the combined MOE.

4. Combined MOE = $1 \div [(1/\text{dermal MOE}) + (1/\text{inhalation MOE}) + (1/\text{incidental oral MOE})]$, 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.

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 = $1 \div [(1/\text{Inhalation MOE}) + (1/\text{Dermal MOE}) + (1/\text{Incidental Oral MOE})]$, 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 chlorpyrifos 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.

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:** $MOE_{\text{food}} = \text{POD}_{\text{food}} (\mu\text{g}/\text{kg}/\text{day}) \div \text{Food Exposure} (\mu\text{g}/\text{kg}/\text{day})$ (from Table 4.2.2.1.2) \div Food Exposure ($\mu\text{g}/\text{kg}/\text{day}$) (from Table 5.4).

$ARI_{\text{food}} = [(MOE_{\text{food}})/(MOE_{\text{target}})]$.

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

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

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

⁵ **DWLOC:** $DWLOC \text{ ppb} = \text{POD}_{\text{water}} (\text{ppb}; \text{from Table 4.2.2.1.2}) \div MOE_{\text{water}}$

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

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:** $MOE_{\text{food}} = \text{POD}_{\text{food}} (\mu\text{g}/\text{kg}/\text{day}) \div \text{Food Exposure} (\mu\text{g}/\text{kg}/\text{day})$ (from Table 4.2.2.1.2) \div Food Exposure ($\mu\text{g}/\text{kg}/\text{day}$) (from Table 5.4).

$ARI_{\text{food}} = [(MOE_{\text{food}})/(MOE_{\text{target}})]$.

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

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

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

⁵ **DWLOC:** $DWLOC \text{ ppb} = \text{POD}_{\text{water}} (\text{ppb}; \text{from Table 4.2.1.2}) \div MOE_{\text{water}}$

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.

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:** $MOE_{food} = POD_{food} (\mu\text{g}/\text{kg}/\text{day}) \div \text{Food Exposure } (\mu\text{g}/\text{kg}/\text{day})$ (from Table 4.2.2.1.2) \div Food Exposure ($\mu\text{g}/\text{kg}/\text{day}$) (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 $MOE_{agg} = \text{Target MOE}$.

⁶ **DWLOC:** $DWLOC \text{ ppb} = PoD_{water} (\text{ppb}; \text{from Table 4.2.2.1.2}) / MOE_{water}$

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:** $MOE_{food} = POD_{food} (\mu\text{g}/\text{kg}/\text{day}) \div \text{Food Exposure } (\mu\text{g}/\text{kg}/\text{day})$ (from Table 4.2.2.1.2) \div Food Exposure ($\mu\text{g}/\text{kg}/\text{day}$) (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 $MOE_{agg} = \text{Target MOE}$.

⁶ **DWLOC:** $DWLOC \text{ ppb} = PoD_{water} (\text{ppb}; \text{from Table 4.2.2.1.2}) / MOE_{water}$

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 ≥ 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 ≥ 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 ≥ 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 ≥ 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 ≥ 10) and no combined (dermal + incidental oral) risks for children 1 to < 2 years old at the field edge (MOEs ≥ 4).

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

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 8.2. Summary of Spray Drift Distances from the Field Edge for Chlorpyrifos MOEs to be > LOCs with FQPA SF Reduced to 1X. ¹										
Application Rate (lb ai/A)	Nozzle Droplet Type/ Canopy Density	Adult Buffer Summary			Children 1 to < 2 Years Old Buffer Summary (Dermal + Incidental Oral)					
		Distance (Feet) from Field Edge Needed for MOE > LOC of 10			Distance (Feet) From Field Edge Needed for MOE > LOC of 4					
		Aerial ²	Groundboom ²	Airblast	Aerial ²	Groundboom ²	Airblast			
6.0	Medium/ Coarse for Aerial and Ground-boom	NA	NA	0	0	NA	0			
4.3			0			0		0		
4.0									0	0
3.76										
3.0			0			0		0	0	
2.3										
2.0										
1.5	Sparse for Airblast	0	0	0	0	0				
1.0										

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-oxon²⁰ 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

¹⁹EPA MRID# 48139303:Acute Inhalation Exposure of Adult CrI: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.

²⁰W. 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): CrI 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):CrI 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 assessment²².

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).

Summary of Occupational Post-Application Dermal Exposure and Risk Estimates

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
CA				0	0 - 1	
Sugar Beet	1.0	MRID 44748102 (sugar beet EC)	MN	0	0 - 1	
			OR	0	0 - 1	
			IL	0 - 1	0 - 3	
Field and Row Crops: Tall	Corn: Sweet; Corn: Field, Including Grown for Seed	1.5	MRID 44748102 (sweet corn EC)	MN	0 - 1	0 - 3
				OR	0 - 1	0 - 2
				IL	0 - 1	0 - 2
	Corn: Sweet; Corn: Field, Including Grown for Seed	1.0	MRID 44748102 (sweet corn EC)	MN	0 - 1	0 - 2
				OR	0 - 1	0 - 2
				IL	0	0 - 1
	Sorghum	1.0	MRID 44748102 (sweet corn EC)	MN	0	0 - 1
				IL	0	1
	Sunflowers	1.5	MRID 44748102 (sweet corn EC)	MN	0	1
CA				0	1	
Tree Fruit: Deciduous	Apples, Cherries, Peaches, Pears, Plums, Prunes, Nectarines	2.0	MRID 44748101 (apple WP)	WA	0	1 - 2
				NY	0	1 - 2
				CA	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)
	(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
				MS (harvesting/seedling production)	0	0
	Citrus	6.0 (CA and AZ)	MRID 43062701 (citrus EC)	CA	0	0 - 2
				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
				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
				GA	0	0
	Filberts, Pecans, Walnuts	2.0	MRID 44748101 (pecan EC)	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	Non-bearing Pineapple	2.0	MRID 44748102 (cotton EC)	MN	0 – 1	1
				OR	0	0 – 1
				MS	0	1
Vine/ Trellis	Grapes (Dormant and Delayed Dormant)	2.0	MRID 43062701 (citrus EC)	CA	0	1
	Grapes (Post-harvest and Prior to Budbreak)					
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 – <i>Liquid Concentrates</i>	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 – <i>Total Release Foggers</i>	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 studies²⁴ 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 assessment²⁵ 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

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 Chlothalonil 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 approach²⁶ 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 ($\mu\text{g}/\text{cm}^2$) = [Chlorpyrifos DFR ($\mu\text{g}/\text{cm}^2$) * TAF] + [Chlorpyrifos DFR ($\mu\text{g}/\text{cm}^2$)]

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.

12.0 References

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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, 2000²⁷) 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 BMD₁₀ is the estimated dose where ChE is inhibited by 10% compared to background. The BMDL₁₀ is the lower confidence bound on the BMD₁₀.

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-](https://www.epa.gov/ingredients-used-pesticides/data)

^[1] <https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances>

^[2] <http://www.oecd.org/env/ehs/testing/oecdguidelinesforhetestingofchemicals.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 California³¹. 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 Bystanders³².” 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 results³⁴. 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.

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 include³⁸.

- 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 dataset³⁹
- 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 center⁴¹.

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 °C	Chlorpyrifos IRED	
pH	NR		
Density (21°C)	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)	1.87x10 ⁻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 <i>per se</i> (<i>O,O</i> - diethyl <i>O</i> -(3,5,6-trichloro- 2-pyridyl) phosphorothioate	<i>O,O</i> -diethyl- <i>O</i> -(3,5,6-trichloro-2- pyridyl) phosphorothioate (apples, grapes, tomatoes) <i>O,O</i> -diethyl- <i>O</i> -(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		Mexico²	Codex³
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					
AGRICULTURAL 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.

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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					
									✓						
				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		

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							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		

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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					
		✓		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

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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					
															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			6						The foliar applications only apply to tart cherries, thus, sweet cherry scenarios (e.g., Pacific NW) annual

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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					
															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

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							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.

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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					
															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		Minimum incorporation is 2 inches
		✓		Preplant, soil incorporated treatment	Ground boom										
		✓		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	2.3	NS	[1] NS	1	30, EC, 21 G				Minimum incorporation is 2 inches
		✓		Post plant, soil application	Ground boom	2.0 EC									
		✓		Foliar broadcast	aircraft, ground boom	1.0 EC	[5.3] NS	3.0	NS	3	21		10		
							2.3	5.3	[5.3] NS	NS	[4] NS	21	24	10	
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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							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/EQUIPMENT. (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		✓	?					
				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									

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							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	<i>0.001-0.021</i> 0.000625 lb a.i./ lb seed WP <i>0.1-1.9</i> 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	<i>0.8-2.2</i> 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

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							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, WDG	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		

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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					
ION PROGRAMS) (TREE FARMS, TREE PLANTATION, ETC.)															
			✓	Foliar, stump treatment	direct spray, drencher	0.34 EC	6.0	NA	[18] NS	NA			7		
			✓	Foliar, broadcast	ground boom, drencher	0.61 EC	3.6	NA	NS	NA	24		7		
FOREST TREES (SOFTWOODS, CONIFERS)			✓	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 spray/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.

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					
															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								
				Foliar, broadcast,	Ground boom, handgun, low pressure and backpack	1.0 EC, G, B	2.0	NA	2	NA		[24] NS	NS		
				Tractor drawn spreader, push type spreader, belly grinder	1.0 G	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

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	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	
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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							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).

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					
															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				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	NS	NS			

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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						
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										

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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					
					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
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.

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							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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							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									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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							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		

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							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	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

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							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		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	10			

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							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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							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.	

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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	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

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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					
					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.

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 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

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					
		✓		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					
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.

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					
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, WDG	[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.

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					
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			66222-19		
				when needed, Drench	Drench	1	NS	NA	NS	NA	NA				NS	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	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	24	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

This is **Exhibit “N”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

Chlorpyrifos

Guideline

The maximum acceptable concentration (MAC) for chlorpyrifos in drinking water is 0.09 mg/L (90 µg/L).

Identity, Use and Sources in the Environment

Chlorpyrifos (C₉H₁₁Cl₃NO₃PS) is an organophosphorus insecticide used for the control of mosquitoes, flies, various crop pests in soil and on foliage, household pests and aquatic larvae. It is also used on sheep and cattle for the control of ectoparasites. Annual use in Canada is in the range of 100 000 to 500 000 kg.¹

The vapour pressure of chlorpyrifos is 2.49×10^{-3} Pa at 25°C, and its solubility in water is 2 mg/L at 25°C.² Reported log octanol–water partition coefficients are high, ranging from 4.82 to 5.11.³

Chlorpyrifos is tightly absorbed by soil and is not expected to leach significantly.⁴ It persists in soil for 60 to 120 days,⁵ with degradation being primarily due to microbial action.⁶ Products of degradation include 3,5,6-trichloro-2-pyridinol, which is subsequently broken down to organochlorine compounds and carbon dioxide.⁷ The rate of hydrolysis of chlorpyrifos in water increases with pH and temperature and is enhanced by the presence of copper.⁵ Between 30 and 60% of the total amount of chlorpyrifos in the aqueous phase may disappear within 24 hours through adsorption, degradation and vaporization.⁸

Exposure

Chlorpyrifos was not detected in a survey of 511 samples from municipal and private drinking water supplies encompassing Metropolitan Toronto (1971 to 1982), Manitoba (1986) and Alberta (1978 to 1985) (detection limits 0.20 and 0.04 µg/L).⁹ It was not found in 446 samples taken from surface waters of the Grand River and Thames River basins, although nearly 3000 and 7500 kg/year, respectively, had been used in these areas (detection limit 0.1 µg/L).¹⁰

Based on the residue tolerance limits set by the Food Directorate of the Department of National Health and Welfare,¹¹ the theoretical maximum daily intake of chlorpyrifos from food is 0.07 mg/d, which represents 10% of the acceptable daily intake (ADI) of 0.7 mg/d for a 70-kg adult.¹² Chlorpyrifos was detected in only 49 of 6391 domestic food samples in the United States, 94% of which had concentrations below 2.0 ppm; in imported foods, chlorpyrifos was detected in 1777 of 12 044 samples, with all but five samples containing concentrations at or below 0.5 µg/g.¹³ The average daily dietary intake of chlorpyrifos has been estimated to be 0.241 µg, based on the U.S. market basket survey.¹⁴

Analytical Methods and Treatment Technology

Organophosphorus insecticides in water may be analysed by extraction separately into hexane and dichloromethane, separation by gas chromatography and flame thermionic or flame photometric detection (detection limit 1 µg/L);¹⁵ separation may also be accomplished by gas/liquid chromatography, followed by flame photometric detection (detection limit 0.1 µg/L).¹⁶

No information was found on the effectiveness of current treatment technologies in removing chlorpyrifos from drinking water.

Health Effects

Chlorpyrifos is readily absorbed from the gastrointestinal tract and is rapidly metabolized. Metabolites are excreted principally in the urine and to a lesser extent in the faeces; the main metabolites are 3,5,6-trichloro-2-pyridylphosphate and 3,5,6-trichloro-2-pyridinol.¹⁷ Small amounts of unmetabolized chlorpyrifos have been detected in the blood, brain and liver after accidental human ingestion.¹⁸

Chlorpyrifos is a cholinesterase inhibitor. Human volunteers (four men per group) were administered oral doses of chlorpyrifos of 0.014 mg/kg bw per day for

27 days, 0.03 mg/kg bw per day for 20 days or 0.10 mg/kg bw per day for nine days.¹⁹ Red blood cell cholinesterase activity was not affected at any level.

Beagle dogs were fed diets containing chlorpyrifos at dose levels of 0, 0.01, 0.03, 0.1, 1.0 or 3.0 mg/kg bw per day for two years.²⁰ Red blood cell cholinesterase was inhibited in males and females at 1.0 and 3.0 mg/kg bw per day. In a similar study,²¹ rats were fed diets containing chlorpyrifos at concentrations of 0, 0.01, 0.03, 0.1, 1.0 and 3.0 mg/kg bw per day for two years. Brain cholinesterase activity was inhibited at 3.0 mg/kg bw per day and slightly depressed at 1.0 mg/kg bw per day. Based on these results, the no-observed-adverse-effect level (NOAEL) for red blood cell and brain cholinesterase inhibition is considered to be 0.1 mg/kg bw per day. The NOAEL in Rhesus monkeys receiving 0.08 mg/kg bw per day of chlorpyrifos by gavage for six months was similar; animals exhibited no depression in red blood cell cholinesterase activity.²²

In a carcinogenicity study in CD-1 mice, chlorpyrifos was not oncogenic when administered at dose levels up to 15 ppm (1.5 mg/kg bw per day) in food for 105 weeks.²³ Chlorpyrifos was not found to be mutagenic in five microbial assay systems.²⁴ In a CF-1 mouse teratogenicity study, chlorpyrifos was not teratogenic at doses up to 25 mg/kg bw per day, although significant reductions in plasma and erythrocyte cholinesterase levels were observed in maternal mice at 1 mg/kg bw per day or greater and in fetuses at 10 mg/kg bw per day or more.²⁵

Rationale

The ADI for chlorpyrifos has been derived by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO)¹² as follows:

$$\text{ADI} = \frac{0.1 \text{ mg/kg bw per day}}{10} = 0.01 \text{ mg/kg bw per day}$$

where:

- 0.1 mg/kg bw per day is the NOAEL derived from two-year studies in the dog and rat^{20,21} and studies with human volunteers¹⁹
- 10 is the uncertainty factor.

The maximum acceptable concentration (MAC) for chlorpyrifos in drinking water is derived from the ADI as follows:

$$\text{MAC} = \frac{0.01 \text{ mg/kg bw per day} \times 70 \text{ kg} \times 0.20}{1.5 \text{ L/d}} \approx 0.09 \text{ mg/L}$$

where:

- 0.01 mg/kg bw per day is the ADI established by the FAO/WHO
- 70 kg is the average body weight of an adult
- 0.20 is the proportion of daily intake of chlorpyrifos allocated to drinking water
- 1.5 L/d is the average daily consumption of drinking water for an adult.

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This is **Exhibit “O”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Canadian Water Quality Guidelines for the Protection of Aquatic Life

CHLORPYRIFOS

Chlorpyrifos (CAS Registry Number 2921-88-2) is an organophosphate insecticide, acaricide, and nematocide. Its chemical formula is $C_9H_{11}NO_3PSCl_3$ and its chemical name is O,O-diethyl O-(3,5,6-trichloro-2-pyridyl) phosphorothioate. Chlorpyrifos is an amber to white, crystalline solid with a molecular weight of 350.6 (Mackay et al. 1999).

Chlorpyrifos was introduced in 1965 by Dow Chemical Company. It is currently produced by Dow Chemical Company, India Medical Corp., Makhteshim-Agan (Israel), and Planter Products, Inc. Chlorpyrifos is registered for use in over 30 products sold under trade/product names such as Dursban, Lorsban, Brodan, Detmol UA, Dowco 179, and Empire (Eisler 2000; EXTOWNET 1996). It is formulated as an emulsifiable concentrate, wettable powder, granule, and microencapsulated formulations.

Uses: Chlorpyrifos was originally used to control pests associated with turfgrass, ornamentals, and indoor environments (EPA 1997; PMRA 2000). Through the 1970s, agricultural applications for chlorpyrifos were developed, including its use on grains, field (e.g., corn, tobacco), fruit, nut and vegetable crops.

The use of chlorpyrifos has changed drastically over the last ten years. Residential/homeowner use has been discontinued as has commercial uses around residential area. Agricultural applications have been reduced. The Pest Management Regulatory Agency (PMRA) will undertake a refined environmental risk assessment by 2008 and will make a final decision on the acceptability for continuing registration of chlorpyrifos after that assessment is completed (PMRA 2007).

Sources to the environment: Direct application of chlorpyrifos to soil, vegetation, and animals can result in exposure to non-target organisms. To control mosquitoes, chlorpyrifos may be applied to temporary pools and flooded areas; application to permanent water bodies is not permitted. The application of chlorpyrifos to temporary or flooded areas, along with accidental spillage, spray drift, leaching and runoff from terrestrial applications has the potential to expose aquatic biota to residues.

Fate, behaviour and partitioning: Chlorpyrifos is moderately soluble in water, with a solubility of $2 \text{ mg}\cdot\text{L}^{-1}$ at 25°C (Kidd and James 1991; Mackay et al. 1999). Jarvinen and Tanner (1982) reported a laboratory half-life of 41 days for chlorpyrifos in solution at water solubility ($1\text{-}2 \text{ mg}\cdot\text{L}^{-1}$). The major routes of chlorpyrifos transformation are aerobic and anaerobic biodegradation, while phototransformation is not an important transformation process (PMRA 2000). Temperature and pH influence chlorpyrifos hydrolysis rates in water, as the rate of hydrolysis increases with increases in both temperature and pH. For instance, hydrolysis half-lives of 73, 77, and 16 days were reported for chlorpyrifos at pH 5 and 7 and 9, respectively (PMRA 2000). The major transformation products of chlorpyrifos in water are 3,5,6-trichloro-2-pyridinol (TCP) and O-ethyl O-(3,5,6-trichloro-2-pyridinol)phosphorothionate (PMRA 2000).

Numerous factors influence soil half-life, such as soil moisture content, microbial activity, and clay and organic content (Eisler 2000). These factors result in a wide range of chlorpyrifos half-lives in soil from <1 week to more than 24 weeks (Eisler 2000). Volatilization from moist soils and surface water is expected, based on a Henry's Law constant of $2.9 \times 10^{-4} \text{ kPa}\cdot\text{m}^3\cdot\text{mol}^{-1}$ (Rice and Chernyak 1995). A vapour pressure of $3.33 \times 10^{-6} \text{ kPa}$ suggests that chlorpyrifos is unlikely to volatilize from dry soils. The high soil adsorption coefficient ($\log K_{oc} = 1.61\text{-}4.72$) and

Table 1. Canadian Water Quality Guidelines for Chlorpyrifos for the Protection of Aquatic Life ($\mu\text{g a.i.}\cdot\text{L}^{-1}$)

	Long-Term Exposure	Short-Term Exposure
Freshwater	0.002*	0.02**
Marine	0.002***	NRG

* value calculated from low-effect data using lowest endpoint approach

** value calculated from LC_{50} data using the SSD approach

*** 1997 marine guideline value

NRG = no recommended guideline

moderate water solubility of chlorpyrifos indicate that it will adsorb to most soils and have low mobility. In addition, these factors limit the persistence of

chlorpyrifos in the water column (HSDB 1999; ATSDR 1997).

The log octanol/water partition coefficient ($\log K_{ow} = 3.31$ to 5.27) of chlorpyrifos indicates an affinity for lipids and thus a potential for bioaccumulation in aquatic organisms. Bioconcentration factors (BCF) reported for aquatic organisms exposed to chlorpyrifos under field conditions range from 100 to 4,667, and those under laboratory conditions range from 58 to 5,100 (Racke 1993). The degree that chlorpyrifos will bioconcentrate varies with species, exposure duration, and dose. Factors that contribute to bioconcentration include metabolic rate, depuration rate, the bioavailability of chlorpyrifos, and the availability of food (Eisler 2000). The BCF values for chlorpyrifos suggest a moderate to very high potential for bioconcentration in fish (Franke et al. 1994).

Under field conditions, chlorpyrifos is non-persistent in the water column. Various field studies from Canada, the United States, and The Netherlands have reported half-lives in aquatic ecosystems from <1 to 3 days (Racke 1993). The short persistence of chlorpyrifos under field conditions is due to its volatility in water, low water solubility, and strong affinity for sediments and suspended solids (ATSDR 1997). Sediment-water half-lives for chlorpyrifos range from 1.2 to 34 days (Schimmel et al. 1983).

Analytical methods: Gas chromatography is typically used to determine sample concentrations of chlorpyrifos, the chlorpyrifos oxygen analog, and 3,5,6-trichloro-2-pyridinol (TCP) (ATSDR 1997). Thin-layer chromatography and high-performance liquid chromatography can also be used. These methods are used in conjunction with selective detection such as flame photometric detection, nitrogen phosphorus thermionic detection, or electron capture detection (ATSDR 1997). The determination of chlorpyrifos concentrations in environmental media begins with liquid/liquid extraction, solid phase extraction (SPE), or Soxhlet extraction. Recoveries from natural waters using SPE can be reduced by the presence of humic material (ATSDR 1997). Further extraction and purification can be accomplished using SPE, gel permeation chromatography, florisil column chromatography, or sweep co-distillation (ATSDR 1997).

Ambient concentrations: Canada's first nation-wide water surveillance project for pesticides was initiated in 2003 by Environment Canada as part of the Pesticide Science Fund. The initiative has been conducted

independently in five regions of Canada (Pacific Yukon Region, Prairie and Northern Region, Ontario Region, Quebec Region, and Atlantic Region) and includes monitoring for chlorpyrifos levels. Samples from the Environment Canada Pacific Yukon Region were collected in areas of high pesticide use following storm events. A total of 140 surface water samples were taken and chlorpyrifos was detected in 56 of these samples. Concentrations ranged from $<0.0000005 \mu\text{g a.i.}\cdot\text{L}^{-1}$ to $0.0183 \mu\text{g a.i.}\cdot\text{L}^{-1}$ (method detection limit = $0.0000005 \mu\text{g a.i.}\cdot\text{L}^{-1}$) (CEI 2006).

Chlorpyrifos was detected in <50% of samples taken in the spring and summer from five reservoirs in Saskatchewan and Alberta, monitored during 2003/2004 in the Prairie Northern Region. Most of the reservoir catchments sampled were seeded to crops. The detection limit used with these samples was not reported.

A maximum concentration of $0.055 \mu\text{g a.i.}\cdot\text{L}^{-1}$ was reported for nine samples taken in the Ontario Region in 2003/2004, and $0.205 \mu\text{g a.i.}\cdot\text{L}^{-1}$ for 160 samples in 2004/2005. These results did not distinguish between samples from agricultural or urban areas. Sampling in the Quebec Region focuses on the tributaries entering the St. Lawrence River. Samples from the St. François River ranged from <0.02 to $0.13 \mu\text{g a.i.}\cdot\text{L}^{-1}$. Chlorpyrifos concentrations in samples from the St. Lawrence River were $<0.006 \mu\text{g a.i.}\cdot\text{L}^{-1}$. The proximity of the sampling locations to sources of chlorpyrifos is not reported.

Mode of action: The primary mechanism of toxicity for organophosphorus pesticides, like chlorpyrifos, is cholinesterase (ChE) inhibition. The inhibition of the enzyme acetylcholinesterase (AChE) results in the buildup of acetylcholine (ACh) at choline receptors, causing continual nerve stimulation (Giesy et al. 1999). Chlorpyrifos is a relatively weak AChE inhibitor compared to its metabolite chlorpyrifos oxon (El-Merhibi et al. 2004), thus toxicity is initiated by the formation of chlorpyrifos oxon by oxidative desulfuration (Eisler 2000; Giesy et al. 1999). Factors influencing the toxicity of chlorpyrifos between species and groups include metabolic rate, the number of target sites available for chlorpyrifos metabolism to chlorpyrifos oxon (Chambers and Carr 1995), organism surface area, and lifestage (El-Merhibi et al. 2004).

Freshwater Toxicity: Vertebrates are generally more tolerant of short-term and long-term exposure than invertebrates (Giesy et al. 1999). Symptoms of chlorpyrifos toxicity include motor incoordination,

delayed maturation and growth, scoliosis, renal histopathology, and reproductive impairment (Eisler 2000).

Toxicity values reported in the literature for freshwater fish ranged from a 96-h LC₅₀ of 1.3 µg a.i.·L⁻¹ for bluegill sunfish (*Lepomis macrochirus*) to a 72-h LC₅₀ of 2,600 µg a.i.·L⁻¹ for mosquitofish (*Gambusia affinis*) (EFED 2005; Davey et al. 1976).

Temperature has been observed to affect the short-term toxicity of chlorpyrifos to fish. In a study examining the effect of temperature on chlorpyrifos toxicity, 96-h LC₅₀s for juvenile rainbow trout (*Oncorhynchus mykiss*) were 7.1, 15, and 51 µg a.i.·L⁻¹ at temperatures of 12.7, 7.2, and 1.6°C, respectively (Macek et al. 1969).

A comparison of chlorpyrifos toxicity to different life stages of walleye (*Stizostedion vitreum*) identified post larvae II as the most sensitive with 48-h LC₅₀s of 12 and 13 µg a.i.·L⁻¹ reported for species from two different hatcheries (Phillips et al., 2002). Ninety-six hour LC₅₀ values for fathead minnows (*Pimephales promelas*) ranged from 120 to 542 µg a.i.·L⁻¹ (Jarvinen and Tanner 1982; Phipps and Holcombe 1985). At concentrations ≥47 µg a.i.·L⁻¹, effects to schooling behaviour were observed after 24 hours of exposure (e.g., location, orientation, grouping pattern), and spinal deformities were apparent after 48 hours of exposure (Holcombe et al. 1982).

Sublethal effects were monitored in coho salmon (*Oncorhynchus kisutch*) exposed to 0.6, 1.2, 1.8, and 2.5 µg a.i./L of chlorpyrifos. Spontaneous swimming was significantly reduced at all test concentrations. Swimming rate during feeding and total food strikes were reduced at ≥1.2 µg a.i.·L⁻¹ and latency to first strike was significantly reduced at 2.5 µg a.i.·L⁻¹ (Sandahl et al. 2005).

The long-term, non-lethal toxicity of chlorpyrifos to fish and other aquatic vertebrates has not been extensively studied. The lowest observed effects concentration (LOEC) for growth inhibition in juvenile fathead minnows decreased from 2.68 to 1.21 µg a.i.·L⁻¹, from 30 to 60 days exposure, respectively (Jarvinen et al., 1983). Jarvinen and Tanner (1982) observed similar results, reporting a 32d-NOEC (embryo/larval growth) of >1.6 and <3.2 µg a.i.·L⁻¹ for fathead minnows.

The larval metamorph was the most sensitive life stage reported for South African clawed frogs (*Xenopus laevis*) (96-h LC₅₀ = 560 µg a.i.·L⁻¹), followed by the embryo (96-h LC₅₀ = 2,410 µg a.i.·L⁻¹), and the

premetamorph life stages (96-h LC₅₀ = 14,600 µg a.i.·L⁻¹) (Richards and Kendall 2002; El-Merhibi et al., 2004). A similar trend in life stage sensitivity was observed in 96-h EC₅₀s for malformations, with values of 240, 511, and 1,710 µg a.i.·L⁻¹ reported for metamorphs, embryos, and premetamorphs, respectively (Richards and Kendall 2002; El-Merhibi et al., 2004).

Among invertebrate species, crustaceans and insect larvae are more sensitive to chlorpyrifos, and molluscs and rotifers are more tolerant (Giesy et al. 1999). Toxicity values for *Hyalalela azteca* (amphipod) ranged from 0.04 to 0.138 µg a.i.·L⁻¹, representing decreasing toxicity with increasing age (Ankley and Collyard 1995; Phipps et al., 1995; Moore et al., 1998; EFED 2005).

The most sensitive water flea species reported in the literature were *Daphnia ambigua* and *Ceriodaphnia dubia*, with 48-h LC₅₀s of 0.035 and 0.05 µg a.i.·L⁻¹, respectively (Harmon et al., 2003; El-Merhibi et al., 2004; Bailey et al., 1997). *Daphnia magna* and *Daphnia pulex* were also sensitive to chlorpyrifos. (EFED 2005; Guilhermino et al. 2000; Gaizik et al., 2001).

Chironomus tentans was the most sensitive midge species with a range in 96-h EC₅₀s from 0.17 to 0.22 µg a.i.·L⁻¹ for swimming behaviour, and a 96-h LC₅₀ of 0.47 µg a.i.·L⁻¹ (Lydy and Austin 2004; Schuler et al. 2005; Ankley and Collyard 1995).

Few studies are available on the long-term effects of chlorpyrifos to invertebrates. Ten-day LC₅₀ values reported for invertebrate species were 0.07 µg a.i.·L⁻¹ for *C. tentans* and *C. dubia* (Phipps et al., 1995; Ankley et al. 1994; Sherrard et al. 2002), 0.086 µg a.i.·L⁻¹ for *H. azteca* (Phipps et al., 1985), and 0.17 µg a.i.·L⁻¹ for *D. pulex* (van der Hoeven and Gerritsen 1997). The long-term value for *C. tentans* was lower than the short-term duration toxicity value (96-h LC₅₀ = 0.47 µg a.i.·L⁻¹) (Ankley and Collyard 1995). The long-term toxicity value for *C. dubia*, 0.07 µg a.i.·L⁻¹, was slightly greater than the 48-h LC₅₀ of 0.05 µg a.i.·L⁻¹ (El-Merhibi et al. 2004).

Laboratory studies have generally shown algae and aquatic plants to be tolerant of chlorpyrifos with EC₅₀ values >100 µg a.i.·L⁻¹ (Giesy et al. 1999). Long-term LC₅₀s ranged from 3.6 µg a.i.·L⁻¹ (96-h) for the plankton *Diaptomis forbesi* (Thankamoni Amma and Kumar 1996), to >10,000 µg a.i.·L⁻¹ (120-h) for the cyanobacterium *Synechococcus leopoliensis* (Van Donk et al. 1992). Within this range are 96-h LC₅₀ values of 140 µg a.i.·L⁻¹ for the alga *Isochrysis galbana* and 150

$\mu\text{g a.i.}\cdot\text{L}^{-1}$ for the diatom *Thalassiosira* sp. (EFED 2005).

Marine Toxicity: Chlorpyrifos is relatively toxic to some marine fish, as seen from short-term toxicity data. For example, 96-h LC₅₀ values are 0.4 and 0.58 $\mu\text{g a.i.}\cdot\text{L}^{-1}$ for 14-d old tidewater silverside (*Menidia peninsulae*) and striped bass (*Morone saxatilis*), respectively (Korn and Earnest 1974; Borthwick et al. 1985). For most species, static 96-h LC₅₀ values are between 2 and 5 $\mu\text{g a.i.}\cdot\text{L}^{-1}$, and flow-through 96-h LC₅₀ values are between 0.5 and 4 $\mu\text{g a.i.}\cdot\text{L}^{-1}$ (Schimmel et al. 1983; Borthwick et al. 1985; Clark et al. 1985).

Long-term tests typically result in reduced weight and survivorship of fish fry exposed to chlorpyrifos. For example, 26-d exposure to 0.62 or 1.3 $\mu\text{g a.i.}\cdot\text{L}^{-1}$ chlorpyrifos reduced weight and survival, respectively, of California grunions (*Leuresthes tenuis*) fry (Goodman et al. 1985). Early life-stage tests also suggest that embryos are more tolerant to chlorpyrifos than fry.

Long-term toxicity data on marine invertebrates are limited to one study in which grass shrimp larvae receiving pulses of chlorpyrifos had a 25-d LC₅₀ of 0.29 $\mu\text{g a.i.}\cdot\text{L}^{-1}$. All larvae exposed to a single pulse of 1.6 $\mu\text{g a.i.}\cdot\text{L}^{-1}$ died (Key and Fulton 1993). Chlorpyrifos pulses, however, did not affect instar number, intermolt duration, developmental duration, or growth.

Information on the toxicity of chlorpyrifos to marine plants is limited to algae. Walsh (1983) reported 50 and 100% growth inhibition in the marine diatom *Skeletonema costatum* exposed to 1200 and 5000 $\mu\text{g a.i.}\cdot\text{L}^{-1}$, respectively.

Water Quality Guideline Derivation: The short-term and long-term freshwater Canadian water quality guidelines (CWQGs) for chlorpyrifos for the protection of aquatic life were developed based on the CCME protocol (CCME 2007). The short-term guideline was developed using the statistical (Type A) approach. The long-term guideline was developed using the lowest-endpoint (Type B) approach. Marine toxicity data was not evaluated to see if there was sufficient data available to update the long-term marine water quality guideline for chlorpyrifos from 1997. No short-term marine water quality guideline was developed in 1997.

Short-term Freshwater Quality Guideline: Short-term exposure guidelines are derived using severe effects data (such as lethality) of defined short-term exposure

periods (24 – 96-h). These guidelines identify estimators of severe effects to the aquatic ecosystem and are intended to give guidance on the impacts of severe, but transient, situations (e.g., spill events to aquatic receiving environments and infrequent releases of short-lived/nonpersistent substances). Short-term guidelines *do not* provide guidance on protective levels of a substance in the aquatic environment, as short-term

Table 2. Endpoints used to determine the short-term CWQG for chlorpyrifos.

Species	Endpoint	Concentration ($\mu\text{g a.i.}\cdot\text{L}^{-1}$)
Fish		
<i>L. macrochirus</i>	96h LC ₅₀	1.3
<i>M. beryllina</i>	96h LC ₅₀	4.2
<i>O. clarkii</i>	96h LC ₅₀	5.4
<i>O. mykiss</i>	96h LC ₅₀	7.1
<i>S.vitreum</i>	48h LC ₅₀	12.5*
<i>L.cyanellus</i>	36h LC ₅₀	22.5
<i>N.crysoleucas</i>	36h LC ₅₀	35
<i>S. namaycush</i>	96h LC ₅₀	73
<i>P. promelas</i>	96h LC ₅₀	140
<i>G. affinis</i>	36h LC ₅₀	215
<i>O. latipes</i>	48h LC ₅₀	250
<i>I. punctatus</i>	96h LC ₅₀	280
Invertebrates		
<i>H. azteca</i>	96h LC ₅₀	0.04
<i>C. dubia</i>	48h LC ₅₀	0.05
<i>S. vittatum</i>	24h LC ₅₀	0.06
<i>G. lacustris</i>	96h LC ₅₀	0.11
<i>C. tentans</i>	96h EC ₅₀ (immobility)	0.193*
<i>D. magna</i>	48h EC ₅₀ (immobility)	0.412*
<i>C. sabulosa</i>	96h LC ₅₀	0.57
<i>A. aegypti</i>	24h LC ₅₀	7.1
<i>P.californica</i>	96h LC ₅₀	10
Amphibians		
<i>X. laevis</i>	96h LC ₅₀	511

*Value shown is the geometric mean of comparable values

guidelines are levels which *do not* protect against adverse effects.

The minimum data requirements for the Type A

Table 3. Short-term CWQG for Chlorpyrifos Resulting from the SSD Method.

	Concentration
SSD 5th percentile	0.023 $\mu\text{g a.i.}\cdot\text{L}^{-1}$
SSD 5th percentile, LFL (5%)	0.009 $\mu\text{g a.i.}\cdot\text{L}^{-1}$
SSD 5th percentile, UFL (95%)	0.048 $\mu\text{g a.i.}\cdot\text{L}^{-1}$

guideline approach were met, and a total of 22 data points were used in the derivation of the guideline. Toxicity studies meeting the requirements for primary and secondary data, according to CCME (2007) protocol, were considered in the derivation of the short-term species sensitivity distribution (SSD). Each species for which appropriate short-term toxicity was available was ranked according to sensitivity, and its centralized position on the SSD was determined using the Hazen plotting position (estimate of the cumulative probability of a data point). Intra-species variability was accounted for by taking the geometric mean of the studies considered to represent the most sensitive lifestage and endpoint. Table 2 presents the final dataset that was used to generate the fitted SSD for chlorpyrifos. Aquatic toxicity studies reported by the U.S. EPA (EFED, 2005) Environmental Fate and Effects Division (EFED) and Health Canada's Pesticide Management Regulatory Agency were classified as primary data, unless erroneous values or other factors raised concerns about data quality.

The log normal model provided the best fit of the twelve models tested (Figure 1). The equation of the fitted normal model is in the form of;

$$y = \frac{1}{2} \left[1 + 0.03268 \left(\frac{x - 3.7666}{1.4898\sqrt{2}} \right) \right]$$

Where x is the log (concentration) and y is the proportion of species affected.

Summary statistics for the short-term SSD are presented in Table 3. The concentration $0.023 \mu\text{g a.i.}\cdot\text{L}^{-1}$, is beyond the range of the data (to which the model was fit). Therefore, the 5th percentile and its fiducial limits (FL) (boundaries within which a parameter is considered to be located) are extrapolations.

Therefore, the short-term CWQG value for protection of aquatic life in surface waters is $0.02 \mu\text{g ai}\cdot\text{L}^{-1}$.

Long-term Freshwater Quality Guideline: Long-term exposure guidelines identify benchmarks in the aquatic ecosystem that are intended to protect all forms of aquatic life for indefinite exposure periods.

Although the persistence of chlorpyrifos in water may be limited under field conditions by factors such as affinity for suspended solids and volatility in water, aquatic

organisms may experience long-term exposure to the pesticide. Aquatic organisms may be chronically exposed to chlorpyrifos if they inhabit the waters receiving pesticide input from multiple sources, or multiple applications.

The acceptable long-term studies identified in this review consisted of one invertebrate species, two fish species, and two amphibian species. Based on the minimum data requirements; there were insufficient data to derive a long-term SSD for chlorpyrifos according to CCME (2007) protocol. There were also insufficient data to derive a long-term guideline using the lowest endpoint approach (Type B1). Therefore, following the tiered approach, the lowest endpoint approach (Type B2) guideline method was used to develop the long-term CWQG.

Under the Type B2 guideline method, for a nonphytotoxic substance such as chlorpyrifos, a guideline may be developed if the available primary and/or secondary studies include two fish species and two invertebrate species. Using the Type B2 guideline method to derive the long-term CWQG, the critical (lowest acceptable) endpoint was identified as a 96h-LC₅₀ of $0.04 \mu\text{g/L}$, for *Hyalella azteca* (Ankley and Collyard 1995). A safety factor of 20 was applied to the lowest data to derive the Type B2 guideline for chlorpyrifos.

Therefore, the long-term CWQG for the protection of freshwater life is $0.002 \mu\text{g a.i.}\cdot\text{L}^{-1}$.

Marine Water Quality Guideline: Marine toxicity data was not re-evaluated to see if there was sufficient data available to derive a short-term or long-term marine water quality guideline for chlorpyrifos. The marine guideline will be revisited in the future when it is believed there is enough data to update the guideline.

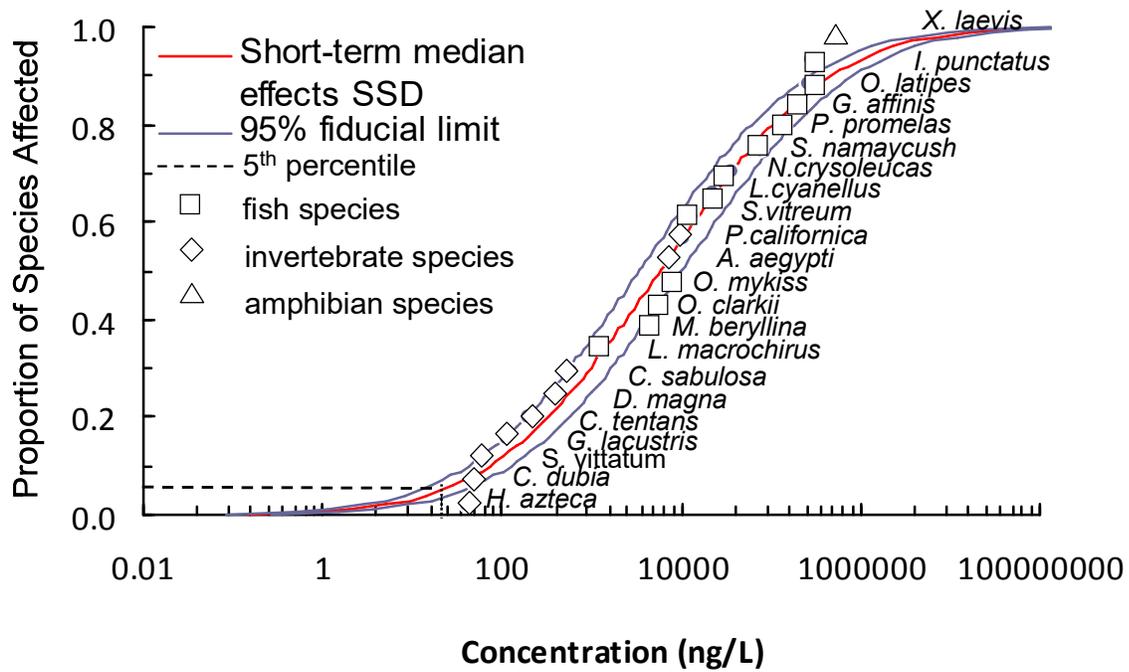


Figure 1. Short-term SSD representing the toxicity of chlorpyrifos in freshwater consisting of acceptable short-term LC50s of 22 aquatic species versus proportion of species affected.

The interim water quality guideline for chlorpyrifos for the protection of marine life is $0.002 \mu\text{g a.i.}\cdot\text{L}^{-1}$ (CCME 1996). It was derived by dividing a 96-h LC_{50} of $0.04 \mu\text{g a.i.}\cdot\text{L}^{-1}$ for mysid shrimp (Schimmel et al. 1983) by a safety factor of 20 (for nonpersistent substance, short-term toxicity study) (CCME 2007). This lowest short-term study, rather than the lowest long-term study, the 25-d LC_{50} of $0.29 \mu\text{g a.i.}\cdot\text{L}^{-1}$ for grass shrimp larvae, was chosen for the guideline derivation because of the lower short-term threshold.

Therefore, the long-term CWQG for the protection of marine life is $0.002 \mu\text{g a.i.}\cdot\text{L}^{-1}$.

Considerations in Guideline Derivation: Based on a review of the literature, Giesy et al. (1999) proposed that providing protection to aquatic organisms from the effects of chlorpyrifos would also prevent effects in aquatic organisms from exposure to its transformation products. Although the activated form of chlorpyrifos, chlorpyrifos oxon, is a more effective inhibitor of AChE than the parent compound, the chlorpyrifos oxon is very sensitive to hydrolytic degradation, and thus occurs at low levels in the environment (Giesy et al., 1999). Moreover, 3,5,6-trichloro-2-pyridinol (TCP), a primary metabolite of chlorpyrifos, does not inhibit AChE and is far less toxic to aquatic organisms than chlorpyrifos (Giesy et al., 1999).

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This is **Exhibit “P”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



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Science Policy Note

SPN2018-02

Cumulative Health Risk Assessment Framework

(publié aussi en français)

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1.0 Executive Summary

This document describes the framework and methodology that Health Canada's Pest Management Regulatory Agency (PMRA) will use for assessing the cumulative health effects of pesticides that have a common mechanism of toxicity. It supersedes Health Canada's 2001 Science Policy Note (SPN2001-01) on Guidance for Identifying Pesticides that have a Common Mechanism of Toxicity for Human Health Risk Assessment. The document also builds upon Health Canada's response to the Commissioner of the Environment and Sustainable Development 2015 audit on pesticide safety, whereby the PMRA indicated its intention to have methodology for cumulative health assessment in place in the 2017-2018 fiscal year.¹ The framework takes into account approaches taken by other chemical regulators and outlines methods for assessing cumulative health risks. A step-wise approach for identifying pesticides that belong to a common mechanism group is presented, including criteria for initial grouping and considerations for refining a common mechanism group. A flexible, tiered framework for assessing the hazard and exposure components of an assessment is presented in order to facilitate further refinement of parameters in a cumulative risk assessment to the extent needed. While the document summarizes elements of cumulative health risk characterization, some of the uncertainties and challenges with respect to cumulative methodology in general are also presented.

In March 2017, the PMRA published a Regulatory Proposal (PRO2017-01) on a Cumulative Risk Assessment Framework for pesticides. A number of comments were received during the consultation period; responses to these comments are summarized in Appendix II of this document. In response to the comments received, modifications were also made to the regulatory proposal, which now serves as the basis for this science policy note.

2.0 Introduction

For the purpose of this policy, cumulative assessment is aimed at identifying the human health risks associated with co-exposures to two or more pesticides² that cause a common toxic effect(s) by the same, or essentially the same, sequence of major biochemical events (that is, a common mechanism of toxicity). Concurrent exposure routes (oral, dermal, inhalation) and pathways (for example, diet, drinking water, residential use) to pesticides that share a common mechanism of toxicity are assessed to determine the potential for cumulative effects, based on the likelihood that people may be exposed to more than one of these pesticides at the same time. Cumulative assessment is undertaken to explore the possibility of whether low-level exposures to multiple pesticides that cause a common toxic effect by a common mechanism, could lead to the same adverse health effect as would a higher level of exposure to any of the pesticides individually.

¹ <http://www.hc-sc.gc.ca/cps-spc/pest/part/protect-protoger/pesticide-safety-securite-pesticide/index-eng.php>

² In the context of this document, the term "pesticides" can refer to conventional and non-conventional chemicals and microbials, including their metabolic derivatives. The term "chemical" has been used in sections of this document that are more generic in nature.

The consideration of the cumulative effects of pesticides was mandated in the modernization of Canadian pesticide legislation and reflects the application of modern science. Specifically, sections 7, 11 and 19 of the *Pest Control Products Act* (PCPA, 2006) require the consideration of “available information on...cumulative effects of the pest control product and other pest control products that have a common mechanism of toxicity” in evaluating the health risks of a pesticide. According to this legislation, cumulative assessments must be undertaken in the context of new evaluations, re-evaluations, and in the establishment of Maximum Residue Limits (MRLs). These assessments may consist of a qualitative or quantitative cumulative risk assessment, or result in a determination that a cumulative risk assessment is not required. For example, situations in which no common mechanism of toxicity exists or that do not involve co-exposures, would not require a cumulative risk assessment. In some scientific circles, exposure to multiple chemicals by multiple routes and pathways is referred to as combined exposure to multiple chemicals rather than cumulative exposure; however, the terminology used throughout this document reflects that used in the *Pest Control Products Act* for the assessment of pesticides. The scope of this policy does not extend to the consideration of mixtures of pesticides that may result in cumulative effects through disparate mechanisms of toxicity; however, it is worth noting that this is an area of interest in the international regulatory community that is being closely monitored by the PMRA.

Assessing the cumulative effects of pesticides to human health differs from aggregate assessment, where the latter considers the risk from exposure (non-occupational) to a single pesticide via all relevant routes and exposure pathways. Aggregate risk assessments have been fully implemented in the review of both new and re-evaluated pesticides and are supported by policy (Health Canada, 2003). Similar to aggregate assessment, cumulative assessment is focussed on non-occupational sources of exposure; however, cumulative assessment considers exposure from multiple pesticides.

It is essential that toxicological and exposure assessments of individual pesticides are up-to-date prior to undertaking the complex task of assessing cumulative health effects. Consequently, cumulative assessments are performed when both toxicity and exposure assessments are available for all pesticides within a common mechanism group. This could occur following the review of new active ingredients or a major new use of a previously registered active ingredient, or following the completion of a re-evaluation. To date, cumulative assessments have been completed primarily through the PMRA’s re-evaluation program. Although this document is focussed on science methodology, some comments received on PRO2017-01 also related to process considerations. To that end, a process map has been included in Appendix III of this document and is further described in the Response to Comments section. The process map identifies the potential paths of evaluation for a cumulative assessment, the decision points for determining the need for a cumulative risk assessment, as well as the opportunities for consultation on proposed cumulative assessment decisions.

This document sets out a framework to facilitate the assessment of cumulative health risks of pesticides that share a common mechanism of toxicity. The framework is not intended to be prescriptive, but rather is intended to function as a guide to those conducting cumulative health risk assessments, as well as a tool to communicate current practices to stakeholders. The

document outlines general methods for cumulative risk assessment, considerations for identifying pesticides that belong to a common mechanism group, a tiered framework consisting of increasing levels of hazard and exposure refinement, elements of risk characterization and a discussion of uncertainties and challenges. The framework contained herein draws from efforts undertaken by other Health Canada programs, North American Free Trade Agreement (NAFTA) partners such as the United States Environmental Protection Agency (USEPA) and by international regulatory and scientific communities.

The PMRA continuously monitors method development as well as specific cumulative assessments at the international level to determine their relevancy to the Canadian context. It is anticipated that by closely aligning the framework and methodology with that of other regulators, the PMRA can make use of cumulative assessments undertaken by those regulators, in whole or in part, provided that the assessments are relevant to the Canadian context.

3.0 Cumulative Risk Assessment Methods

In assessing the risks of pesticides with a common mechanism of toxicity, it is not necessary to have a full understanding of the entire molecular sequence of events required to produce a specific biological outcome. Rather, a more important aspect is having an understanding of the key cytological and biochemical events following chemical interaction. In this sense, the concept of mode of action, often used in cancer risk assessment, and generally considered to require less detail in the description of events than at the molecular level, is applicable. More recently, the term adverse outcome pathway has been employed to link the molecular initiating event(s) to progressive levels of biological organization at the individual or population level. Mechanism of toxicity, mode of action and adverse outcome pathway are all conceptually similar constructs for establishing the key events that define a common mechanism group.

Fundamentally, exposure to more than one chemical at a time is required for there to be a cumulative effect. When combined, chemicals can act jointly, resulting in three distinct types of action: independent, as an interaction or in an additive manner. Chemicals that act independently typically do so through different modes of action and are referred to as complex mixtures. Independently-acting chemicals, by definition, are not addressed by cumulative assessment as mandated under current pesticide legislation.

Interactions refer to synergistic or antagonistic actions between or among chemicals. From a public health perspective, synergistic interactions are of concern, as default assumptions of additivity could lead to an under-prediction of risk; however, synergistic interactions are quite rare. Data analysis suggests that when present, the magnitude of the under-prediction is relatively small (EC, 2009; EC, 2012).

Chemicals that act via the same mode of action, referred to as simple mixtures when combined, can be characterized as behaving in an additive manner. The concept of dose or concentration addition assumes no chemical interactions, but acknowledges that the combination of effects will be greater than that of each individual chemical. For the purpose of cumulative assessment, as described herein, an additive action is the default assumption used by most regulatory authorities (USEPA, 2002; EFSA, 2008).

The most common dose/concentration addition approaches are the hazard index method, margin of exposure method or relative potency factor method. These methods are described herein in further detail. The choice of method used by the PMRA in a cumulative risk assessment will be influenced primarily by the context of the assessment, the available data and the level of refinement required in the assessment. The use of an alternate approach is not precluded, but it is paramount that any alternate approach is scientifically defensible, well-documented and communicated in a transparent manner. The maximum cumulative ratio is also described herein as a tool for identifying the relative significance of cumulative toxicity compared to the toxicity of an individual chemical in the common mechanism group.

3.1 Hazard Index Method

The hazard index (HI) method is a simple and flexible approach that sums the individual hazard quotients (HQ) of individual chemicals in a cumulative assessment group. The HQ is the ratio of an individual chemical's exposure to its reference value. The reference value is the point of departure, (that is, the No Observed Adverse Effect level [NOAEL], Lowest Observed Adverse Effect level [LOAEL], or lower confidence limit on the benchmark dose [BMDL]), divided by the composite assessment factor (that is, the product of the uncertainty factors and the *Pest Control Products Act* factor (PCPA factor)). The PCPA factor is a legally-mandated margin of safety intended to afford particular protection of infants and children (Health Canada, 2008). A HI greater than one would indicate a potential health risk concern. It is worth emphasizing that the points of departure used in a cumulative risk assessment, using any method, may be different from those used in the risk assessment of an individual chemical given the focus on common effect.

$$\text{HQ} = \frac{\text{Exposure}}{\text{Reference Value}} \quad \text{Reference Value} = \frac{\text{Point of Departure}}{\text{Composite Assessment Factor}}$$

$$\text{HI} = \frac{\text{Exposure}_1}{\text{Reference Value}_1} + \frac{\text{Exposure}_2}{\text{Reference Value}_2} + \dots + \dots + \frac{\text{Exposure}_n}{\text{Reference Value}_n}$$

The approach allows for the application of chemical-specific uncertainty factors; however, the application of these uncertainty factors can mask the relative potency of the chemicals in a common mechanism group and thus, can inflate the overall uncertainty in the group.

3.2 Margin of Exposure (MOE) Method

The margin of exposure of a chemical is the ratio of its point of departure to its exposure. The adequacy of the MOE is determined by comparing it to a target MOE, the latter being the product of the uncertainty factors and the PCPA factor associated with that chemical. The margin of exposure method (MOE_{Total}) calculates the reciprocal of the sum of the reciprocals of the MOEs of individual chemicals in a cumulative assessment group (see equation below). This method does not include consideration of the uncertainty and PCPA factors associated with each individual assessment. The uncertainty and PCPA factors associated with the common mechanism group at large are taken into account in determining the target MOE for the group.

A potential health concern would be flagged if the MOE_{Total} is less than the target MOE or composite assessment factor (that is, the product of the uncertainty factors and the PCPA factor) for the group of chemicals.

$$MOE = \frac{\text{Point of Departure}}{\text{Exposure}}$$

$$MOE_{Total} = \frac{1}{\frac{1}{MOE_1} + \frac{1}{MOE_2} + \dots + \frac{1}{MOE_n}}$$

This method is currently used by the PMRA in conducting aggregate assessments of individual pesticides. Although, as previously noted, the uncertainty and PCPA factors for each chemical in the assessment group are not quantified in this approach, it remains a simple and flexible method to assess cumulative risk.

When the target MOEs are different for the individual chemicals in a cumulative assessment group, the aggregate risk index method (ARI) can be used to assess risk. The MOEs are calculated separately and then combined using the equation below. This method accounts for the uncertainty and PCPA factors for each individual chemical in the assessment group. A potential health concern would be flagged if the ARI is less than one for the group of chemicals.

$$ARI = \frac{1}{\frac{\text{Target MOE}_1}{MOE_1} + \frac{\text{Target MOE}_2}{MOE_2} + \dots + \frac{\text{Target MOE}_n}{MOE_n}}$$

3.3 Relative Potency Factor Method

The relative potency factor method is a more complex approach that capitalizes on the occurrence of similar effects seen in chemicals with a common mechanism of action. This approach relies upon the selection of an index chemical within a cumulative assessment group, against which the other members of the group are compared. The index chemical should have a robust database and be representative of the chemicals in the assessment group. The relative potency factor (RPF), or scaling factor, for each chemical is derived by dividing the point of departure for a common measure of effect for the index chemical, termed the effective dose (ED), by the point of departure for the same measure of effect for the individual chemical. For example, the effective dose of the index chemical that results in a 10% response is compared to the effective dose of each test chemical in the assessment group that also results in a 10% response.

$$RPF_1 = \frac{ED_{index}}{ED_1}$$

In cases where the magnitude of the uncertainty and PCPA factors is the same for each chemical of the assessment group, this magnitude would be reflected as the target MOE for the combined exposures (see Table 1, Example 1). In situations where the uncertainty and PCPA factors vary among the chemicals, the relative potency factor for each chemical can be multiplied by the respective factor to yield an adjusted RPF (see Table 1, Example 2). Any factor used to adjust the RPF should not be double-counted in the target MOE for the combined exposures. For example, as illustrated in Table 1, Example 2, the uncertainty factor for interspecies extrapolation and the PCPA factors differ among the three chemicals. Therefore, the adjusted RPF for each chemical is calculated by multiplying the RPF by the chemical-specific uncertainty factor for interspecies extrapolation and PCPA factor. As the uncertainty factor for intraspecies variability for all three chemicals is the same (that is, 10-fold), and was not used to calculate the adjusted RPF, it forms the basis of the target MOE for the combined exposures.

Once the relative potency factor (adjusted or not) for each individual chemical has been derived, exposures of these chemicals can be converted to an index chemical equivalent exposure (by multiplying the chemical-specific exposure estimates by their respective RPF) and compared to the point of departure for the index chemical and the target MOE for the combined exposures.

Table 1 Examples of Uncertainty Factor Incorporation in RPF Methodology.

Chemical	RPF	UF _A	UF _H	PCPA Factor	Adjusted RPF	Target MOE
Example 1						
Index Chemical A	1	10	10	1	-	100 (UF _A × UF _H × PCPA)
Chemical B	2.5	10	10	1	-	
Chemical C	0.4	10	10	1	-	
Example 2						
Index Chemical X	1	10	10	1	10	10 (UF _H)
Chemical Y	3	3	10	1	9	
Chemical Z	0.01	10	10	3	0.3	

UF_A – uncertainty factor for interspecies extrapolation (that is, animal to human extrapolation)

UF_H – uncertainty factor for intraspecies variability (that is, within human variability)

PCPA factor - legally-mandated margin of safety intended to afford particular protection of infants and children (Health Canada, 2008)

The RPF approach provides a more refined method for standardizing the dose metrics for chemicals in an assessment group, but is heavily reliant on the quality and availability of appropriate toxicology data. Although it allows for the consideration of potency and uncertainties of individual chemicals, a limitation of the approach is the assumption of similarly shaped dose-response curves. This approach has been utilized by the USEPA in their cumulative assessment of various pesticide classes such as the organophosphates and N-methyl carbamates.

3.4 Maximum Cumulative Ratio (MCR)

The MCR is a tool that can be used in cumulative assessment to identify chemicals that may drive the risk assessment (Price et al 2012). The MCR is the ratio of the hazard index (HI) of a group of chemicals (that is, the sum of the hazard quotients (HQ) of each chemical in that group) to the maximum hazard quotient within that group, where the hazard index is used to normalize exposures across chemicals.

$$\text{MCR} = \frac{\text{HI}}{\text{Maximum HQ}}$$

MCR values range from one to the number of chemicals in the common mechanism group. Values close to one indicate that one chemical dominates the toxicity of the group, whereas values that approximate the number of chemicals in the group indicate an equitoxic hazard among those chemicals. As the MCR is hazard-focussed, it is less useful for identifying exposure scenarios that influence the risk assessment.

4.0 Selection Considerations for Common Mechanism Groups

A common mechanism of toxicity pertains to two or more chemicals that share a common toxic effect that results from the same, or essentially the same, sequence of major biochemical events. Care must be taken not to confuse mechanism of toxicity with site of toxic action. Likewise, for some chemicals, the site of toxic effect may be different than the site of toxic action. For instance, the anterior pituitary gland would be the site of toxic action for a chemical inhibiting the thyroid stimulating hormone (mechanism of toxicity) whereas the thyroid would be the site of toxic effect for the ensuing hypothyroidism. Another chemical could share the common toxic effect of hypothyroidism but have a different mechanism of toxicity such as the inhibition of thyroxine and triiodothyronine; in this case, the site of toxic effect and site of toxic action would be the same.

Many chemicals can cause more than one toxic effect, depending on the level of exposure, and do so by different mechanisms of toxicity at different sites of toxic action. However, a chemical may also cause multiple toxic effects at multiple sites from a single mechanism of toxicity taking place at a single site of toxic action. An example of the latter would be the downstream effects occurring from inhibiting the conversion of cholesterol to corticosteroid hormones in the adrenal cortex.

The PMRA follows a “weight-of-evidence” approach to support the development of hypotheses pertaining to mechanisms of toxicity. Generally, a single piece of information is insufficient on its own to support the characterization of a specific or common mechanism of toxicity; this finding will require support by the analysis and interrelationships of multiple pieces of information. Toxicity data generated in support of regulatory submissions will be the primary source of information used by the PMRA. Toxicity data obtained from other studies, such as those described in reports from other regulatory authorities, or the published scientific literature will also be used. Available epidemiological and mechanistic studies are also considered.

The totality of the evidence is assessed to ensure that the mechanism is consistent with current toxicological theory and knowledge and deemed scientifically plausible by the PMRA for these purposes.

In dealing with uncertainties that arise during the process of integrating multiple lines of evidence, the PMRA employs a precautionary approach from both a hazard and exposure perspective, as described in other regulatory documents (refer to SPN series: SPN2000-01 through SPN2008-01).

4.1 Preliminary Grouping

Identification of a preliminary grouping of pesticides that might cause a common toxic effect by a common mechanism of toxicity is undertaken early in the process of cumulative assessment. This preliminary grouping of pesticides is based upon at least one of the following criteria, considered within a weight-of-evidence context.

Structural similarity

It is assumed that pesticides that are structurally analogous could contain a common toxophore and may interact analogously with cellular molecular sites to cause a common toxic effect. This would also include any pesticides that are biotransformed by mammals to yield a common toxophore upon metabolism. Data on structure-activity relationships, quantitative structure-activity relationship modelling and structural alerts can contribute to the identification of structural analogs.

Similarity of mechanism of action

- (a) General mechanism of toxicity in pests: the mechanisms by which some pesticides are toxic to humans can be fundamentally similar or, in some cases, identical to their mechanisms of intended toxicity to pests.
- (b) General mechanism of mammalian toxicity: this is based on the possibility that pesticides that share a known general mechanism of toxicity may cause a common toxic effect. A general mechanism of toxicity may include, for example, pesticides that uncouple oxidative phosphorylation.

Similarity of toxic effect

It is possible that a particular toxic effect known to occur in experimental animals or humans could be common (that is, concordant in both site and nature) to many pesticides, and that this commonality in toxicity could be due to a common mechanism. Since this type of grouping is functionally based, not structurally based, it enables the identification of structurally unrelated pesticides that cause a common toxic effect from a common mechanism that otherwise might not be identifiable from groupings based on structural similarity or mode of pesticidal action alone.

Not all toxic effects can be used as a preliminary basis for grouping pesticides. Toxic effects that have many possible unrelated causes, or that could be defined as nonspecific in origin, are not appropriate as the primary basis for the initial grouping of pesticides. These effects, such as body weight changes or death, can result from many unrelated factors and are usually of limited value in understanding the mechanism of toxicity. Such generalized effects, therefore, will not typically be used as a basis for an initial grouping. The PMRA groups pesticides that cause multiple toxic effects by a common mechanism from a common site of toxic action for purposes of the preliminary grouping, provided at least one of the toxic effects is common among the pesticides.

Following the initial grouping of pesticides, a detailed evaluation of available toxicology data for each pesticide within the group will be undertaken to identify and characterize the toxic effects caused by each, and to determine which of the pesticides cause toxic effects that are common with other pesticides (that is, toxic effects that are concordant in both site and nature). Pesticides may be placed in more than one group in instances where they cause more than one common toxic effect.

The PMRA does not make a determination of common mechanism of toxicity solely on the basis of the preliminary grouping; rather, it is important that a preliminary group proceed through the refined grouping phase to confirm or narrow the list of pesticides that belong to a common mechanism group. Hence, only those pesticides that cause a common toxic effect by a common mechanism (through the in-depth review described below) will be considered by the PMRA for cumulative risk assessment.

4.2 Refined Grouping

The next phase of the review process is to determine the mechanisms by which the pesticides of the preliminary group cause the common toxic effect(s). Once the critical biochemical/molecular events pertaining to toxicity are understood for each pesticide in the preliminary group, they can be compared and those pesticides that cause toxicity through a common mechanism can be identified.

For those pesticides whose toxic mechanisms are not known or not well understood, or for which there is an absence of direct mechanistic data, the PMRA will analyze available structural data, pharmacokinetic data, and toxicity data for the pesticide, its toxophore, and its analogs. A weight-of-evidence approach will be undertaken to determine the major biochemical events that are most critical in causing toxicity. Mechanistic similarities that would support a finding of a common toxic mechanism include, for example, analogous interactions of the pesticide with identical or similar biological targets, and the occurrence of similar metabolic transformations that yield common or structurally analogous metabolites that interact with similar biological targets, or that are otherwise involved in causing toxicity. Pesticides that cause a common toxic effect by different mechanisms will be excluded from the refined grouping.

5.0 Considerations for Determination of Cumulative Exposure

The challenges posed by complex exposure scenarios require approaches that allow the assessment of the health effects of multiple pesticides via multiple routes and exposure pathways, and over multiple time frames. Risk assessments should consider all non-occupational sources, pathways, and routes of exposure that could contribute materially to a person's total exposure. It is appropriate to integrate only those exposures that are likely to occur within the critical time window for the common toxicological effect. Toxicokinetic and toxicodynamic data can inform whether consecutive, separate or partially-overlapping exposures need to be considered in a cumulative assessment.

Exposures may originate from a single route (for example, oral exposure from a dietary pathway) or they may originate from multiple routes (oral, dermal and inhalation), all of which may vary over time and space. Determination of the combination of exposures and routes is an important step for cumulative risk assessments. Identification of use patterns of active ingredients will inform the exposure scenarios for assessment, data collection, or modelling strategies. Co-exposures will be identified on the basis of data that support temporality of exposure.

The consideration of co-exposures will be an iterative process. At the earliest stages of the cumulative assessment, it will be determined whether there is dietary or residential exposure or whether exposure is limited to occupational scenarios. As the review progresses, principles for inclusion or exclusion of exposure scenarios, similar to those used in aggregate risk assessments (SPN2003-04), will be applied to the cumulative risk assessments.

6.0 Cumulative Health Risk Assessment Framework

The PMRA supports the use of the WHO/IPCS framework to maximize efficiency in performing cumulative health risk assessment (Meek et al, 2011). The framework involves a tiered approach to the assessment of exposure and hazard, with each tier being more refined (that is, less conservative and uncertain) than the previous tier. As the tiers of assessment increase, the effort to perform the assessment generally increases, as do the data required to support the refinements. The WHO/IPCS framework has also been employed by regulators responsible for Canada's Chemical Management Plan (Health Canada, Environment Canada, 2015). This iterative process is also similar to the screening analysis framework put forth by the USEPA (USEPA, 2015).

A conceptual representation of the framework, as constructed by WHO/IPCS, is presented in Appendix I and forms the foundation of the PMRA's approach. The elements of the framework are not fixed and will vary depending on the available data. It is not necessary for the hazard and exposure components to be assessed at similar tiers of refinement; rather, the available data will dictate the extent to which either component can be refined. The risk assessor needs only to progress through the tiers to the point where risk does not exceed the level of concern. This process may include consideration of viable mitigation measures. If unacceptable risk is still present with the maximal level of refinement, then further regulatory action is warranted.

As part of the approach to conserving resources in assessment and focussing on critical areas, the PMRA will leverage assessments (or parts of assessments) from other jurisdictions that have undertaken a cumulative health assessment. In these cases, the assessments must be applicable to the Canadian context and consistent with current policy.

A narrative is provided below to illustrate levels of refinement in both the hazard and exposure components of an assessment. The content of each tier is not meant to be prescriptive or fixed, but is intended to show the progressive steps that could be undertaken in a cumulative health risk assessment.

6.1 Hazard Assessment

At the least refined level (Tier 0), it is assumed that all pesticides in a common mechanism group have the same potency and the point of departure of the most potent member of the group is used in the assessment. This assumption, while conservative, can be used as an initial screening method to determine if further refinement is necessary and if so, to what degree. Similarly, selecting the lowest point of departure for a pesticide, rather than the most relevant point of departure, can be used at an early screening stage.

At the next level of refinement (Tier 1), information on each of the pesticides in the common mechanism group can be integrated into the assessment to provide relative measures of potency. Points of departure such as the NOAELs or LOAELS for the apical effect of the individual pesticides can be used.

At a higher tier of refinement (Tier 2), additional refinements can be made by incorporating information on mode of action where available. The use of benchmark dosing can allow for a more refined comparison of potencies in that it can determine the dose associated with a defined response level (for example, a 10% change in the parameter of interest) for each pesticide of the common mechanism group. This facilitates the comparison of potency of each pesticide against an index pesticide in the common mechanism group, which is then expressed as an equivalent of the index pesticide or relative potency factor.

At the highest level of refinement (Tier 3), analyses can be quite sophisticated and include further consideration of mode of action data, toxicokinetics and toxicodynamics. Data modelling and probabilistic techniques can be employed, although the extent of these advanced analyses will depend on the data availability, quality, strength and reliability.

6.2 Exposure Assessment

At the least refined level (Tier 0), it is assumed that exposure is based on simple semi-quantitative estimates of exposure. Semi-quantitative estimates are based on limited data and a few very simple assumptions to determine a worst-case scenario. Similarly, determining a best-case scenario can be used at an early screening stage.

At the next level of refinement (Tier 1), generic exposure scenarios are assessed using conservative point estimates. These are developed based on assumptions and modelled data, rather than measured data. These assumptions provide a conservative risk assessment in the absence of more specific, reliable exposure data, addressing a range of similar uses with limited numbers of parameters being included. However, if the risk estimates from these conservative assumptions are considered acceptable, no further evaluation is necessary.

At the next level of refinement (Tier 2), pesticide-specific and more detailed and reliable data for key parameters, in conjunction with risk mitigation factors are incorporated to refine the exposure and risk assessment. These data may include biomonitoring data from the Canadian Health Measures Survey (CHMS), food residue data from the Canadian Food Inspection Agency (CFIA) and the United States Department of Agriculture's Pesticide Data Program (USDA PDP), and water monitoring data. Additional data for refinement may be drawn from the Residential Joint Venture (REJV) homeowner survey data and use data from the Canadian Pest Management Association (CPMA). Trade data, for imported food commodities and for common mechanism group active ingredients not registered in Canada, can also be utilized. Although still conservative, this results in more realistic exposure estimates.

At the highest level of refinement (Tier 3), probabilistic techniques and more sophisticated data modelling can be employed. This approach requires representative information on exposure for the scenarios of interest, and for the relevant populations and different uses across populations. At this tier, more defined and tailored exposure estimates are developed using fewer assumptions. More emphasis is placed on measured data and modelling software such as Calendex, CARES NG (Cumulative and Aggregate Risk Evaluation System Next Generation), SHEDs (Stochastic Human Exposure and Dose Simulation), and purpose built algorithms, if available. The extent of these advanced analyses will depend on the data availability, quality, strength and reliability.

6.3 Risk Characterization

In case studies undertaken by the WHO/IPCS, it has been demonstrated that refinements in the exposure assessment lead to the largest gains in characterizing risk (Meek, 2013). There is likely to be a greater difference between the lower and upper tiers of exposure assessment than there is for the tiers of hazard assessment, due to the higher reliance on assumptions in the exposure assessment. Hazard refinement, particularly at the uppermost tier, is more constrained by the absence of data on mode of action or toxicokinetics and toxicodynamics.

Given the complexity of cumulative risk assessment, the characterization of risk is of utmost importance. Each assessment must clearly identify the pesticides and exposure scenarios addressed, the types and quality of data available, and the methods of estimation. It is critical that the strengths and limitations associated with the data and analyses be discussed together with the uncertainties and assumptions. The overall level of risk can be expressed in different ways, depending on whether deterministic or probabilistic methods were used, and can reflect a series or range of estimates in light of the numerous input parameters in the assessment. These risk estimates can be specific to different age groups, durations of exposure and/or geographic regions where data permit. The target against which the cumulative health risk estimates are

compared should incorporate uncertainty factors that represent the cumulative assessment group as a whole (such as the factors for interspecies extrapolation and intraspecies variability), as well as the PCPA factor.

Acceptability of cumulative health risk estimates must also take into account direction and magnitude of bias in the data and confidence in the data. Sensitivity analyses can assist in determining the impact of various parameters in the assessment and can contribute to the development of risk mitigation options by identifying drivers of risk. As with individual pesticide risk assessments, the finding of unacceptable risk in a cumulative health risk assessment will warrant risk mitigation. Risk mitigation can include a host of measures ranging from label amendments to cancellation of uses or products, as well as MRL amendments.

In those cases where the PMRA has leveraged a cumulative health assessment from another jurisdiction, a narrative that characterizes the risk and its acceptability in the Canadian context is vital. Regardless of the approach utilized, cumulative health assessments will be subject to consultation prior to final decisions as per established processes; accordingly, it is imperative that the assessments are transparent and clearly communicated.

7.0 Uncertainties and Challenges

Cumulative risk assessment represents a complex series of analyses; as such, varying degrees of uncertainty are unavoidable. These sources of uncertainty can be generic or pesticide-specific.

In the case of the hazard assessment, generic sources of uncertainty can include the assumptions of dose-additivity or similar-shaped dose-response curves of pesticides within a common mechanism group and the lack of data on mode of action. Pesticide-specific sources of uncertainty in hazard assessment can include the adequacy of the toxicological data to define appropriate points of departure (that is, points of departure that are temporally relevant, age relevant, etc.) as well as lack of knowledge regarding human relevance.

Uncertainties in the cumulative exposure assessment include, but are not limited to, the following:

- the level of accuracy with which exposure to different pesticides can be characterised;
- the degree of understanding on the extent and profile of co-exposure to different pesticides. Different pesticides have different persistence in the environment and in the body, and therefore, duration of exposure will vary; in other words, it may be episodic for one pesticide and continuous for another; and
- the variability and uncertainty within the algorithms used to estimate exposure, which are compounded across substances in a cumulative context and may also lead to overestimates of exposure.

The legislative requirement for precaution will be applied in cumulative assessment in a manner similar to that applied for individual pesticide assessments. Accordingly, conservative assumptions and methods will be employed in the absence of data.

8.0 Conclusions

Cumulative health risk assessment methodology is a rapidly developing field as more regulatory authorities incorporate cumulative assessment into their practices. It is expected that methodology will continue to evolve with increased experience in conducting cumulative health risk assessment; hence, the current framework is considered a starting point upon which the methodology will be further developed as approaches and scientific understanding progress.

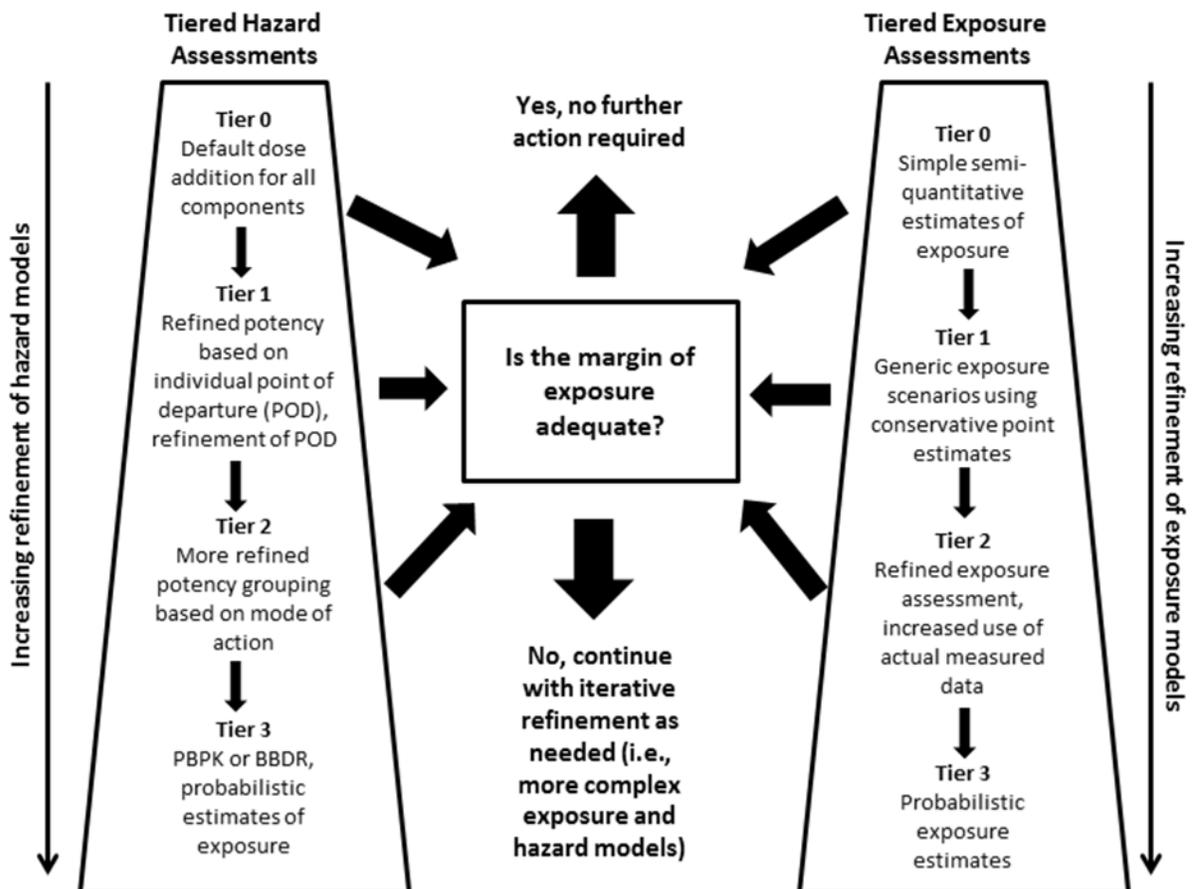
Appendix I WHO/IPCS Framework for Risk Assessment of Combined Exposure to Multiple Chemicals (modified from M.E. Meek et al., (2011) Regulatory Toxicology and Pharmacology, 60: S1-S14).

Problem Formulation: Cumulative Risk Assessment

- What is the nature of exposure?
- Is exposure likely, taking into account the context?
- Is there a likelihood of co-exposure within a relevant timeframe?
- What is the rationale for considering compounds in an assessment group?



Tiered Exposure and Hazard Considerations



Appendix II Response to Comments

Seven sets of comments were received during the consultation period for PRO2017-01. Commenters represented a wide array of stakeholders including the pesticide industry and non-governmental organisations representing the interests of public health and the environment. All commenters were supportive of the proposed framework and methodology outlined in PRO2017-01. Additional comments were provided that were general in nature or specific to certain sections. These comments have been summarized and where relevant, grouped by theme. The summarized comments and the PMRA's responses are outlined below; where appropriate, the PMRA has modified the science policy to address these comments.

General Comments

1. Comment related to the applicability of the policy to cumulative environmental assessment

Several commenters questioned whether the policy was limited to cumulative human health risk assessment. Some commenters indicated that, over time, the PMRA should expand its framework to enable the assessment of cumulative environmental risks, consistent with other international regulatory bodies such as the European Union.

PMRA Response:

The legislative requirement to consider the cumulative effects of pesticides is restricted to the evaluation of health risks; accordingly, the policy is focussed on human health risk assessment. That said, the PMRA recognizes that there is scientific merit in also considering the cumulative effects of pesticides on the environment. The PMRA has previously conducted cumulative assessments for the environment on a case-by-case basis where there has been clear evidence of pesticides with the same mode of action co-occurring in environmental media. Moving forward, the PMRA will be exploring potential options for developing a more formal approach for conducting these cumulative assessments.

2. The PMRA is encouraged to work with international partners in developing the policy

One commenter encouraged the PMRA to work with NAFTA and Organization for Economic Co-operation and Development (OECD) partners to ensure consistent approaches.

PMRA Response:

The PMRA is committed to maintaining engagement with international partners on this issue. The PMRA has recently provided comments on an OECD guidance document on assessing the risks of combined exposure to multiple chemicals, and this is also a topic of ongoing dialogue with USEPA counterparts. In addition, from an intradepartmental perspective, the PMRA maintains linkages with other programs interested in cumulative health assessment (for example, the Chemical Management Program [CMP]).

3. Comments related to the applicability of the cumulative health risk assessment framework to genetically modified (GM) crops/traits

One commenter suggested that the use of herbicide-tolerant crops is relevant to the proposed cumulative health risk assessment framework, and made several recommendations regarding the use of GM crops and traits, and their relationship to herbicide use.

PMRA Response:

Plants with novel traits are regulated separately by the Canadian Food Inspection Agency (CFIA), and by Health Canada under the *Food and Drugs Act*. As such, the regulation of genetically or otherwise modified crops and traits falls outside the scope of the *Pest Control Products Act*, as well as the SPN2018-02. However, the impact of the novel trait on how a pesticide may be used on the growing crop is factored into all pesticide risk assessments conducted by the PMRA.

Herbicide-tolerant traits extend the window of application for a herbicide to the growing crop. For example, transgenic crops may be tolerant to both pre- and post-emergent herbicide applications, whereas conventional crops may be tolerant to only pre-emergent treatments. The increased intensity of herbicide use is accounted for in pesticide risk assessments. Plant metabolism studies and residue data are required for both types of crops in order to identify and delineate differences in how plants metabolise the pesticide, as well as differences in the potential residue levels between transgenic and conventional crops. Use data are also factored into the assessment so as to account for the fraction of the total amount of crop treated with the specific herbicide. In situations where reliable use data are not available, a health protective estimate of 100 per cent crop treated is assumed for risk assessment purposes.

4. Comments related to the process for conducting cumulative health risk assessments, including opportunities for consultation and timelines

Several comments were related to the process for conducting cumulative health risk assessments. These included queries regarding how the findings of a cumulative health risk assessment are integrated into the regulatory process, whether such assessments would be conducted as part of a

re-evaluation, and whether the framework would include a “gatekeeper” step as outlined in Solomon et al, 2016³ and Moretto et al, 2017⁴. Commenters also highlighted the importance of consultation at various points in the assessment, as well as the establishment of timelines.

PMRA Response:

The PMRA has developed a process map for cumulative health assessments to address the received comments (see Appendix III). Cumulative health assessments that can be addressed within the context of the individual pesticide documentation (Proposed Registration Decision [PRD] or Proposed Re-evaluation Decision [PRVD]) will continue in this manner as per current practice. Those assessments that are more complex will be handled as stand-alone re-evaluations for a cumulative assessment group. For the latter type, the PMRA will undertake a scoping assessment to identify the available evidence relating to both the evidence for common toxicity and evidence for co-exposure. This step is an initial collection of information and is analogous to the gatekeeper step referred to in the cited publications. Based on this information, the PMRA determines whether a cumulative health risk assessment is required, and, if so, the PMRA then undertakes a problem formulation to identify the scope and depth of the necessary analysis. Upon completion of the problem formulation, the PMRA will announce the proposed cumulative assessment group, and request toxicological, exposure and use pattern information relevant to the cumulative health risk assessment. Following this information-gathering step, the PMRA will publish a project plan which will include timelines for completion of the cumulative health risk assessment and then proceed with the review. Regardless of which path an assessment follows, there will be an opportunity for interested stakeholders to comment on the proposed decision prior to the publication of the final decision.

5. Comment on completion of re-evaluations without a cumulative health assessment

One set of comments recommended that the re-evaluation of individual pesticides within the same group not be considered complete until cumulative health risks have been assessed.

PMRA Response:

As indicated in the process map (Appendix III), in some cases, cumulative health assessments will be undertaken within the scope of the re-evaluation for individual pesticides. In other cases that require a more complex assessment, the PMRA will initiate a separate re-evaluation for a

³ Solomon KR, Wilks MF, Bachman A, Boobis A, Moretto A, Pastoor TP, Phillips R and Embry MR. (2016). Problem formulation for risk assessment of combined exposures to chemicals and other stressors in humans. *Crit Rev Toxicol* 46(10): 835-844.

⁴ Moretto A, Bachman A, Boobis A, Solomon KR, Pastoor TP, Wilks MF and Embry MR. (2017). A framework for cumulative risk assessment in the 21st century. *Crit Rev Toxicol* 47(2):85-97.

cumulative assessment group, after completing the re-evaluations of the individual pesticides within that group. The latter process will ensure that there is no delay in implementing required risk mitigation measures for individual pesticides, while at the same time maintaining regulatory authority for the subsequent evaluation of cumulative health risk.

6. Comment related to updating the framework, including the consideration of a “gatekeeper” step

One commenter recommended updating the framework to reflect the processes outlined in Solomon et al., 2016⁵ and Moretto et al., 2017⁶. Specifically, the commenter recommended inclusion of a gatekeeper step which involves assembling available information on toxicity and exposure to determine if sufficient evidence is available to warrant a cumulative risk assessment.

PMRA Response

There will be a scoping step in the cumulative health risk assessment process aimed at identifying the available toxicological, exposure, and use information relevant to a determination of co-exposure and common mechanisms of action. This information will be used to determine if a cumulative health risk assessment is required and if it is required, a problem formulation will define the scope and the depth of the risk assessment. A cumulative health risk assessment is deemed unnecessary if the information indicates either a lack of co-exposure or common mode of toxic action. The scoping step does not involve a complete assessment, but rather documents the initial collection and summary of the data in-hand for the cumulative assessment group.

7. Comments related to how and when cumulative health risk assessments are triggered/required

Several commenters recommended that the framework should specify the conditions that would trigger the need for a cumulative health risk assessment, and identify points in the decision-making process where the need for a cumulative health risk assessment is determined.

PMRA Response:

According to the *Pest Control Product Act*, cumulative assessments of health effects for pesticides must be undertaken for new evaluations, re-evaluations and in the establishment of MRLs. These assessments may consist of a qualitative or quantitative cumulative health risk

⁵ Solomon KR, Wilks MF, Bachman A, Boobis A, Moretto A, Pastoor TP, Phillips R, Embry MR. (2016). Problem formulation for risk assessment of combined exposures to chemicals and other stressors in humans. *Crit Rev Toxicol* 46(10): 835-844.

⁶ Moretto A, Bachman A, Boobis A, Solomon KR, Pastoor TP, Wilks MF and Embry MR. (2017). A framework for cumulative risk assessment in the 21st century. *Crit Rev Toxicol* 47(2):85-97.

assessment, or result in a determination that a cumulative health risk assessment is not required, as further outlined in the process map that has been developed for cumulative health assessments (see Appendix III). The process map highlights conditions under which a cumulative health risk assessment would not be required (for example, lack of a common mechanism of action, or on the basis of use pattern). It also details the process that will be followed in situations that require a more complex cumulative health risk assessment, for example, where several pesticides have been identified to belong to a cumulative assessment group, and it is anticipated that co-exposure will occur. Moving forward, the process identified in Appendix III will be undertaken for all re-evaluations, for evaluations of new pesticide active ingredients, as well as those involving major new uses of previously registered pesticide active ingredients.

8. Comment on regulatory impact

Several commenters recommended that the PMRA indicate how conclusions about cumulative health risk will influence regulatory decisions.

PMRA Response:

As with individual pesticide risk assessments, the finding of unacceptable risk in a cumulative health risk assessment will warrant risk mitigation. Risk mitigation measures can include a host of possible measures ranging from label amendments to cancellation of uses or products, as well as MRL amendments. Given the potential complexity of a cumulative health risk assessment, the need to identify risk drivers will be of paramount importance in a finding of unacceptable risk. Sensitivity analyses can help to discern whether risks are driven by one pesticide in the common mechanism group or by certain uses, pathways of exposure or other factors, such as whether risks are specific to a certain population. Regulatory actions would be tailored to address the risk of concern. The PMRA recognizes that the challenges will increase in identifying appropriate risk mitigation options with larger common mechanism groups and increased number of potential co-exposure events. For these reasons, stakeholder consultation will be vital to developing appropriate mitigation options.

9. Comments relating to the incorporation of a precautionary approach in cumulative health risk assessments

One commenter recommended describing the application of the legislative requirement for precaution in the framework document. Another commenter indicated that a precautionary approach is a more appropriate way to proceed than relying on a weight-of-evidence approach when assessing common mechanisms of action.

PMRA Response:

The legislative requirement for precaution will be applied in cumulative health risk assessments in a manner similar to that applied for individual pesticide assessments. Accordingly, conservative assumptions and methods will be employed in the absence of data, acceptability of risk will be determined and unacceptable risks will be mitigated. These features have been reflected in the SPN2018-02.

The PMRA does not consider the weight-of-evidence approach and the precautionary approach to be mutually exclusive. The weight-of-evidence approach is a qualitative process of integrating multiple lines of evidence to reach a conclusion using professional judgement. Uncertainties that result from incomplete or absent scientific data during this integration frequently require scientists to make inferences, assumptions and judgements in order to characterize risk. As noted above, the PMRA employs a precautionary approach in the absence of data through the use of conservative assumptions and methods.

10. Comment related to the level of conservatism in the proposed approaches

One commenter indicated that the flexibility provided in the cumulative health risk assessment framework with regards to the proposed options for assessment methods was appreciated. However, the commenter indicated that it was important that the PMRA not default to the use of overly-conservative approaches.

PMRA Response:

The PMRA will be mindful to not introduce unnecessary conservatism into cumulative health risk assessments through the choice of assessment methods. However, the choice of methods will be largely driven by the quality and amount of data that are available, and the level of refinement that is deemed necessary. According to the proposed tiered approach outlined in the cumulative health risk assessment framework, more conservative approaches for assessing the hazard and exposure components of an assessment generally will be used in the earlier stages of the cumulative health risk assessment, with refinement of these parameters undertaken as needed, in an effort toward efficient use of resources.

11. Request to include real-life examples in the document including the determination of relevant exposure scenarios and data

One commenter indicated that it would be useful to provide real-life examples in the document including the determination of relevant exposure scenarios and data, as this information will impact the risk assessment the most.

PMRA Response:

Given the high level of interest in publishing the framework document in an expeditious manner, the PMRA has chosen to not include real-life examples at this time. However, as the PMRA will be publishing and consulting on cumulative health assessments, stakeholders will have the opportunity to provide further comments on the approach to cumulative assessment.

12. Comment on backlog of pesticides without a cumulative health risk assessment

Several commenters recommended that the PMRA establish timelines for addressing the backlog of currently registered pesticides for which cumulative health risks have not been assessed.

PMRA Response:

The PMRA acknowledges that cumulative health assessments for some pesticides in the re-evaluation program (for example, the N-methyl carbamates or organophosphates) were deferred. The reason for this deferral was to ensure that risks associated with individual pesticides within a group had been adequately characterized by way of a modern assessment and mitigated to acceptable levels. The PMRA will review past assessments for pesticides belonging to already-known common mechanism groups and will develop a strategic plan to address those with outstanding cumulative health risk assessments. New active ingredients that have been registered since the requirement for conducting cumulative health assessments, will be addressed in future re-evaluations and in the assessment of new active ingredients.

13. Suggestion to develop an evaluation strategy for the cumulative health risk assessment framework

One commenter recommended the inclusion of an evaluation strategy to determine the effectiveness of the framework and identify areas for future analysis and assessment.

PMRA Response:

Recognizing that the area of cumulative health risk assessment is an evolving science, the PMRA will update related policies as necessary. Continued involvement with international partners will ensure that the PMRA stays abreast of key developments.

14. Comment related to the maintenance of a cumulative health assessment database

One set of commenters recommended that the PMRA maintain a publicly accessible database of pesticide toxic effects and associated hypotheses about mechanisms of toxicity, including groupings of pesticides for cumulative health assessments.

PMRA Response:

The PMRA will explore mechanisms for tracking cumulative health assessments and providing public access to such records.

15. Comments related to expanding and updating the PMRA’s cumulative health risk assessment approach in the future

It was recommended that a timeline be included for the development of more advanced methodologies in the future. Commenters suggested that the scope of cumulative health risk assessments should be expanded in the future to include consideration of cumulative health risks associated with pesticide formulations, mixtures of pesticides with disparate mechanisms but similar toxic effects, as well as mixtures of pesticides with other chemicals that share common toxic effects and/or mechanisms of toxicity. It was also suggested that future methods should consider synergistic effects of pesticide mixtures, regardless of their mechanisms of toxicity and individual toxic effects, as well as alternate modes of action for individual pesticides.

PMRA Response:

The PMRA’s current focus remains the prompt completion and implementation of the SPN2018-02, which includes currently recognized and widely adopted methods. The PMRA acknowledges that methodology in this subject area will continue to evolve, and will continue to update cumulative health risk assessment methods accordingly. With regards to the suggestion that future methods should consider alternate modes of action for individual pesticides, it should be noted that this point is already addressed in the current framework. The SPN2018-02 indicates that pesticides may be placed in more than one group in instances where pesticides cause more than one common toxic effect.

Specific Comments**Comments on Section 2 - Introduction****16. Comment related to use of the wording “increased health risk”**

One commenter asked for clarification of the term “increased health risk” in the statement “Cumulative assessment is undertaken to explore the possibility that low level exposures to specific multiple chemicals could lead to the same or increased health risk relative to a higher level of exposure to any of these chemicals individually.”

PMRA Response:

The PMRA has modified the statement to clarify its meaning. The sentence now reads “Cumulative assessment is undertaken to explore the possibility of whether low-level exposures to multiple pesticides that cause a common toxic effect by a common mechanism, could lead to the same adverse health effect as would a higher level of exposure to any of the pesticides individually”.

Comments on Section 3 - Cumulative Risk Assessment Methods**17. Comment related to selection of the appropriate cumulative health risk assessment method**

One commenter requested that the PMRA provide clarification regarding how the method of assessment would be selected for a given cumulative health risk assessment. This commenter suggested that the problem formulation methods outlined in Solomon et al (2016)⁷ could be used to inform method selection.

PMRA Response:

The cited reference (Solomon et al, 2016)⁸ focusses on the subject of problem formulation, rather than on method selection for cumulative risk assessments. Problem formulation has now been incorporated into the PMRA’s process map for cumulative health assessment (see Appendix III). The choice of method for cumulative health risk assessment will be influenced primarily by the context of the assessment (for example, whether the assessment involves single or multiple exposure pathways), the quality and extent of the available data, and the level of refinement required in the assessment.

18. Comment related to maximum cumulative ratio approaches

One commenter requested that the PMRA consider the papers of Price et al (2011⁹, 2012¹⁰ and 2014¹¹) which discuss the maximum cumulative ratio (MCR) approach and its applicability to cumulative health assessment.

⁷ Solomon KR, Wilks MF, Bachman A, Boobis A, Moretto A, Pastoor TP, Phillips R, Embry MR. (2016). Problem formulation for risk assessment of combined exposures to chemicals and other stressors in humans. *Crit Rev Toxicol* 46(10): 835-844.

⁸ Ibid.

⁹ Price PS and Han X. (2011). Maximum Cumulative Ratio (MCR) as a Tool for Assessing the Value of Performing a Cumulative Risk Assessment. *Int. J. Environ. Res. Public Health* 8:2212-2225.

¹⁰ Price P, Dhein E, Hamer M, Han X, Heneweer M, Junghans M, Kunz P, Magyar C, Penning H and Rodriguez C. (2012). A decision tree for assessing effects from exposures to multiple substances. *Environmental Sciences Europe* 24:26.

PMRA Response

The MCR is the ratio of the hazard index of a group of chemicals (that is, the sum of the hazard quotients of each chemical in that group) to the maximum hazard quotient within that group, where the hazard index is used to normalize exposures across chemicals. The PMRA concurs that this approach provides an additional tool that can be used in the tiers of assessment to identify pesticides that may drive the risk assessment and for which refinements may be of greater importance. As the MCR is hazard-focussed, it is less useful for identifying exposure scenarios that influence the risk assessment. Additional text has been included in the SPN2018-02 referencing this method.

Comments on Section 4 – Selection Considerations for Common Mechanism Groups

19. Comments related to preliminary grouping

One commenter recommended a tiered approach to preliminary grouping. The commenter suggested that grouping should not be based on only one of the listed criteria, particularly not structural similarity. They further stated that common mechanism of toxic effect and co-exposure are the most important determinants in grouping, and should be prerequisites for conducting cumulative health risk assessments.

Another commenter suggested the following addition (in underline) “The PMRA does not regard the preliminary grouping alone to be sufficient to reliably conclude that such chemicals have a common mechanism of toxicity.”

PMRA Response:

A tiered approach is already outlined in the framework in that a cumulative assessment group identified during preliminary grouping undergoes further analysis at the refined grouping step to determine whether there is sufficient support for a common mechanism group. Notwithstanding this iterative approach, structural similarity is a useful criterion for screening at the preliminary grouping step, given the potential for common toxophores. As outlined in Appendix III, stakeholders will have an opportunity to provide additional information during the process regarding the proposed common mechanism groups.

¹¹ Price P, Zaleski R, Hollnagel H, Ketelslegers H and Han X. (2014). Assessing the safety of co-exposure to food packaging migrants in food and water using the maximum cumulative ratio and an established decision tree. *Food Additives & Contaminants, Part A*, 31(3):414-421.

The PMRA concurs that common mechanism of toxic effect and co-exposure are important determinants in grouping. For this reason, complex cumulative health assessments will incorporate a scoping step to elaborate on these elements prior to undertaking a full review.

Regarding the suggested text modification, the intent of the original sentence was to indicate that it was necessary to further consider a preliminary grouping, as per Section 4.2. Refined Grouping, prior to making a common mechanism determination. The insertion of the suggested text would alter the meaning of the sentence, such that it would imply that a preliminary group could never be considered sufficient to conclude that such pesticides have a common mechanism of toxicity. The PMRA has not made this modification, as it is plausible that a preliminary group could be confirmed at the refined grouping stage for a common mechanism finding. The text has been modified in the SPN2018-02 to clarify the intent.

20. Comments related to use of the precautionary approach in grouping

One set of comments recommended adoption of a precautionary approach to grouping. It was suggested that the PMRA should proceed with the cumulative health risk assessment if there is uncertainty regarding the mechanism of toxicity with the onus on the registrant to disprove hypotheses on common mechanisms.

PMRA Response:

The PMRA is exploring options to solicit information on mechanisms of action from the registrant earlier in the evaluation and re-evaluation process of individual pesticides. For complex assessments, the preliminary evidence on common toxicity and co-exposure is identified during the scoping step and a problem formulation is created. This information will be published at the information gathering step at which point there will be a request for any additional information to inform the cumulative health risk assessment and address uncertainties. If it is decided at any point in the process that a cumulative health risk assessment is not required, this proposed decision will also be published to allow for consultation.

21. Comment related to basis for grouping pesticides

One commenter recommended that grouping pesticides for cumulative health risk assessments should be based on findings on a ‘tissue level’ rather than being defined at the level of a particular biochemical reaction.

PMRA Response:

The PMRA acknowledges that there is interest in considering common findings on a tissue level when grouping pesticides for cumulative health risk assessment. As outlined in the SPN2018-02, information regarding similar toxic effects is considered during the preliminary grouping step to assess whether further investigation is warranted at the refined grouping step.

22. Comment related to grouping pesticides that have more than one mechanism of toxicity

One commenter asked the PMRA to clarify how pesticides for which more than one mechanism of toxicity has been identified would be handled under the cumulative health risk assessment framework.

PMRA Response:

The PMRA recognizes that some pesticides may exert toxic effects via more than one mechanism of action. If this is the case, and the identified mechanisms of action are shared by one or more other pesticides, then the pesticide will be included in each applicable cumulative health risk assessment, as outlined in the SPN2018-02.

23. Comment related to the types of health effects that would be considered relevant for cumulative health risk assessments, and the methods used to conduct literature-based health assessments

One commenter asked whether the cumulative health risk assessment framework will be applicable to adverse health outcomes such as endocrine disruption, neurodevelopmental effects and cancer. The commenter recommended that a weight-of-evidence approach that considers epidemiologic data, in addition to in vivo animal studies, in vitro genotoxicity assays, and mechanistic studies be used to assess the potential for such health effects, and to elucidate their mechanisms of action. It was further recommended that systematic review methods and reporting, such as described by Rooney et al (2014),¹² be used in such weight-of-evidence approaches to ensure transparency, rigour and confidence.

PMRA Response:

The cumulative health risk assessment framework is applicable to any toxicity endpoints that are the result of a common mechanism of toxicity, except those that are non-specific in origin or those that could have many possible unrelated causes. The PMRA currently considers, and

¹² Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. (2014). Systematic review and evidence integration for literature-based environmental health science assessments. *Environ Health Perspect* 122 (7): 711-18.

utilizes as appropriate, all of the types of data suggested by the commenter in a weight-of-evidence approach when evaluating health effects associated with individual pesticides, and will continue to use this approach in the context of cumulative health risk assessments, as further described in the SPN2018-02.

The PMRA acknowledges the benefits and sound principles of the systematic review methods described in the cited reference (Rooney et al, 2014). In general, the principles will be followed to the extent possible for cumulative health risk assessments, using a ‘fit for purpose’ approach. Some of the principles, although not formally documented, are routinely taken into consideration during the PMRA’s health assessment of individual pesticides, including many of the factors described for determining the level of confidence in the available data.

Comments on Section 5 – Cumulative Risk Assessment Framework

24. Comment related to providing more detail on types of data or models used to estimate exposure at each tier and how the proposed models will accommodate new active ingredients

Commenters requested that the PMRA provide more detail on the types of data or models used to estimate exposure at each tier and include a discussion on the use of the Residential Joint Venture (REJV) homeowner survey data. There was also a concern expressed regarding the ability to refine exposure estimates for new active ingredients due to the lack of information on use patterns and market share.

PMRA Response:

The typical data and assumptions used to conduct risk assessments for individual pesticides will, to a large extent, also be used to determine exposure estimates for cumulative health risk assessments. This approach will apply to cumulative health assessments for new active ingredients, as well as those assessed through the re-evaluation process. Exposure information generally will be derived from the submitted regulatory data package and assessed in accordance with SPN2014-01 General Exposure Factor Inputs for Dietary, Occupational and Residential Exposure Assessments. These data include registrant field trial data, drinking water residue estimates derived from modelling, demographic and food intake data from the National Health and Nutrition Examination Survey (NHANES), and generic exposure algorithms from the USEPA Residential Standard Operating Procedures.

The derivation of exposure estimates can progress from the use of deterministic methods at lower tiers, to more complex probabilistic assessments at higher tiers. This has been described more fully in the SPN2018-02. Notwithstanding the lack of information regarding the extent of use and market share data on new pesticides, much of the data cited in the SPN2018-02 are used as generic and/or surrogate data to refine risk assessments for all pesticides.

25. Comments related to how the proposed models would accommodate multi-route exposure scenarios

Commenters suggested that clear examples of multi-route exposure analyses with recommendations be provided and also noted the USEPA's Aggregate Risk Index (ARI) as an additional method that can be used when uncertainty factors differ by route.

PMRA Response:

As described in the SPN2018-02, exposures may originate from a single route (for example, oral exposure from a dietary pathway) or multiple routes (oral, dermal and inhalation), all of which may vary over time and space. Determination of the combination of exposures and routes is an important step for cumulative health risk assessments. Identification of use patterns of active ingredients is required to develop exposure scenarios for assessment (including route, duration, and frequency of exposure), data collection, or modelling strategies. The problem formulation will address questions regarding the route, duration, and frequency of exposure to the exposed target populations being considered and the probability of co-occurrence of exposures within a relevant timeframe. If information is not available to make this determination, it will be requested by the PMRA during the information gathering stage. When combining the different routes of exposure for multiple pesticides, methods similar to those used for combining multi-route exposures for individual pesticide risk assessments will be employed. These methods include the combined MOE and the ARI approaches, depending on the toxicological profile of the group of pesticides. The ARI method has been added to the SPN2018-02.

26. Comments related to the need for access to exposure monitoring data

Some commenters want to ensure that Canadian monitoring programs have capacity and funding to collect information, strengthen reporting, and co-ordinate programs to meet the needs of the PMRA.

PMRA Response:

The PMRA is engaged with partners to generate and collect information relevant to pesticide exposures. This includes monitoring and surveillance activities conducted under the CMP, such as the Canadian Health Measure Survey (CHMS), food residue monitoring conducted by the

CFIA under the National Chemical Residue Monitoring Program, demographic instruments such as the Canadian Community Health Surveys, and water quality monitoring data collected by Federal, Provincial and Territorial partners. The PMRA supports these publicly funded monitoring and surveillance activities, and is active in providing recommendations on the selection of monitored parameters. However, the funding and capacity-building aspects are broader than the PMRA's role, and fall more within the scope of Government of Canada initiatives such as the CMP. Where appropriate, the PMRA may also rely on data from international programs such as the United States Department of Agriculture's Pesticide Data Program (USDA PDP) for residues on foods imported into Canada, and the Centers for Disease Control and Prevention's NHANES for food intake estimates.

Monitoring and surveillance programs can provide data critical for the refinement of exposure estimates, however, pesticide registrants have the responsibility to provide the toxicology and exposure data required to support their registered products. The PMRA will use the most reliable and relevant available data to inform cumulative health assessments, which is consistent with the approach currently used for individual pesticide risk assessments. That is, the data sources will include both publicly generated information, as well as registrant-supplied data.

27. Comment related to criteria for identifying co-exposures

Several commenters asked for clarification of how, and at which point in the process, co-exposures will be identified. Another commenter requested that the "critical time window" be defined and the approach to assessing cumulative chronic exposure be clarified.

PMRA Response:

Exposure scenarios and the likelihood of co-exposure, along with the common toxicity determination, will be considered by the PMRA at the beginning of the cumulative health assessment process. At the earliest stages of the cumulative health assessment, it will be determined whether there is dietary or residential exposure, or whether exposure is limited to occupational scenarios. This initial analysis will determine if the cumulative health risk assessment is required and if so, whether it can be addressed within the individual pesticide documentation. For those groups that are addressed within the individual pesticide documentation, co-exposures are assessed concurrently with the review of exposure information supporting the individual pesticide. For groups for which the assessments are anticipated to be more complex, co-exposures will be identified, along with a common toxicity determination, at a scoping and problem formulation step. This step also represents a decision point at which there is a determination of whether a cumulative health risk assessment is required.

Timing of exposures to multiple pesticides sharing a common mechanism of toxicity is a major determinant of risks in cumulative health assessment. Co-exposures will be identified on the basis of the data that demonstrate temporality of exposure. The routes, pathways, amounts, frequency and intensity of exposure are all factors that must be considered in determining the likelihood of co-exposure. Relevant co-exposures target the same population within the same timeframe. The exposure period should be concordant with the exposure duration for which adverse effects are observed in animal toxicity studies. Toxicokinetic and toxicodynamic data can inform whether consecutive, separate or partially-overlapping exposures need to be considered in a cumulative health assessment. The critical time window will be based on actual or anticipated conditions of use and will be included in the problem formulation, if the information is available to make that determination. Otherwise, information will be requested to determine the critical time window during the information gathering step.

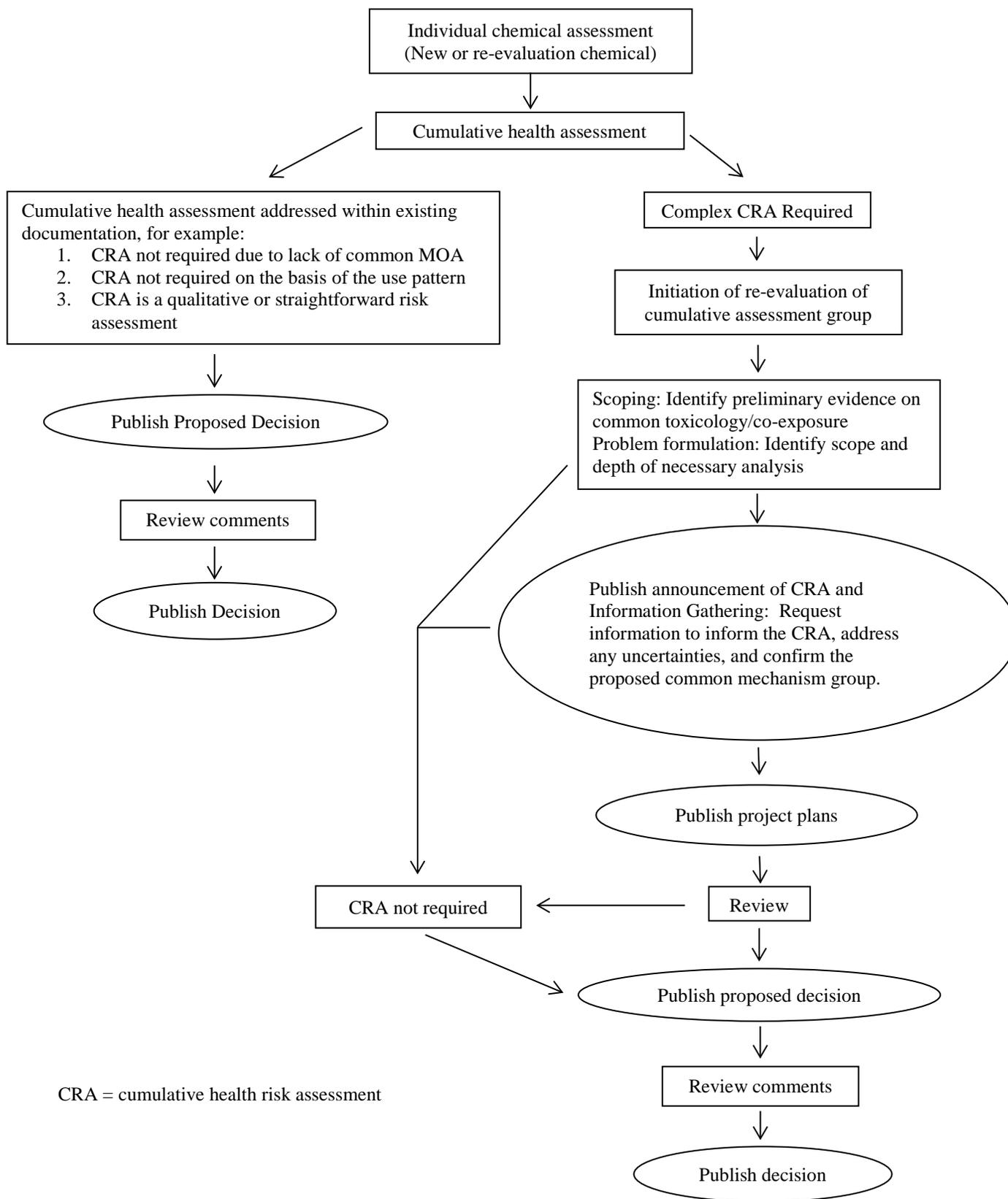
28. Comment related to overly conservative risk assessments

One commenter recommended not summing exposures from too many separate scenarios for the screening-level residential exposure analysis. They indicated that the cumulative health risk assessment should not assume that multiple active ingredients with the same mode of action are concurrently applied to the same sites in the same temporal period.

PMRA Response:

The focus of the cumulative health risk assessments will be on exposures that are likely to co-occur, rather than those that may possibly co-occur. Information on product use and co-use profiles is essential for determining a realistic scenario of combined exposure for a given population and avoiding overestimation of exposure. Principles for inclusion or exclusion of exposure scenarios, similar to those used in aggregate risk assessments (SPN2003-04), will be applied to the cumulative health risk assessments. As the PMRA will be consulting on the outcomes of cumulative health assessments, stakeholders will have the opportunity to provide further comments on the likelihood of any given co-exposures.

Appendix III Process Map for Cumulative Health Assessment



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Glossary

Adverse Outcome Pathway: A linear representation of key events between a molecular initiating event and an adverse outcome

Analog(s): A generic term used to describe chemicals that are chemically closely related. Structural analogs are chemicals that have similar or nearly identical molecular structures. Structural analogs may or may not have similar or identical biological properties.

Common Mechanism Group: Pertains to two or more chemicals that cause a common toxic effect to human health by the same, or essentially the same, sequence of major biochemical events. Hence, the underlying basis of the toxicity is the same, or essentially the same, for each chemical.

Common Toxic Effect: Two or more chemicals that are known to cause the same toxic effect (that is, concordant in the nature of the effect) in or at the same anatomical or physiological site or location (for example, same organ or tissue).

Composite Assessment Factor: The product of the uncertainty factors and the PCPA factor; used to establish reference values for use in dietary, aggregate and cumulative risk assessments.

Cumulative Assessment Group: Two or more chemicals grouped together for the purpose of conducting a cumulative health assessment.

Cumulative Toxic Effect: The net change in magnitude of a common toxic effect resulting from the exposure to two or more chemicals acting by a common mechanism, relative to the magnitude of the common toxic effect caused by exposure to any of the chemicals individually.

Hazard Index: The sum of the individual hazard quotients of individual chemicals in a cumulative assessment group

Hazard Quotient: The ratio of an individual chemical's exposure to its reference value.

Lower Confidence Limit on a Benchmark Dose: The lower confidence limit on a benchmark dose. The benchmark dose is the dose or concentration that corresponds with a specified level of response. Both the benchmark dose and its lower limit are derived through statistical modelling of dose-response data.

Lowest Observed Adverse Effect Level: The lowest level of exposure in an organism that causes an adverse alteration of morphology, function, capacity, growth, development or lifespan.

Maximum Cumulative Ratio: The ratio of the hazard index of a group of chemicals (that is, the sum of the hazard quotients of each chemical in that group) to the maximum hazard quotient within that group, where the hazard index is used to normalize exposures across chemicals.

Margin of Exposure: The ratio of a chemical's point of departure to its predicted or estimated exposure.

Mechanism of Toxicity or Action: The molecular sequence of events that produces a specific biological outcome.

Mode of Action: A plausible hypothesis about measurable key events by which a chemical exerts its biological effects. It does not imply full understanding of mechanism of action at the molecular level. In the context of this document, mode of action refers to the key cytological and biochemical events by which a pesticide is toxic to humans or experimental animals, and not the mode of action by which it is toxic to target or intended species (that is, its pesticidal action).

No Observed Adverse Effect Level: A level of exposure in an organism at which there is no biologically or statistically significant increase in the frequency or severity of an adverse effect.

Point of Departure: A dosage or concentration of a single chemical used in regulatory toxicology for estimating tolerable exposures to humans. The point of departure is typically based on a NOAEL, No observed Adverse Effect Concentration (NOAEC) or benchmark dose.

Reference Value: The reference value is the point of departure, (that is, the NOAEL, LOAEL, or BMDL), divided by the composite assessment factor (that is, the product of the uncertainty factors and the PCPA factor).

Relative Potency Factor: The ratio of the toxic potency of a given chemical to that of an index chemical in a cumulative assessment group.

Site of Toxic Action: The anatomical or physiological site(s) or location(s) at which the interaction of the chemical with its biological targets occurs that leads to a toxic effect.

Site of a Toxic Effect: The specific anatomical or physiological site or location (e.g., organ or tissue) at which the effect occurs.

Target Margin of Exposure: The product of the uncertainty factors and the PCPA factor; used in occupational, residential, aggregate and cumulative risk assessments.

Toxic Action: The interaction of a given chemical with biological targets that leads to a toxic effect.

Toxic Effect: An effect known (or can reasonably be expected) to occur from exposure to a chemical and that will or can reasonably be expected to endanger or adversely affect the quality of life. Some examples of toxic effects are acute lethality, loss of hearing, renal tubule necrosis, and cardiomyopathy.

Toxophore: A structural feature or moiety of a chemical that bestows the toxic property through interaction with a molecular site (e.g., receptor) in cells of tissue or organs. The resulting biochemical changes or alterations lead to the disruption of physiological processes performed by the tissue or organs and, ultimately, to the toxic effect. The toxophoric portion of a chemical may interact reversibly or irreversibly with its molecular site, depending upon its reactivity and the molecular site. For some chemicals, toxicity results from the metabolism of a structural substituent to a toxophore. Metabolic pathways that lead to toxicity are often called bioactivation pathways.

Weight-of-Evidence: A qualitative evaluation that takes into account the nature and quality of scientific information regarding a chemical for a specific purpose. A weight-of-evidence evaluation can involve a detailed analysis of several data elements, such as data from different toxicity tests, pharmacokinetic data, and chemistry data, followed by a conclusion in which a hypothesis is developed or selected from previous hypotheses.

List of Abbreviations

ARI: Aggregate Risk Index

BMDL: Lower Confidence Limit on a Benchmark Dose

CAG: Cumulative Assessment Group

CARES NG: Cumulative and Aggregate Risk Evaluation System Next Generation

CFIA: Canadian Food Inspection Agency

CHMS: Canadian Health Measure Survey

CMG: Common Mechanism Group

CMP: Chemical Management Program

CPMA: Canadian Pest Management Association

EC: European Commission

ED: Effective Dose

EFSA: European Food Safety Authority

HI: Hazard Index

HQ: Hazard Quotient

LOAEL: Lowest Observed Adverse Effect Level

MCR: Maximum Cumulative Ratio

MOA: Mode of Action

MOE: Margin of Exposure

MRL: Maximum Residue Limit

NAFTA: North American Free Trade Agreement

NOAEC: No Observed Adverse Effect Concentration

NOAEL: No Observed Adverse Effect Level

NHANES: National Health and Nutrition Examination Survey

OECD: Organization for Economic Development

PCPA: Pest Control Products Act

PMRA: Pest Management Regulatory Agency

POD: Point of Departure

PRD: Proposed Registration Decision

PRO: Regulatory Proposal

PRVD: Proposed Re-evaluation Decision

REJV: Residential Join Venture

RPF: Relative Potency Factor

SHEDS: Stochastic Human Exposure and Dose Simulation

SPN: Science Policy Note

UF: Uncertainty Factor

USEPA: United States Environmental Protection Agency

WHO/IPCS: World Health Organization/International Program on Chemical Safety

WOE: Weight of Evidence

USDA PDP: United States Department of Agriculture's Pesticide Data Program

This is **Exhibit “Q”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy

The purpose of this Directive is to inform registrants, user groups, and other stakeholders about the Pest Management Regulatory Agency's strategy for the implementation of the Federal Government's Toxic Substances Management Policy (TSMP) for products regulated under the *Pest Control Products Act*.

In June 1995, the federal government released the TSMP - a policy developed to provide direction on the management of toxic substances and other substances of concern that are released into the environment. The policy applies to all substances that are subject to federal regulation. Although the impetus for the TSMP was to provide a means for managing substances that are not well regulated, the principles of the TSMP are relevant to chemicals that are used as pest control products.

The enclosed strategy was distributed as Regulatory Proposal Pro98-03 in November 1998, for information and comment. Many of the comments have been incorporated.

(publié aussi en français)

March 12, 1999

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Introduction

The Pest Management Regulatory Agency (PMRA) was established within Health Canada on April 1, 1995, by amalgamating the resources from the federal departments that were formerly involved in pesticide regulation: Agriculture, Health, Environment and Natural Resources. The mandate of the PMRA is to protect human health, safety and the environment by minimizing the risks associated with pesticides, while enabling access to pest management tools, namely, pest control products and sustainable pest management strategies. The PMRA uses a risk-management approach for the regulation of pest control products, consistent with the manner in which Health Canada undertakes regulatory activities for other products in the area of chemicals management.

The Toxic Substances Management Policy

The Toxic Substances Management Policy¹ is a federal government policy developed to provide direction on the management of substances that have been found to be toxic and other substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that are CEPA-toxic² or equivalent, predominantly anthropogenic, persistent and bio-accumulative) and full life cycle management to prevent or minimize releases of Track 2 substances (those that do not meet all of the four Track 1 criteria).

This policy applies to all substances that are subject to federal regulation, including those used as pest control products. The TSMP and the *Pest Control Products Act* (PCPA) have the same fundamental purpose: to protect human health and the environment. The PCPA is administered by the PMRA within Health Canada. The protection of human health and the environment is of primary importance in the regulation of pest control products in Canada.

Substances Regulated Under the *Pest Control Products Act*

Any substance that claims to have a pest control use is regulated under the PCPA. There are substances that have both pesticide and non-pesticide uses. Only the pesticide uses are regulated under the PCPA. Other substances that are contained in pest control products, e.g., formulants, adjuvants and contaminants, are also regulated as part of the pest control product under the PCPA.

Pest control products differ from many other substances that enter the environment, in that they are not by-products of another process but are intentionally released for a specific purpose.

¹ Appendix I provides a general description of the TSMP and its objectives.

² As defined under the *Canadian Environmental Protection Act*, and described in Appendix I

The biological activity of most pest control products is what makes them valuable to Canadian society, while at the same time, it means the release of these products must be closely controlled. For this reason, the PCPA and policies affecting pest control products recognize and consider the environmental and human health risks as well as the value of the product.

PMRA Implementation of the Principles of the TSMP

Through detailed pre-market assessment and post-registration monitoring activities, pest control products have for many years been closely regulated. Many of the principles found in the TSMP are similar to those established for pest control products. The consolidation of pesticide regulatory activities within the PMRA (April 1995) and the planned revision of the PCPA are strengthening the life cycle management of pest control products in Canada. In accordance with the mandate given to the PMRA, the Agency is fostering sustainability in the context of pest management. The PMRA facilitates access to alternative products and coordinates development of long-term sustainable pest management strategies in a variety of user sectors, and thus provides a further catalyst for achieving the objectives of the TSMP.

Before making a registration decision regarding a new pest control product, the PMRA conducts a comprehensive assessment of the risk and value specific to the proposed use. The value assessment considers whether the use of the product contributes to pest management, and if the application rates are the lowest they can be to effectively control the target pest. The risk assessment considers the inherent toxicity, persistence and bioaccumulative nature of the pest control product. It addresses human health and environmental concerns and, for each of these, considers the possible hazards associated with the product as well as the degree to which humans and the non-target environment may be exposed. Exposure estimates are a key component of the risk assessment process. As pest control products are deliberately introduced into the environment at quantifiable rates, potential short-term impacts of environmental exposures can be closely estimated. For long-term environmental exposure, the PMRA relies on persistence and bioaccumulation data as qualitative indicators as well as on any monitoring data that may be available. With the introduction of the TSMP, increased emphasis will be placed on assessing the long-term risks associated with the release of substances into the environment. Through this process and the criteria established in the TSMP, the PMRA determines whether active ingredients in new pest control products are likely to be considered candidates for Track 1 or Track 2 classification. Consistent with the TSMP, where a Track 1 substance results from the degradation or transformation of a parent substance in the environment, the parent substance may also be considered for Track 1 by the PMRA.

Pest control products will only be registered if the data requirements for assessing value and safety have been adequately addressed, evaluation indicates that the product has merit and value, and the human health and environmental risks associated with the proposed use are acceptable.

For registered products, ongoing surveillance, advances in analytical methods and improved evaluation processes already provide the means to uncover environmental or health concerns, particularly with older products. In implementing the TSMP, the PMRA will systematically screen registered products using the TSMP criteria for persistence and bioaccumulation to identify those that contain active ingredients that are candidates for Track 1. The results of this screening process will then be taken into consideration along with the surveillance data, in the setting of priorities for re-evaluation or special review by the PMRA. Once this assessment is complete, and Track 1 or 2 classification is assigned, the next step will be to work in consultation with stakeholders to develop appropriate management strategies in accordance with the long-term goal of virtual elimination or that of life cycle management, as appropriate.

The PMRA manages the risks associated with the use of pest control products through several means, including: setting conditions of registration, monitoring compliance with these conditions, and label improvement programs to support best management practices, including integrated pest management (IPM) strategies. Non-compliance with conditions of registration is a violation of the PCPA and may lead to suspension, cancellation, use restriction or phase out of pest control products. These management practices of the PMRA reflect the principles of the TSMP and meet the TSMP requirements for Track 2 substances. For Track 1 substances, these same management tools allow the PMRA to work towards the goal of virtual elimination. Outlined below are several examples of how these tools will be applied in managing Track 1 substances.

Identifying Track 1 Substances in Pest Control Products

Track 1 substances in pest control products may be identified in three ways, namely, by:

- comparing active ingredients, formulants and contaminants against the federal government's list of Track 1 substances (Appendix II);
- evaluating new active ingredients against the TSMP criteria for Track 1 designation; or
- evaluating currently registered active ingredients to identify those, if any, that meet the TSMP criteria for Track 1 designation.

As other Track 1 substances are officially identified by the federal government, the list of substances in Appendix II will be amended, and the additional substances will be included in the PMRA's TSMP activities.

Managing New Pest Control Products Containing Track 1 Substances

i) Active Ingredients and Formulants (non-active ingredients)

The risks associated with a pest control product containing an active ingredient or a formulant, that is a Track 1 substance, would generally be considered unacceptable, and such products would not be registered.

A product containing a Track 1 substance as an active ingredient or formulant may be registered only:

- in exceptional circumstances, e.g., emergency³ or critical need⁴ situations, and with the imposition of conditions of registration designed to minimize the risks associated with its use; or
- where significant risk reduction can be achieved, e.g., a product offering a significant reduction of health or environmental risks over those posed by an existing product registered for the same use.

In these situations, new pest control products containing a Track 1 substance as an active ingredient or formulant may be registered on a temporary basis, for one year. Registration would only be permitted provided that the conditions of registration can be designed to ensure that risks would be acceptable.

The conditions of registration may include a requirement to provide specific information, including environmental monitoring data. Consistent with the goal of virtual elimination of Track 1 substances, any request for continued registration of the product would be reviewed in light of the required information as well as any new information concerning health and environmental risks, and the continuing existence of exceptional circumstances.

³ Under provisions of Section 17(1) of the PCP Regulations, the Minister may register a product for a period not exceeding one year for the emergency control of pest infestations that are seriously detrimental to public health, domestic animals, natural resources or other things (cf. Regulatory Directive Dir94-05, *Registration of Pesticides for Emergency Use*, March 3, 1994).

⁴ A product is deemed to be critically needed if it is to control a new pest problem or one for which registered products are no longer effective or acceptable in international markets, and the inability to manage the pest problem effectively would lead to severe economic hardship to the potential user. Consideration is also given to registration of additional products in situations where the availability of more than one product is required to manage the pest problem or the development of pest resistance.

ii) *Microcontaminants*

New pest control products containing a Track 1 substance as a microcontaminant may be registered:

- in exceptional circumstances, e.g., emergency or critical need situations, and with the imposition of conditions of registration designed to minimize the risks associated with its use;
- where significant risk reduction can be achieved, e.g., a product offers a significant reduction of health or environmental risks over those posed by an existing product registered for the same use, or a product replaces an existing product with a higher level of the same microcontaminant, resulting in a lower overall release of the substance; or
- where the Track 1 substance has been virtually eliminated. Conditions of registration will require that:
 - < the level of microcontaminant in the product is very low⁵;
 - < the registrant demonstrates that the level of microcontaminant in the product is as low as can be achieved by the application of the best available technology from a manufacturing perspective; and
 - < the use of the product in accordance with its proposed label is not expected to present unacceptable risks.

Provision to the PMRA of routine microcontaminant Quality Control data and environmental monitoring data may also be required. In all cases, conditions of registration would be imposed that are specific to the use scenario and are designed to ensure that risks are acceptable.

The registration validity period specified would not exceed five years. Consistent with the goal of virtual elimination of Track 1 substances, registration of the product would be reviewed as a condition of renewal in light of environmental-monitoring data, available alternatives and any new information concerning health and environmental risks

⁵ Limits of quantification (LOQs) may be used as guidance for this purpose.

Managing Track 1 Substances Contained in Currently Registered Pest Control Products

The TSMP recognizes that social, economic and technical considerations must be taken into account in any management decision. Virtual elimination of Track 1 substances is a long-term goal to be implemented through a common sense approach.

In working towards the goal of virtual elimination, actions that may be taken include:

i) Track 1 Active Ingredients

- A systematic screening of registered active ingredients using the TSMP criteria for persistence and bioaccumulation to identify those that contain substances that are candidates for Track 1.
- Use of the TSMP criteria for persistence and bioaccumulation in the setting of priorities for re-evaluation or special review under the PCPA.
- Strengthen partnerships with industry, researchers, provinces and users to achieve reduction in use and replacement of actives of concern.

Note: Additional registrations would only be permitted in specific situations and provided conditions of registration can be designed to ensure that risks would be acceptable. For example, exceptional circumstances such as emergency or critical need situations, or where the products replaces an existing product for which it is a toxicologically or environmentally preferable alternative, or where the market is shared by products of similar chemistry and the total amount of the Track 1 substance entering the environment from pesticidal sources will not increase.

ii) Track 1 Formulants (non-active ingredients)

- In cooperation with registrants, strengthen the existing program to replace/reduce/eliminate formulants of concern, including Track 1 substances.

Note: Additional registrations would only be permitted in specific situations and provided conditions of registration can be designed to ensure that risks would be acceptable. For example, exceptional circumstances such as emergency or critical need situations, or where the products replaces an existing product for which it is a toxicologically or environmentally preferable alternative, or where the market is shared by products of similar chemistry and the total amount of

the Track 1 substance entering the environment from pesticidal sources will not increase.

iii) Track 1 Microcontaminants

- Review current levels of microcontaminants in pest control products for their continued acceptability.
- Work in partnership with registrants to reduce/eliminate microcontaminants of concern in line with the best available technology from a manufacturing perspective and encourage the development of new technology.
- If the level of the microcontaminant remains unacceptable, work in partnership with registrants and other stakeholders to develop alternative products and/or pest control strategies to prevent or minimize releases, with the ultimate goal of virtual elimination.

Note: Provided conditions of registration can be designed to ensure that risks would be acceptable, additional registrations may be permitted.

The TSMP and Canada's International Position

International Trade

The ability of Canadian services and products to compete for domestic and international markets is critical to the Canadian economy. Pest control products often play a vital role in ensuring the high quality and acceptability of Canadian goods. The PMRA includes socio-economic and technical considerations in formulating regulatory decisions that are consistent with the responsibility to protect human health and safety and the environment. The PMRA is committed to a system of open communication and transparency, and will strive for a cooperative approach to move towards the goal of virtual elimination of Track 1 substances.

Environmental Initiatives

Canada will continue to actively participate in international fora, such as the risk reduction initiatives under the United Nations, North American Free Trade Agreement, and the Organisation for Economic Co-operation and Development Pesticide Programme. These activities address health and environmental problems associated with pesticide use as well as concerns about risks to users and the general public.

The long-range transport of persistent organic pollutants (POPs) is a high priority issue for the Government of Canada, particularly the Ministers of Health and Indian and Northern Affairs. The TSMP is critical to Canada's position in discussions and negotiations with the world community on managing toxic substances. The clarification of how the TSMP will be implemented by the PMRA will facilitate the development of consistent national positions and provide increased opportunities to influence approaches taken in international fora, and indeed, in other countries.

APPENDIX I *Canadian Environmental Protection Act* and Toxic Substances Management Policy (TSMP)

The *Canadian Environmental Protection Act* (CEPA), administered jointly by the Ministers of Health and Environment, provides a federal regulatory role in the management of toxic substances. CEPA was developed to ensure coverage of substances not captured under other federal legislation. Section 11 of CEPA defines “toxic” as follows:

For the purposes of this Part, a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions

- a) *having or that may have an immediate or long-term harmful effect on the environment;*
- b) *constituting or that may constitute a danger to the environment on which human life depends; or*
- c) *constituting or that may constitute a danger in Canada to human life or health.*

For a substance to be classified as toxic under CEPA there must be a possibility: that the substance will enter the environment; that living organisms will be exposed to the substance; and that a harmful effect will result from that exposure. The TSMP relies on the CEPA definition of toxic. Under the TSMP, a substance is “toxic” if, after scientific assessment and based on decisions taken under federal programs, it either conforms or is equivalent to “toxic” as defined in CEPA.

The TSMP has two key management objectives:

1. **Virtual Elimination of Track 1 Substances:** The TSMP may identify a substance as Track 1 if it is CEPA-toxic or equivalent, persistent, bioaccumulative and primarily the result of human activity. If all four criteria are met, the substance will be deemed Track 1 and designated for virtual elimination. Socio-economic factors are not considered when setting the ultimate goal of virtual elimination; however, the TSMP does recognize that social, economic, and technical considerations must be taken into account in any management decision. Therefore, virtual elimination of *Track 1 substances* is a long-term goal to be implemented through a common sense approach.
2. **Life Cycle Management of Track 2 Substances:** A substance may be identified as Track 2 if it does not meet all of the four criteria. The ultimate objective for *Track 2 substances* is life cycle management to prevent or minimize release.

APPENDIX II List of currently identified Track 1 substances

Aldrin
Chlordane
Dieldrin
DDT
Endrin
Heptachlor
Hexachlorobenzene
Mirex
Toxaphene
Polychlorinated dibenzo-p-dioxins substituted in at least the 2,3,7,8 positions
Polychlorinated dibenzofurans substituted in at least the 2,3,7,8 positions
Polychlorinated Biphenyls

None of these Track 1 substances are registered as active ingredients under the PCPA.

This is **Exhibit “R”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

STOCKHOLM CONVENTION

ON PERSISTENT ORGANIC POLLUTANTS (POPS)

TEXT AND ANNEXES

REVISED IN 2019



STOCKHOLM CONVENTION

ON PERSISTENT ORGANIC POLLUTANTS (POPS)

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INTRODUCTION

The Stockholm Convention on Persistent Organic Pollutants was adopted at a Conference of Plenipotentiaries on 22 May 2001 in Stockholm, Sweden. The Convention entered into force on 17 May 2004.

Article 18 of the Convention requires the Conference of the Parties to adopt arbitration and conciliation procedures to govern the settlement of disputes between Parties to the Convention. At its first meeting, held from 2 to 6 May 2005 in Punta del Este, Uruguay, the Conference of the Parties adopted decision SC-1/2, by which it established such procedures. The procedures are set out in a new annex to the Convention, Annex G, Part I of which sets forth the arbitration procedure and Part II of which sets forth the conciliation procedure. Annex G entered into force on 31 October 2007, i.e. one year after the date of the communication of its adoption by the depositary for the Convention.

Amendments to Annexes A, B or C to the Convention enter into force one year from the date of communication of their adoption by the depositary, except for those Parties that submit either: a notification of non-acceptance in accordance with the provisions of paragraph 3 (b) of Article 22; or a declaration in accordance with paragraph 4 of Article 22 and paragraph 4 of Article 25 of the Convention.

This revised booklet reflects the amendments to the Annexes A, B and C to the Convention adopted at the fourth, fifth, sixth, seventh, eighth and ninth meetings of the Conference of the Parties.

The version of the Stockholm Convention contained in this booklet is for information purposes and does not substitute the original authentic texts of the Convention and amendments thereto as deposited with the Secretary-General in New York. Should you wish to access the authentic texts of the Convention, obtain a certified true copy of the Convention or, more generally, have access to amendments and modifications to the certified true copies, rectifications of authentic texts or any other relevant formalities circulated under the cover of depositary notifications (CNS), you are advised to visit the United Nations Treaty Section online (<https://treaties.un.org>) or kindly contact the Treaty Section for further assistance.

The Secretariat of the Stockholm Convention, September 2020.

STOCKHOLM CONVENTION ON PERSISTENT ORGANIC POLLUTANTS

The Parties to this Convention,

Recognizing that persistent organic pollutants possess toxic properties, resist degradation, bioaccumulate and are transported, through air, water and migratory species, across international boundaries and deposited far from their place of release, where they accumulate in terrestrial and aquatic ecosystems,

Aware of the health concerns, especially in developing countries, resulting from local exposure to persistent organic pollutants, in particular impacts upon women and, through them, upon future generations,

Acknowledging that the Arctic ecosystems and indigenous communities are particularly at risk because of the biomagnification of persistent organic pollutants and that contamination of their traditional foods is a public health issue,

Conscious of the need for global action on persistent organic pollutants,

Mindful of decision 19/13 C of 7 February 1997 of the Governing Council of the United Nations Environment Programme to initiate international action to protect human health and the environment through measures which will reduce and/or eliminate emissions and discharges of persistent organic pollutants,

Recalling the pertinent provisions of the relevant international environmental conventions, especially the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, and the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal including the regional agreements developed within the framework of its Article 11,

Recalling also the pertinent provisions of the Rio Declaration on Environment and Development and Agenda 21,

Acknowledging that precaution underlies the concerns of all the Parties and is embedded within this Convention,

Recognizing that this Convention and other international agreements in the field of trade and the environment are mutually supportive,

Reaffirming that States have, in accordance with the Charter of the United Nations and the principles of international law, the sovereign right to exploit their own resources pursuant to their own environmental and developmental policies, and the responsibility to ensure that activities within their jurisdiction or control do not cause damage to the environment of other States or of areas beyond the limits of national jurisdiction,

Taking into account the circumstances and particular requirements of developing countries, in particular the least developed among them, and countries with economies in transition, especially the need to strengthen their national capabilities for the management of chemicals, including through the transfer of technology, the provision of financial and technical assistance and the promotion of cooperation among the Parties,

Taking full account of the Programme of Action for the Sustainable Development of Small Island Developing States, adopted in Barbados on 6 May 1994,

Noting the respective capabilities of developed and developing countries, as well as the common but differentiated responsibilities of States as set forth in Principle 7 of the Rio Declaration on Environment and Development,

Recognizing the important contribution that the private sector and non-governmental organizations can make to achieving the reduction and/or elimination of emissions and discharges of persistent organic pollutants,

Underlining the importance of manufacturers of persistent organic pollutants taking responsibility for reducing adverse effects caused by their products and for providing information to users, Governments and the public on the hazardous properties of those chemicals,

Conscious of the need to take measures to prevent adverse effects caused by persistent organic pollutants at all stages of their life cycle,

Reaffirming Principle 16 of the Rio Declaration on Environment and Development which states that national authorities should endeavour to promote the internalization of environmental costs and the use of economic instruments, taking into account the approach that the polluter should, in principle, bear the cost of pollution, with due regard to the public interest and without distorting international trade and investment,

Encouraging Parties not having regulatory and assessment schemes for pesticides and industrial chemicals to develop such schemes,

Recognizing the importance of developing and using environmentally sound alternative processes and chemicals,

Determined to protect human health and the environment from the harmful impacts of persistent organic pollutants,

Have agreed as follows:

ARTICLE 1

Objective

Mindful of the precautionary approach as set forth in Principle 15 of the Rio Declaration on Environment and Development, the objective of this Convention is to protect human health and the environment from persistent organic pollutants.

ARTICLE 2

Definitions

For the purposes of this Convention:

- (a) “Party” means a State or regional economic integration organization that has consented to be bound by this Convention and for which the Convention is in force;
- (b) “Regional economic integration organization” means an organization constituted by sovereign States of a given region to which its member States have transferred competence in respect of matters governed by this Convention and which has been duly authorized, in accordance with its internal procedures, to sign, ratify, accept, approve or accede to this Convention;
- (c) “Parties present and voting” means Parties present and casting an affirmative or negative vote.

ARTICLE 3

Measures to reduce or eliminate releases from intentional production and use

1. Each Party shall:
 - (a) Prohibit and/or take the legal and administrative measures necessary to eliminate:
 - (i) Its production and use of the chemicals listed in Annex A subject to the provisions of that Annex; and
 - (ii) Its import and export of the chemicals listed in Annex A in accordance with the provisions of paragraph 2; and
 - (b) Restrict its production and use of the chemicals listed in Annex B in accordance with the provisions of that Annex.
2. Each Party shall take measures to ensure:
 - (a) That a chemical listed in Annex A or Annex B is imported only:
 - (i) For the purpose of environmentally sound disposal as set forth in paragraph 1 (d) of Article 6; or
 - (ii) For a use or purpose which is permitted for that Party under Annex A or Annex B;
 - (b) That a chemical listed in Annex A for which any production or use specific exemption is in effect or a chemical listed in Annex B for which any production or use specific exemption or acceptable purpose is in effect, taking into account any relevant provisions in existing international prior informed consent instruments, is exported only:
 - (i) For the purpose of environmentally sound disposal as set forth in paragraph 1 (d) of Article 6;
 - (ii) To a Party which is permitted to use that chemical under Annex A or Annex B; or

(iii) To a State not Party to this Convention which has provided an annual certification to the exporting Party. Such certification shall specify the intended use of the chemical and include a statement that, with respect to that chemical, the importing State is committed to:

- a. Protect human health and the environment by taking the necessary measures to minimize or prevent releases;
- b. Comply with the provisions of paragraph 1 of Article 6; and
- c. Comply, where appropriate, with the provisions of paragraph 2 of Part II of Annex B.

The certification shall also include any appropriate supporting documentation, such as legislation, regulatory instruments, or administrative or policy guidelines. The exporting Party shall transmit the certification to the Secretariat within sixty days of receipt.

(c) That a chemical listed in Annex A, for which production and use specific exemptions are no longer in effect for any Party, is not exported from it except for the purpose of environmentally sound disposal as set forth in paragraph 1 (d) of Article 6;

(d) For the purposes of this paragraph, the term “State not Party to this Convention” shall include, with respect to a particular chemical, a State or regional economic integration organization that has not agreed to be bound by the Convention with respect to that chemical.

3. Each Party that has one or more regulatory and assessment schemes for new pesticides or new industrial chemicals shall take measures to regulate with the aim of preventing the production and use of new pesticides or new industrial chemicals which, taking into consideration the criteria in paragraph 1 of Annex D, exhibit the characteristics of persistent organic pollutants.

4. Each Party that has one or more regulatory and assessment schemes for pesticides or industrial chemicals shall, where appropriate, take into consideration within these schemes the criteria in paragraph 1 of Annex D when conducting assessments of pesticides or industrial chemicals currently in use.

5. Except as otherwise provided in this Convention, paragraphs 1 and 2 shall not apply to quantities of a chemical to be used for laboratory-scale research or as a reference standard.

6. Any Party that has a specific exemption in accordance with Annex A or a specific exemption or an acceptable purpose in accordance with Annex B shall take appropriate measures to ensure that any production or use under such exemption or purpose is carried out in a manner that prevents or minimizes human exposure and release into the environment. For exempted uses or acceptable purposes that involve intentional release into the environment under conditions of normal use, such release shall be to the minimum extent necessary, taking into account any applicable standards and guidelines.

ARTICLE 4

Register of specific exemptions

1. A Register is hereby established for the purpose of identifying the Parties that have specific exemptions listed in Annex A or Annex B. It shall not identify Parties that make use of the provisions in Annex A or Annex B that may be exercised by all Parties. The Register shall be maintained by the Secretariat and shall be available to the public.

2. The Register shall include:

(a) A list of the types of specific exemptions reproduced from Annex A and Annex B;

(b) A list of the Parties that have a specific exemption listed under Annex A or Annex B; and

(c) A list of the expiry dates for each registered specific exemption.

3. Any State may, on becoming a Party, by means of a notification in writing to the Secretariat, register for one or more types of specific exemptions listed in Annex A or Annex B.

4. Unless an earlier date is indicated in the Register by a Party, or an extension is granted pursuant to paragraph 7, all registrations of specific exemptions shall

expire five years after the date of entry into force of this Convention with respect to a particular chemical.

5. At its first meeting, the Conference of the Parties shall decide upon its review process for the entries in the Register.

6. Prior to a review of an entry in the Register, the Party concerned shall submit a report to the Secretariat justifying its continuing need for registration of that exemption. The report shall be circulated by the Secretariat to all Parties. The review of a registration shall be carried out on the basis of all available information. Thereupon, the Conference of the Parties may make such recommendations to the Party concerned as it deems appropriate.

7. The Conference of the Parties may, upon request from the Party concerned, decide to extend the expiry date of a specific exemption for a period of up to five years. In making its decision, the Conference of the Parties shall take due account of the special circumstances of the developing country Parties and Parties with economies in transition.

8. A Party may, at any time, withdraw an entry from the Register for a specific exemption upon written notification to the Secretariat. The withdrawal shall take effect on the date specified in the notification.

9. When there are no longer any Parties registered for a particular type of specific exemption, no new registrations may be made with respect to it.

ARTICLE 5

Measures to reduce or eliminate releases from unintentional production

Each Party shall at a minimum take the following measures to reduce the total releases derived from anthropogenic sources of each of the chemicals listed in Annex C, with the goal of their continuing minimization and, where feasible, ultimate elimination:

- (a) Develop an action plan or, where appropriate, a regional or subregional action plan within two years of the date of entry into force of this Convention for it, and subsequently implement it as part of its implementation plan

specified in Article 7, designed to identify, characterize and address the release of the chemicals listed in Annex C and to facilitate implementation of subparagraphs (b) to (e). The action plan shall include the following elements:

- (i) An evaluation of current and projected releases, including the development and maintenance of source inventories and release estimates, taking into consideration the source categories identified in Annex C;
 - (ii) An evaluation of the efficacy of the laws and policies of the Party relating to the management of such releases;
 - (iii) Strategies to meet the obligations of this paragraph, taking into account the evaluations in (i) and (ii);
 - (iv) Steps to promote education and training with regard to, and awareness of, those strategies;
 - (v) A review every five years of those strategies and of their success in meeting the obligations of this paragraph; such reviews shall be included in reports submitted pursuant to Article 15;
 - (vi) A schedule for implementation of the action plan, including for the strategies and measures identified therein;
- (b) Promote the application of available, feasible and practical measures that can expeditiously achieve a realistic and meaningful level of release reduction or source elimination;
 - (c) Promote the development and, where it deems appropriate, require the use of substitute or modified materials, products and processes to prevent the formation and release of the chemicals listed in Annex C, taking into consideration the general guidance on prevention and release reduction measures in Annex C and guidelines to be adopted by decision of the Conference of the Parties;
 - (d) Promote and, in accordance with the implementation schedule of its action plan, require the use of best available techniques for new sources within source categories which a Party has identified as warranting such action in

its action plan, with a particular initial focus on source categories identified in Part II of Annex C. In any case, the requirement to use best available techniques for new sources in the categories listed in Part II of that Annex shall be phased in as soon as practicable but no later than four years after the entry into force of the Convention for that Party. For the identified categories, Parties shall promote the use of best environmental practices. When applying best available techniques and best environmental practices, Parties should take into consideration the general guidance on prevention and release reduction measures in that Annex and guidelines on best available techniques and best environmental practices to be adopted by decision of the Conference of the Parties;

- (e) Promote, in accordance with its action plan, the use of best available techniques and best environmental practices:
 - (i) For existing sources, within the source categories listed in Part II of Annex C and within source categories such as those in Part III of that Annex; and
 - (ii) For new sources, within source categories such as those listed in Part III of Annex C which a Party has not addressed under subparagraph (d).

When applying best available techniques and best environmental practices, Parties should take into consideration the general guidance on prevention and release reduction measures in Annex C and guidelines on best available techniques and best environmental practices to be adopted by decision of the Conference of the Parties;

- (f) For the purposes of this paragraph and Annex C:
 - (i) “Best available techniques” means the most effective and advanced stage in the development of activities and their methods of operation which indicate the practical suitability of particular techniques for providing in principle the basis for release limitations designed to prevent and, where that is not practicable, generally to reduce releases of chemicals listed in Part I of Annex C and their impact on the environment as a whole. In this regard:
 - (ii) “Techniques” includes both the technology used and the way in which the installation is designed, built, maintained, operated and decommissioned;

- (iii) “Available” techniques means those techniques that are accessible to the operator and that are developed on a scale that allows implementation in the relevant industrial sector, under economically and technically viable conditions, taking into consideration the costs and advantages; and
- (iv) “Best” means most effective in achieving a high general level of protection of the environment as a whole;
- (v) “Best environmental practices” means the application of the most appropriate combination of environmental control measures and strategies;
- (vi) “New source” means any source of which the construction or substantial modification is commenced at least one year after the date of:
 - a. Entry into force of this Convention for the Party concerned; or
 - b. Entry into force for the Party concerned of an amendment to Annex C where the source becomes subject to the provisions of this Convention only by virtue of that amendment.
- (g) Release limit values or performance standards may be used by a Party to fulfill its commitments for best available techniques under this paragraph.

ARTICLE 6

Measures to reduce or eliminate releases from stockpiles and wastes

1. In order to ensure that stockpiles consisting of or containing chemicals listed either in Annex A or Annex B and wastes, including products and articles upon becoming wastes, consisting of, containing or contaminated with a chemical listed in Annex A, B or C, are managed in a manner protective of human health and the environment, each Party shall:

- (a) Develop appropriate strategies for identifying:
 - (i) Stockpiles consisting of or containing chemicals listed either in Annex A or Annex B; and

- (ii) Products and articles in use and wastes consisting of, containing or contaminated with a chemical listed in Annex A, B or C;
- (b) Identify, to the extent practicable, stockpiles consisting of or containing chemicals listed either in Annex A or Annex B on the basis of the strategies referred to in subparagraph (a);
- (c) Manage stockpiles, as appropriate, in a safe, efficient and environmentally sound manner. Stockpiles of chemicals listed either in Annex A or Annex B, after they are no longer allowed to be used according to any specific exemption specified in Annex A or any specific exemption or acceptable purpose specified in Annex B, except stockpiles which are allowed to be exported according to paragraph 2 of Article 3, shall be deemed to be waste and shall be managed in accordance with subparagraph (d);
- (d) Take appropriate measures so that such wastes, including products and articles upon becoming wastes, are:
 - (i) Handled, collected, transported and stored in an environmentally sound manner;
 - (ii) Disposed of in such a way that the persistent organic pollutant content is destroyed or irreversibly transformed so that they do not exhibit the characteristics of persistent organic pollutants or otherwise disposed of in an environmentally sound manner when destruction or irreversible transformation does not represent the environmentally preferable option or the persistent organic pollutant content is low, taking into account international rules, standards, and guidelines, including those that may be developed pursuant to paragraph 2, and relevant global and regional regimes governing the management of hazardous wastes;
 - (iii) Not permitted to be subjected to disposal operations that may lead to recovery, recycling, reclamation, direct reuse or alternative uses of persistent organic pollutants; and
 - (iv) Not transported across international boundaries without taking into account relevant international rules, standards and guidelines;

- (e) Endeavour to develop appropriate strategies for identifying sites contaminated by chemicals listed in Annex A, B or C; if remediation of those sites is undertaken it shall be performed in an environmentally sound manner.
2. The Conference of the Parties shall cooperate closely with the appropriate bodies of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal to, inter alia:
- (a) Establish levels of destruction and irreversible transformation necessary to ensure that the characteristics of persistent organic pollutants as specified in paragraph 1 of Annex D are not exhibited;
 - (b) Determine what they consider to be the methods that constitute environmentally sound disposal referred to above; and
 - (c) Work to establish, as appropriate, the concentration levels of the chemicals listed in Annexes A, B and C in order to define the low persistent organic pollutant content referred to in paragraph 1 (d) (ii).

ARTICLE 7

Implementation plans

1. Each Party shall:
- (a) Develop and endeavour to implement a plan for the implementation of its obligations under this Convention;
 - (b) Transmit its implementation plan to the Conference of the Parties within two years of the date on which this Convention enters into force for it; and
 - (c) Review and update, as appropriate, its implementation plan on a periodic basis and in a manner to be specified by a decision of the Conference of the Parties.
2. The Parties shall, where appropriate, cooperate directly or through global, regional and subregional organizations, and consult their national stakeholders, including women's groups and groups involved in the health of children, in order to facilitate the development, implementation and updating of their implementation plans.

3. The Parties shall endeavour to utilize and, where necessary, establish the means to integrate national implementation plans for persistent organic pollutants in their sustainable development strategies where appropriate.

ARTICLE 8

Listing of chemicals in Annexes A, B and C

1. A Party may submit a proposal to the Secretariat for listing a chemical in Annexes A, B and/or C. The proposal shall contain the information specified in Annex D. In developing a proposal, a Party may be assisted by other Parties and/or by the Secretariat.

2. The Secretariat shall verify whether the proposal contains the information specified in Annex D. If the Secretariat is satisfied that the proposal contains the information so specified, it shall forward the proposal to the Persistent Organic Pollutants Review Committee.

3. The Committee shall examine the proposal and apply the screening criteria specified in Annex D in a flexible and transparent way, taking all information provided into account in an integrative and balanced manner.

4. If the Committee decides that:

(a) It is satisfied that the screening criteria have been fulfilled, it shall, through the Secretariat, make the proposal and the evaluation of the Committee available to all Parties and observers and invite them to submit the information specified in Annex E; or

(b) It is not satisfied that the screening criteria have been fulfilled, it shall, through the Secretariat, inform all Parties and observers and make the proposal and the evaluation of the Committee available to all Parties and the proposal shall be set aside.

5. Any Party may resubmit a proposal to the Committee that has been set aside by the Committee pursuant to paragraph 4. The resubmission may include any concerns of the Party as well as a justification for additional consideration by the Committee. If, following this procedure, the Committee again sets the proposal aside, the Party may challenge the decision of the Committee and the Conference of the

Parties shall consider the matter at its next session. The Conference of the Parties may decide, based on the screening criteria in Annex D and taking into account the evaluation of the Committee and any additional information provided by any Party or observer, that the proposal should proceed.

6. Where the Committee has decided that the screening criteria have been fulfilled, or the Conference of the Parties has decided that the proposal should proceed, the Committee shall further review the proposal, taking into account any relevant additional information received, and shall prepare a draft risk profile in accordance with Annex E. It shall, through the Secretariat, make that draft available to all Parties and observers, collect technical comments from them and, taking those comments into account, complete the risk profile.

7. If, on the basis of the risk profile conducted in accordance with Annex E, the Committee decides:

(a) That the chemical is likely as a result of its long-range environmental transport to lead to significant adverse human health and/or environmental effects such that global action is warranted, the proposal shall proceed. Lack of full scientific certainty shall not prevent the proposal from proceeding. The Committee shall, through the Secretariat, invite information from all Parties and observers relating to the considerations specified in Annex F. It shall then prepare a risk management evaluation that includes an analysis of possible control measures for the chemical in accordance with that Annex; or

(b) That the proposal should not proceed, it shall, through the Secretariat, make the risk profile available to all Parties and observers and set the proposal aside.

8. For any proposal set aside pursuant to paragraph 7 (b), a Party may request the Conference of the Parties to consider instructing the Committee to invite additional information from the proposing Party and other Parties during a period not to exceed one year. After that period and on the basis of any information received, the Committee shall reconsider the proposal pursuant to paragraph 6 with a priority to be decided by the Conference of the Parties. If, following this procedure, the Committee again sets the proposal aside, the Party may challenge the decision of the Committee and the Conference of the Parties shall consider the matter at its next session. The Conference of the Parties may decide, based on the risk profile prepared

in accordance with Annex E and taking into account the evaluation of the Committee and any additional information provided by any Party or observer, that the proposal should proceed. If the Conference of the Parties decides that the proposal shall proceed, the Committee shall then prepare the risk management evaluation.

9. The Committee shall, based on the risk profile referred to in paragraph 6 and the risk management evaluation referred to in paragraph 7 (a) or paragraph 8, recommend whether the chemical should be considered by the Conference of the Parties for listing in Annexes A, B and/or C. The Conference of the Parties, taking due account of the recommendations of the Committee, including any scientific uncertainty, shall decide, in a precautionary manner, whether to list the chemical, and specify its related control measures, in Annexes A, B and/or C.

ARTICLE 9

Information exchange

1. Each Party shall facilitate or undertake the exchange of information relevant to:
 - (a) The reduction or elimination of the production, use and release of persistent organic pollutants; and
 - (b) Alternatives to persistent organic pollutants, including information relating to their risks as well as to their economic and social costs.
2. The Parties shall exchange the information referred to in paragraph 1 directly or through the Secretariat.
3. Each Party shall designate a national focal point for the exchange of such information.
4. The Secretariat shall serve as a clearing-house mechanism for information on persistent organic pollutants, including information provided by Parties, intergovernmental organizations and non-governmental organizations.
5. For the purposes of this Convention, information on health and safety of humans and the environment shall not be regarded as confidential. Parties that exchange other information pursuant to this Convention shall protect any confidential information as mutually agreed.

ARTICLE 10

Public information, awareness and education

1. Each Party shall, within its capabilities, promote and facilitate:
 - (a) Awareness among its policy and decision makers with regard to persistent organic pollutants;
 - (b) Provision to the public of all available information on persistent organic pollutants, taking into account paragraph 5 of Article 9;
 - (c) Development and implementation, especially for women, children and the least educated, of educational and public awareness programmes on persistent organic pollutants, as well as on their health and environmental effects and on their alternatives;
 - (d) Public participation in addressing persistent organic pollutants and their health and environmental effects and in developing adequate responses, including opportunities for providing input at the national level regarding implementation of this Convention;
 - (e) Training of workers, scientists, educators and technical and managerial personnel;
 - (f) Development and exchange of educational and public awareness materials at the national and international levels; and
 - (g) Development and implementation of education and training programmes at the national and international levels.
2. Each Party shall, within its capabilities, ensure that the public has access to the public information referred to in paragraph 1 and that the information is kept up-to-date.
3. Each Party shall, within its capabilities, encourage industry and professional users to promote and facilitate the provision of the information referred to in paragraph 1 at the national level and, as appropriate, subregional, regional and global levels.
4. In providing information on persistent organic pollutants and their alternatives, Parties may use safety data sheets, reports, mass media and other means of communication, and may establish information centres at national and regional levels.

5. Each Party shall give sympathetic consideration to developing mechanisms, such as pollutant release and transfer registers, for the collection and dissemination of information on estimates of the annual quantities of the chemicals listed in Annex A, B or C that are released or disposed of.

ARTICLE 11

Research, development and monitoring

1. The Parties shall, within their capabilities, at the national and international levels, encourage and/or undertake appropriate research, development, monitoring and cooperation pertaining to persistent organic pollutants and, where relevant, to their alternatives and to candidate persistent organic pollutants, including on their:

- (a) Sources and releases into the environment;
- (b) Presence, levels and trends in humans and the environment;
- (c) Environmental transport, fate and transformation;
- (d) Effects on human health and the environment;
- (e) Socio-economic and cultural impacts;
- (f) Release reduction and/or elimination; and
- (g) Harmonized methodologies for making inventories of generating sources and analytical techniques for the measurement of releases.

2. In undertaking action under paragraph 1, the Parties shall, within their capabilities:

- (a) Support and further develop, as appropriate, international programmes, networks and organizations aimed at defining, conducting, assessing and financing research, data collection and monitoring, taking into account the need to minimize duplication of effort;
- (b) Support national and international efforts to strengthen national scientific and technical research capabilities, particularly in developing countries

and countries with economies in transition, and to promote access to, and the exchange of, data and analyses;

- (c) Take into account the concerns and needs, particularly in the field of financial and technical resources, of developing countries and countries with economies in transition and cooperate in improving their capability to participate in the efforts referred to in subparagraphs (a) and (b);
- (d) Undertake research work geared towards alleviating the effects of persistent organic pollutants on reproductive health;
- (e) Make the results of their research, development and monitoring activities referred to in this paragraph accessible to the public on a timely and regular basis; and
- (f) Encourage and/or undertake cooperation with regard to storage and maintenance of information generated from research, development and monitoring.

ARTICLE 12

Technical assistance

1. The Parties recognize that rendering of timely and appropriate technical assistance in response to requests from developing country Parties and Parties with economies in transition is essential to the successful implementation of this Convention.
2. The Parties shall cooperate to provide timely and appropriate technical assistance to developing country Parties and Parties with economies in transition, to assist them, taking into account their particular needs, to develop and strengthen their capacity to implement their obligations under this Convention.
3. In this regard, technical assistance to be provided by developed country Parties, and other Parties in accordance with their capabilities, shall include, as appropriate and as mutually agreed, technical assistance for capacity-building relating to implementation of the obligations under this Convention. Further guidance in this regard shall be provided by the Conference of the Parties.

4. The Parties shall establish, as appropriate, arrangements for the purpose of providing technical assistance and promoting the transfer of technology to developing country Parties and Parties with economies in transition relating to the implementation of this Convention. These arrangements shall include regional and subregional centres for capacity-building and transfer of technology to assist developing country Parties and Parties with economies in transition to fulfil their obligations under this Convention. Further guidance in this regard shall be provided by the Conference of the Parties.

5. The Parties shall, in the context of this Article, take full account of the specific needs and special situation of least developed countries and small island developing states in their actions with regard to technical assistance.

ARTICLE 13

Financial resources and mechanisms

1. Each Party undertakes to provide, within its capabilities, financial support and incentives in respect of those national activities that are intended to achieve the objective of this Convention in accordance with its national plans, priorities and programmes.

2. The developed country Parties shall provide new and additional financial resources to enable developing country Parties and Parties with economies in transition to meet the agreed full incremental costs of implementing measures which fulfill their obligations under this Convention as agreed between a recipient Party and an entity participating in the mechanism described in paragraph 6. Other Parties may also on a voluntary basis and in accordance with their capabilities provide such financial resources. Contributions from other sources should also be encouraged. The implementation of these commitments shall take into account the need for adequacy, predictability, the timely flow of funds and the importance of burden sharing among the contributing Parties.

3. Developed country Parties, and other Parties in accordance with their capabilities and in accordance with their national plans, priorities and programmes, may also provide and developing country Parties and Parties with economies in transition avail themselves of financial resources to assist in their implementation of this Convention through other bilateral, regional and multilateral sources or channels.

4. The extent to which the developing country Parties will effectively implement their commitments under this Convention will depend on the effective implementation by developed country Parties of their commitments under this Convention relating to financial resources, technical assistance and technology transfer. The fact that sustainable economic and social development and eradication of poverty are the first and overriding priorities of the developing country Parties will be taken fully into account, giving due consideration to the need for the protection of human health and the environment.

5. The Parties shall take full account of the specific needs and special situation of the least developed countries and the small island developing states in their actions with regard to funding.

6. A mechanism for the provision of adequate and sustainable financial resources to developing country Parties and Parties with economies in transition on a grant or concessional basis to assist in their implementation of the Convention is hereby defined. The mechanism shall function under the authority, as appropriate, and guidance of, and be accountable to the Conference of the Parties for the purposes of this Convention. Its operation shall be entrusted to one or more entities, including existing international entities, as may be decided upon by the Conference of the Parties. The mechanism may also include other entities providing multilateral, regional and bilateral financial and technical assistance. Contributions to the mechanism shall be additional to other financial transfers to developing country Parties and Parties with economies in transition as reflected in, and in accordance with, paragraph 2.

7. Pursuant to the objectives of this Convention and paragraph 6, the Conference of the Parties shall at its first meeting adopt appropriate guidance to be provided to the mechanism and shall agree with the entity or entities participating in the financial mechanism upon arrangements to give effect thereto. The guidance shall address, inter alia:

- (a) The determination of the policy, strategy and programme priorities, as well as clear and detailed criteria and guidelines regarding eligibility for access to and utilization of financial resources including monitoring and evaluation on a regular basis of such utilization;
- (b) The provision by the entity or entities of regular reports to the Conference of the Parties on adequacy and sustainability of funding for activities relevant to the implementation of this Convention;

- (c) The promotion of multiple-source funding approaches, mechanisms and arrangements;
- (d) The modalities for the determination in a predictable and identifiable manner of the amount of funding necessary and available for the implementation of this Convention, keeping in mind that the phasing out of persistent organic pollutants might require sustained funding, and the conditions under which that amount shall be periodically reviewed; and
- (e) The modalities for the provision to interested Parties of assistance with needs assessment, information on available sources of funds and on funding patterns in order to facilitate coordination among them.

8. The Conference of the Parties shall review, not later than its second meeting and thereafter on a regular basis, the effectiveness of the mechanism established under this Article, its ability to address the changing needs of the developing country Parties and Parties with economies in transition, the criteria and guidance referred to in paragraph 7, the level of funding as well as the effectiveness of the performance of the institutional entities entrusted to operate the financial mechanism. It shall, based on such review, take appropriate action, if necessary, to improve the effectiveness of the mechanism, including by means of recommendations and guidance on measures to ensure adequate and sustainable funding to meet the needs of the Parties.

ARTICLE 14

Interim financial arrangements

The institutional structure of the Global Environment Facility, operated in accordance with the Instrument for the Establishment of the Restructured Global Environment Facility, shall, on an interim basis, be the principal entity entrusted with the operations of the financial mechanism referred to in Article 13, for the period between the date of entry into force of this Convention and the first meeting of the Conference of the Parties, or until such time as the Conference of the Parties decides which institutional structure will be designated in accordance with Article 13. The institutional structure of the Global Environment Facility should fulfill this function through operational measures related specifically to persistent organic pollutants taking into account that new arrangements for this area may be needed.

ARTICLE 15

Reporting

1. Each Party shall report to the Conference of the Parties on the measures it has taken to implement the provisions of this Convention and on the effectiveness of such measures in meeting the objectives of the Convention.
2. Each Party shall provide to the Secretariat:
 - (a) Statistical data on its total quantities of production, import and export of each of the chemicals listed in Annex A and Annex B or a reasonable estimate of such data; and
 - (b) To the extent practicable, a list of the States from which it has imported each such substance and the States to which it has exported each such substance.
3. Such reporting shall be at periodic intervals and in a format to be decided by the Conference of the Parties at its first meeting.

ARTICLE 16

Effectiveness evaluation

1. Commencing four years after the date of entry into force of this Convention, and periodically thereafter at intervals to be decided by the Conference of the Parties, the Conference shall evaluate the effectiveness of this Convention.
2. In order to facilitate such evaluation, the Conference of the Parties shall, at its first meeting, initiate the establishment of arrangements to provide itself with comparable monitoring data on the presence of the chemicals listed in Annexes A, B and C as well as their regional and global environmental transport. These arrangements:
 - (a) Should be implemented by the Parties on a regional basis when appropriate, in accordance with their technical and financial capabilities, using existing monitoring programmes and mechanisms to the extent possible and promoting harmonization of approaches;

- (b) May be supplemented where necessary, taking into account the differences between regions and their capabilities to implement monitoring activities; and
 - (c) Shall include reports to the Conference of the Parties on the results of the monitoring activities on a regional and global basis at intervals to be specified by the Conference of the Parties.
3. The evaluation described in paragraph 1 shall be conducted on the basis of available scientific, environmental, technical and economic information, including:
- (a) Reports and other monitoring information provided pursuant to paragraph 2;
 - (b) National reports submitted pursuant to Article 15; and
 - (c) Non-compliance information provided pursuant to the procedures established under Article 17.

ARTICLE 17

Non-compliance

The Conference of the Parties shall, as soon as practicable, develop and approve procedures and institutional mechanisms for determining non-compliance with the provisions of this Convention and for the treatment of Parties found to be in non-compliance.

ARTICLE 18

Settlement of disputes

1. Parties shall settle any dispute between them concerning the interpretation or application of this Convention through negotiation or other peaceful means of their own choice.
2. When ratifying, accepting, approving or acceding to the Convention, or at any time thereafter, a Party that is not a regional economic integration organization may declare in a written instrument submitted to the depositary that, with respect to any

dispute concerning the interpretation or application of the Convention, it recognizes one or both of the following means of dispute settlement as compulsory in relation to any Party accepting the same obligation:

(a) Arbitration in accordance with procedures to be adopted by the Conference of the Parties in an annex as soon as practicable;

(b) Submission of the dispute to the International Court of Justice.

3. A Party that is a regional economic integration organization may make a declaration with like effect in relation to arbitration in accordance with the procedure referred to in paragraph 2 (a).

4. A declaration made pursuant to paragraph 2 or paragraph 3 shall remain in force until it expires in accordance with its terms or until three months after written notice of its revocation has been deposited with the depositary.

5. The expiry of a declaration, a notice of revocation or a new declaration shall not in any way affect proceedings pending before an arbitral tribunal or the International Court of Justice unless the parties to the dispute otherwise agree.

6. If the parties to a dispute have not accepted the same or any procedure pursuant to paragraph 2, and if they have not been able to settle their dispute within twelve months following notification by one party to another that a dispute exists between them, the dispute shall be submitted to a conciliation commission at the request of any party to the dispute. The conciliation commission shall render a report with recommendations. Additional procedures relating to the conciliation commission shall be included in an annex to be adopted by the Conference of the Parties no later than at its second meeting.

ARTICLE 19

Conference of the Parties

1. A Conference of the Parties is hereby established.

2. The first meeting of the Conference of the Parties shall be convened by the Executive Director of the United Nations Environment Programme no later than one year after the entry into force of this Convention. Thereafter, ordinary meetings of

the Conference of the Parties shall be held at regular intervals to be decided by the Conference.

3. Extraordinary meetings of the Conference of the Parties shall be held at such other times as may be deemed necessary by the Conference, or at the written request of any Party provided that it is supported by at least one third of the Parties.

4. The Conference of the Parties shall by consensus agree upon and adopt at its first meeting rules of procedure and financial rules for itself and any subsidiary bodies, as well as financial provisions governing the functioning of the Secretariat.

5. The Conference of the Parties shall keep under continuous review and evaluation the implementation of this Convention. It shall perform the functions assigned to it by the Convention and, to this end, shall:

- (a) Establish, further to the requirements of paragraph 6, such subsidiary bodies as it considers necessary for the implementation of the Convention;
- (b) Cooperate, where appropriate, with competent international organizations and intergovernmental and non-governmental bodies; and
- (c) Regularly review all information made available to the Parties pursuant to Article 15, including consideration of the effectiveness of paragraph 2 (b) (iii) of Article 3;
- (d) Consider and undertake any additional action that may be required for the achievement of the objectives of the Convention.

6. The Conference of the Parties shall, at its first meeting, establish a subsidiary body to be called the Persistent Organic Pollutants Review Committee for the purposes of performing the functions assigned to that Committee by this Convention. In this regard:

- (a) The members of the Persistent Organic Pollutants Review Committee shall be appointed by the Conference of the Parties. Membership of the Committee shall consist of government-designated experts in chemical assessment or management. The members of the Committee shall be appointed on the basis of equitable geographical distribution;
- (b) The Conference of the Parties shall decide on the terms of reference, organization and operation of the Committee; and

(c) The Committee shall make every effort to adopt its recommendations by consensus. If all efforts at consensus have been exhausted, and no consensus reached, such recommendation shall as a last resort be adopted by a two-thirds majority vote of the members present and voting.

7. The Conference of the Parties shall, at its third meeting, evaluate the continued need for the procedure contained in paragraph 2 (b) of Article 3, including consideration of its effectiveness.

8. The United Nations, its specialized agencies and the International Atomic Energy Agency, as well as any State not Party to this Convention, may be represented at meetings of the Conference of the Parties as observers. Any body or agency, whether national or international, governmental or non-governmental, qualified in matters covered by the Convention, and which has informed the Secretariat of its wish to be represented at a meeting of the Conference of the Parties as an observer may be admitted unless at least one third of the Parties present object. The admission and participation of observers shall be subject to the rules of procedure adopted by the Conference of the Parties.

ARTICLE 20

Secretariat

1. A Secretariat is hereby established.
2. The functions of the Secretariat shall be:
 - (a) To make arrangements for meetings of the Conference of the Parties and its subsidiary bodies and to provide them with services as required;
 - (b) To facilitate assistance to the Parties, particularly developing country Parties and Parties with economies in transition, on request, in the implementation of this Convention;
 - (c) To ensure the necessary coordination with the secretariats of other relevant international bodies;
 - (d) To prepare and make available to the Parties periodic reports based on information received pursuant to Article 15 and other available information;

- (e) To enter, under the overall guidance of the Conference of the Parties, into such administrative and contractual arrangements as may be required for the effective discharge of its functions; and
 - (f) To perform the other secretariat functions specified in this Convention and such other functions as may be determined by the Conference of the Parties.
3. The secretariat functions for this Convention shall be performed by the Executive Director of the United Nations Environment Programme, unless the Conference of the Parties decides, by a three-fourths majority of the Parties present and voting, to entrust the secretariat functions to one or more other international organizations.

ARTICLE 21

Amendments to the Convention

1. Amendments to this Convention may be proposed by any Party.
2. Amendments to this Convention shall be adopted at a meeting of the Conference of the Parties. The text of any proposed amendment shall be communicated to the Parties by the Secretariat at least six months before the meeting at which it is proposed for adoption. The Secretariat shall also communicate proposed amendments to the signatories to this Convention and, for information, to the depositary.
3. The Parties shall make every effort to reach agreement on any proposed amendment to this Convention by consensus. If all efforts at consensus have been exhausted, and no agreement reached, the amendment shall as a last resort be adopted by a three-fourths majority vote of the Parties present and voting.
4. The amendment shall be communicated by the depositary to all Parties for ratification, acceptance or approval.
5. Ratification, acceptance or approval of an amendment shall be notified to the depositary in writing. An amendment adopted in accordance with paragraph 3 shall enter into force for the Parties having accepted it on the ninetieth day after the date of deposit of instruments of ratification, acceptance or approval by at least three-fourths of the Parties. Thereafter, the amendment shall enter into force for any other Party on the ninetieth day after the date on which that Party deposits its instrument of ratification, acceptance or approval of the amendment.

ARTICLE 22

Adoption and amendment of annexes

1. Annexes to this Convention shall form an integral part thereof and, unless expressly provided otherwise, a reference to this Convention constitutes at the same time a reference to any annexes thereto.

2. Any additional annexes shall be restricted to procedural, scientific, technical or administrative matters.

3. The following procedure shall apply to the proposal, adoption and entry into force of additional annexes to this Convention:

(a) Additional annexes shall be proposed and adopted according to the procedure laid down in paragraphs 1, 2 and 3 of Article 21;

(b) Any Party that is unable to accept an additional annex shall so notify the depositary, in writing, within one year from the date of communication by the depositary of the adoption of the additional annex. The depositary shall without delay notify all Parties of any such notification received. A Party may at any time withdraw a previous notification of non-acceptance in respect of any additional annex, and the annex shall thereupon enter into force for that Party subject to subparagraph (c); and

(c) On the expiry of one year from the date of the communication by the depositary of the adoption of an additional annex, the annex shall enter into force for all Parties that have not submitted a notification in accordance with the provisions of subparagraph (b).

4. The proposal, adoption and entry into force of amendments to Annex A, B or C shall be subject to the same procedures as for the proposal, adoption and entry into force of additional annexes to this Convention, except that an amendment to Annex A, B or C shall not enter into force with respect to any Party that has made a declaration with respect to amendment to those Annexes in accordance with paragraph 4 of Article 25, in which case any such amendment shall enter into force for such a Party on the ninetieth day after the date of deposit with the depositary of its instrument of ratification, acceptance, approval or accession with respect to such amendment.

5. The following procedure shall apply to the proposal, adoption and entry into force of an amendment to Annex D, E or F:

(a) Amendments shall be proposed according to the procedure in paragraphs 1 and 2 of Article 21;

- (b) The Parties shall take decisions on an amendment to Annex D, E or F by consensus; and
- (c) A decision to amend Annex D, E or F shall forthwith be communicated to the Parties by the depositary. The amendment shall enter into force for all Parties on a date to be specified in the decision.

6. If an additional annex or an amendment to an annex is related to an amendment to this Convention, the additional annex or amendment shall not enter into force until such time as the amendment to the Convention enters into force.

ARTICLE 23

Right to vote

1. Each Party to this Convention shall have one vote, except as provided for in paragraph 2.
2. A regional economic integration organization, on matters within its competence, shall exercise its right to vote with a number of votes equal to the number of its member States that are Parties to this Convention. Such an organization shall not exercise its right to vote if any of its member States exercises its right to vote, and vice versa.

ARTICLE 24

Signature

This Convention shall be open for signature at Stockholm by all States and regional economic integration organizations on 23 May 2001, and at the United Nations Headquarters in New York from 24 May 2001 to 22 May 2002.

ARTICLE 25

Ratification, acceptance, approval or accession

1. This Convention shall be subject to ratification, acceptance or approval by States and by regional economic integration organizations. It shall be open for accession by States and by regional economic integration organizations from the day after the

date on which the Convention is closed for signature. Instruments of ratification, acceptance, approval or accession shall be deposited with the depositary.

2. Any regional economic integration organization that becomes a Party to this Convention without any of its member States being a Party shall be bound by all the obligations under the Convention. In the case of such organizations, one or more of whose member States is a Party to this Convention, the organization and its member States shall decide on their respective responsibilities for the performance of their obligations under the Convention. In such cases, the organization and the member States shall not be entitled to exercise rights under the Convention concurrently.

3. In its instrument of ratification, acceptance, approval or accession, a regional economic integration organization shall declare the extent of its competence in respect of the matters governed by this Convention. Any such organization shall also inform the depositary, who shall in turn inform the Parties, of any relevant modification in the extent of its competence.

4. In its instrument of ratification, acceptance, approval or accession, any Party may declare that, with respect to it, any amendment to Annex A, B or C shall enter into force only upon the deposit of its instrument of ratification, acceptance, approval or accession with respect thereto.

ARTICLE 26

Entry into force

1. This Convention shall enter into force on the ninetieth day after the date of deposit of the fiftieth instrument of ratification, acceptance, approval or accession.

2. For each State or regional economic integration organization that ratifies, accepts or approves this Convention or accedes thereto after the deposit of the fiftieth instrument of ratification, acceptance, approval or accession, the Convention shall enter into force on the ninetieth day after the date of deposit by such State or regional economic integration organization of its instrument of ratification, acceptance, approval or accession.

3. For the purpose of paragraphs 1 and 2, any instrument deposited by a regional economic integration organization shall not be counted as additional to those deposited by member States of that organization.

ARTICLE 27

Reservations

No reservations may be made to this Convention.

ARTICLE 28

Withdrawal

1. At any time after three years from the date on which this Convention has entered into force for a Party, that Party may withdraw from the Convention by giving written notification to the depositary.
2. Any such withdrawal shall take effect upon the expiry of one year from the date of receipt by the depositary of the notification of withdrawal, or on such later date as may be specified in the notification of withdrawal.

ARTICLE 29

Depositary

The Secretary-General of the United Nations shall be the depositary of this Convention.

ARTICLE 30

Authentic texts

The original of this Convention, of which the Arabic, Chinese, English, French, Russian and Spanish texts are equally authentic, shall be deposited with the Secretary-General of the United Nations.

IN WITNESS WHEREOF the undersigned, being duly authorized to that effect, have signed this Convention.

Done at Stockholm on this twenty-second day of May, two thousand and one.



ANNEXES

ANNEX A¹

ELIMINATION

Part I

Chemical	Activity	Specific exemption ²
Aldrin* CAS No: 309-00-2	Production	None
	Use	Local ectoparasiticide Insecticide
Alpha hexachlorocyclohexane* CAS No: 319-84-6	Production	None
	Use	None
Beta hexachlorocyclohexane* CAS No: 319-85-7	Production	None
	Use	None
Chlordane* CAS No: 57-74-9	Production	As allowed for the Parties listed in the Register
	Use	Local ectoparasiticide Insecticide Termiticide Termiticide in buildings and dams Termiticide in roads Additive in plywood adhesives
Chlordecone* CAS No: 143-50-0	Production	None
	Use	None

¹ As amended by decisions SC-4/10 to SC-4/18 of 8 May 2009; SC-5/3 of 29 April 2011; SC-6/13 of 10 May 2013; SC-7/12 to SC-7/14 of 15 May 2015; and SC-8/10 to SC-8/12 of 5 May 2017; and SC-9/4, SC-9/11 and SC-9/12 of 10 May 2019.

² Please note that, in accordance with paragraph 9 of Article 4 of the Convention, when there are no longer any Parties registered for a particular type of specific exemption no new registrations may be made with respect to such exemptions, which appear in gray text in the table.

Chemical	Activity	Specific exemption ²
Decabromodiphenyl ether (BDE-209) present in commercial decabromodiphenyl ether (CAS No: 1163-19-5)	Production	As allowed for the Parties listed in the Register
	Use	In accordance with Part IX of this Annex: <ul style="list-style-type: none"> • Parts for use in vehicles specified in paragraph 2 of Part IX of this Annex • Aircraft for which type approval has been applied for before December 2018 and has been received before December 2022 and spare parts for those aircraft • Textile products that require anti-flammable characteristics, excluding clothing and toys • Additives in plastic housings and parts used for heating home appliances, irons, fans, immersion heaters that contain or are in direct contact with electrical parts or are required to comply with fire retardancy standards, at concentrations lower than 10 per cent by weight of the part • Polyurethane foam for building insulation
Dicofol CAS No: 115-32-2 CAS No: 10606-46-9	Production	None
	Use	None
Dieldrin* CAS No: 60-57-1	Production	None
	Use	In agricultural operations

Chemical	Activity	Specific exemption ²
Endrin* CAS No: 72-20-8	Production	None
	Use	None
Heptachlor* CAS No: 76-44-8	Production	None
	Use	Termiticide Termiticide in structures of houses Termiticide (subterranean) Wood treatment In use in underground cable boxes
Hexabromobiphenyl * CAS No: 36355-01-8	Production	None
	Use	None
Hexabromocyclododecane	Production	As allowed for the Parties listed in the Register in accordance with the provisions of Part VII of this Annex
	Use	Expanded polystyrene and extruded polystyrene in buildings in accordance with the provisions of Part VII of this Annex
Hexabromodiphenyl ether* and heptabromodiphenyl ether*	Production	None
	Use	Articles in accordance with the provisions of Part IV of this Annex
Hexachlorobenzene CAS No: 118-74-1	Production	As allowed for the Parties listed in the Register
	Use	Intermediate Solvent in pesticide Closed system site limited intermediate
Hexachlorobutadiene CAS No: 87-68-3	Production	None
	Use	None

Chemical	Activity	Specific exemption ²
Lindane* CAS No: 58-89-9	Production	None
	Use	Human health pharmaceutical for control of head lice and scabies as second line treatment
Mirex* CAS No: 2385-85-5	Production	As allowed for the Parties listed in the Register
	Use	Termiticide
Pentachlorobenzene* CAS No: 608-93-5	Production	None
	Use	None
Pentachlorophenol and its salts and esters	Production	As allowed for the Parties listed in the Register in accordance with the provisions of Part VIII of this Annex
	Use	Pentachlorophenol for utility poles and cross-arms in accordance with the provisions of Part VIII of this Annex

Chemical	Activity	Specific exemption ²
<p>The following compounds are not included as PFOA-related compounds:</p> <p>(i) C₈F₁₇-X, where X= F, Cl, Br;</p> <p>(ii) Fluoropolymers that are covered by CF₃[CF₂]_n-R', where R'=any group, n>16;</p> <p>(iii) Perfluoroalkyl carboxylic and phosphonic acids (including their salts, esters, halides and anhydrides) with ≥8 perfluorinated carbons;</p> <p>(iv) Perfluoroalkane sulfonic acids (including their salts, esters, halides and anhydrides) with ≥9 perfluorinated carbons;</p> <p>(v) Perfluorooctane sulfonic acid (PFOS), its salts and perfluorooctane sulfonyl fluoride (PFOSF), as listed in Annex B to the Convention.</p>	<p>Use</p>	<ul style="list-style-type: none"> • Use of perfluorooctyl iodide for the production of perfluorooctyl bromide for the purpose of producing pharmaceutical products, in accordance with the provisions of paragraph 3 of part X of this Annex • Manufacture of polytetrafluoroethylene (PTFE) and polyvinylidene fluoride (PVDF) for the production of: <ul style="list-style-type: none"> ▪ High-performance, corrosion-resistant gas filter membranes, water filter membranes and membranes for medical textiles ▪ Industrial waste heat exchanger equipment ▪ Industrial sealants capable of preventing leakage of volatile organic compounds and PM2.5 particulates • Manufacture of polyfluoroethylene propylene (FEP) for the production of high-voltage electrical wire and cables for power transmission • Manufacture of fluoroelastomers for the production of O-rings, v-belts and plastic accessories for car interiors

Chemical	Activity	Specific exemption ²
Polychlorinated Biphenyls (PCB)*	Production	None
	Use	Articles in use in accordance with the provisions of Part II of this Annex
Polychlorinated naphthalenes, including dichlorinated naphthalenes, trichlorinated naphthalenes, tetrachlorinated naphthalenes, pentachlorinated naphthalenes, hexachlorinated naphthalenes, heptachlorinated naphthalenes, octachlorinated naphthalene	Production	Intermediates in production of polyfluorinated naphthalenes, including octafluoronaphthalene
	Use	Production of polyfluorinated naphthalenes, including octafluoronaphthalene

Chemical	Activity	Specific exemption ²
<p>Short-chain chlorinated paraffins (Alkanes, C₁₀₋₁₃, chloro) ⁺: straight-chain chlorinated hydrocarbons with chain lengths ranging from C₁₀ to C₁₃ and a content of chlorine greater than 48 per cent by weight</p> <p>For example, the substances with the following CAS numbers may contain short-chain chlorinated paraffins: CAS No. 85535-84-8; CAS No. 68920-70-7; CAS No. 71011-12-6; CAS No. 85536-22-7; CAS No. 85681-73-8; CAS No. 108171-26-2.</p>	Production	As allowed for the Parties listed in the Register
	Use	<ul style="list-style-type: none"> • Additives in the production of transmission belts in the natural and synthetic rubber industry • Spare parts of rubber conveyor belts in the mining and forestry industries • Leather industry, in particular fatliquoring in leather • Lubricant additives, in particular for engines of automobiles, electric generators and wind power facilities, and for drilling in oil and gas exploration, petroleum refinery to produce diesel oil • Tubes for outdoor decoration bulbs • Waterproofing and fire-retardant paints • Adhesives • Metal processing • Secondary plasticizers in flexible polyvinyl chloride, except in toys and children's products
<p>Technical endosulfan* (CAS No: 115-29-7) and its related isomers* (CAS No: 959-98-8 and CAS No: 33213-65-9)</p>	Production	As allowed for the Parties listed in the Register
	Use	Crop-pest complexes as listed in accordance with the provisions of part VI of this Annex
<p>Tetrabromodiphenyl ether* and pentabromodiphenyl ether*</p>	Production	None
	Use	Articles in accordance with the provisions of Part V of this Annex

Chemical	Activity	Specific exemption ²
Toxaphene* CAS No: 8001-35-2	Production	None
	Use	None

Notes:

- (i) Except as otherwise specified in this Convention, quantities of a chemical occurring as unintentional trace contaminants in products and articles shall not be considered to be listed in this Annex;
- (ii) This note shall not be considered as a production and use specific exemption for purposes of paragraph 2 of Article 3. Quantities of a chemical occurring as constituents of articles manufactured or already in use before or on the date of entry into force of the relevant obligation with respect to that chemical, shall not be considered as listed in this Annex, provided that a Party has notified the Secretariat that a particular type of article remains in use within that Party. The Secretariat shall make such notifications publicly available;
- (iii) This note, which does not apply to a chemical that has an asterisk following its name in the Chemical column in Part I of this Annex, shall not be considered as a production and use specific exemption for purposes of paragraph 2 of Article 3. Given that no significant quantities of the chemical are expected to reach humans and the environment during the production and use of a closed-system site-limited intermediate, a Party, upon notification to the Secretariat, may allow the production and use of quantities of a chemical listed in this Annex as a closed-system site-limited intermediate that is chemically transformed in the manufacture of other chemicals that, taking into consideration the criteria in paragraph 1 of Annex D, do not exhibit the characteristics of persistent organic pollutants. This notification shall include information on total production and use of such chemical or a reasonable estimate of such information and information regarding the nature of the closed-system site-limited process including the amount of any non-transformed and unintentional trace contamination of the persistent organic pollutant-starting material in

the final product. This procedure applies except as otherwise specified in this Annex. The Secretariat shall make such notifications available to the Conference of the Parties and to the public. Such production or use shall not be considered a production or use specific exemption. Such production and use shall cease after a ten-year period, unless the Party concerned submits a new notification to the Secretariat, in which case the period will be extended for an additional ten years unless the Conference of the Parties, after a review of the production and use decides otherwise. The notification procedure can be repeated;

- (iv) All the specific exemptions in this Annex may be exercised by Parties that have registered exemptions in respect of them in accordance with Article 4 with the exception of the use of polychlorinated biphenyls in articles in use in accordance with the provisions of Part II, and the use of hexabromodiphenyl ether and heptabromodiphenyl ether in accordance with the provisions of Part IV of this Annex, and the use of tetrabromodiphenyl ether and pentabromodiphenyl ether in accordance with the provisions of Part V of this Annex, which may be exercised by all Parties.
- (v) Technical endosulfan (CAS No: 115-29-7), its related isomers (CAS No: 959-98-8 and CAS No: 33213-65-9) and endosulfan sulfate (CAS No: 1031-07-8) were assessed and identified as persistent organic pollutants.
- (vi) Pentachlorophenol (CAS No: 87-86-5), sodium pentachlorophenate (CAS No: 131-52-2 and 27735-64-4 (as monohydrate)) and pentachlorophenyl laurate (CAS No: 3772-94-9), when considered together with their transformation product pentachloroanisole (CAS No: 1825-21-4), were identified as persistent organic pollutants.
- (vii) Note (i) does not apply to quantities of a chemical that has a plus sign (“+”) following its name in the “Chemical” column in Part I of this Annex that occurs in mixtures at concentrations greater than or equal to 1 per cent by weight.

Part II

Polychlorinated biphenyls

Each Party shall:

- (a) With regard to the elimination of the use of polychlorinated biphenyls in equipment (e.g. transformers, capacitors or other receptacles containing liquid stocks) by 2025, subject to review by the Conference of the Parties, take action in accordance with the following priorities:
 - (i) Make determined efforts to identify, label and remove from use equipment containing greater than 10 per cent polychlorinated biphenyls and volumes greater than 5 litres;
 - (ii) Make determined efforts to identify, label and remove from use equipment containing greater than 0.05 per cent polychlorinated biphenyls and volumes greater than 5 litres;
 - (iii) Endeavour to identify and remove from use equipment containing greater than 0.005 per cent polychlorinated biphenyls and volumes greater than 0.05 litres;
- (b) Consistent with the priorities in subparagraph (a), promote the following measures to reduce exposures and risk to control the use of polychlorinated biphenyls:
 - (i) Use only in intact and non-leaking equipment and only in areas where the risk from environmental release can be minimised and quickly remedied;
 - (ii) Not use in equipment in areas associated with the production or processing of food or feed;
 - (iii) When used in populated areas, including schools and hospitals, all reasonable measures to protect from electrical failure which could result in a fire, and regular inspection of equipment for leaks;
- (c) Notwithstanding paragraph 2 of Article 3, ensure that equipment containing polychlorinated biphenyls, as described in subparagraph (a), shall not be exported or imported except for the purpose of environmentally sound waste management;

- (d) Except for maintenance and servicing operations, not allow recovery for the purpose of reuse in other equipment of liquids with polychlorinated biphenyls content above 0.005 per cent;
- (e) Make determined efforts designed to lead to environmentally sound waste management of liquids containing polychlorinated biphenyls and equipment contaminated with polychlorinated biphenyls having a polychlorinated biphenyls content above 0.005 per cent, in accordance with paragraph 1 of Article 6, as soon as possible but no later than 2028, subject to review by the Conference of the Parties;
- (f) In lieu of note (ii) in Part I of this Annex, endeavour to identify other articles containing more than 0.005 per cent polychlorinated biphenyls (e.g. cable-sheaths, cured caulk and painted objects) and manage them in accordance with paragraph 1 of Article 6;
- (g) Provide a report every five years on progress in eliminating polychlorinated biphenyls and submit it to the Conference of the Parties pursuant to Article 15;
- (h) The reports described in subparagraph (g) shall, as appropriate, be considered by the Conference of the Parties in its reviews relating to polychlorinated biphenyls. The Conference of the Parties shall review progress towards elimination of polychlorinated biphenyls at five year intervals or other period, as appropriate, taking into account such reports.

Part III

Definitions

For the purpose of this Annex:

- (a) “Hexabromodiphenyl ether and heptabromodiphenyl ether” mean 2,2',4,4',5,5'-hexabromodiphenyl ether (BDE-153, CAS No: 68631-49-2), 2,2',4,4',5,6'-hexabromodiphenyl ether (BDE-154, CAS No: 207122-15-4), 2,2',3,3',4,5',6-heptabromodiphenyl ether (BDE-175, CAS No: 446255-22-7), 2,2',3,4,4',5',6-heptabromodiphenyl ether (BDE-183, CAS No: 207122-16-5) and other hexa- and heptabromodiphenyl ethers present in commercial octabromodiphenyl ether.

- (b) “Tetrabromodiphenyl ether and pentabromodiphenyl ether” means 2,2',4,4'-tetrabromodiphenyl ether [BDE-47, CAS No: 5436-43-1] and 2,2',4,4',5-pentabromodiphenyl ether [BDE-99, CAS No: 60348-60-9] and other tetra- and pentabromodiphenyl ethers present in commercial pentabromodiphenyl ether.
- (c) “Hexabromocyclododecane” means hexabromocyclododecane [CAS No: 25637-99-4], 1, 2, 5, 6, 9, 10-hexabromocyclododecane [CAS No: 3194-55-6] and its main diastereoisomers: alpha-hexabromocyclododecane [CAS No: 134237-50-6]; beta-hexabromocyclododecane [CAS No: 134237-51-7]; and gamma-hexabromocyclododecane [CAS No: 134237-52-8].

Part IV

Hexabromodiphenyl ether and heptabromodiphenyl ether

1. A Party may allow recycling of articles that contain or may contain hexabromodiphenyl ether and heptabromodiphenyl ether, and the use and final disposal of articles manufactured from recycled materials that contain or may contain hexabromodiphenyl ether and heptabromodiphenyl ether, provided that:

- (a) The recycling and final disposal is carried out in an environmentally sound manner and does not lead to recovery of hexabromodiphenyl ether and heptabromodiphenyl ether for the purpose of their reuse;
- (b) The Party takes steps to prevent exports of such articles that contain levels/ concentrations of hexabromodiphenyl ether and heptabromodiphenyl ether exceeding those permitted for the sale, use, import or manufacture of those articles within the territory of the Party; and
- (c) The Party has notified the Secretariat of its intention to make use of this exemption.

2. At its sixth ordinary meeting and at every second ordinary meeting thereafter the Conference of the Parties shall evaluate the progress that Parties have made towards achieving their ultimate objective of elimination of hexabromodiphenyl ether and heptabromodiphenyl ether contained in articles and review the continued need for this specific exemption. This specific exemption shall in any case expire at the latest in 2030.

Part V

Tetrabromodiphenyl ether and pentabromodiphenyl ether

1. A Party may allow recycling of articles that contain or may contain tetrabromodiphenyl ether and pentabromodiphenyl ether, and the use and final disposal of articles manufactured from recycled materials that contain or may contain tetrabromodiphenyl ether and pentabromodiphenyl ether, provided that:

- (a) The recycling and final disposal is carried out in an environmentally sound manner and does not lead to recovery of tetrabromodiphenyl ether and pentabromodiphenyl ether for the purpose of their reuse;
- (b) The Party does not allow this exemption to lead to the export of articles containing levels/concentrations of tetrabromodiphenyl ether and pentabromodiphenyl ether that exceed those permitted to be sold within the territory of the Party; and
- (c) The Party has notified the Secretariat of its intention to make use of this exemption.

2. At its sixth ordinary meeting and at every second ordinary meeting thereafter the Conference of the Parties shall evaluate the progress that Parties have made towards achieving their ultimate objective of elimination of tetrabromodiphenyl ether and pentabromodiphenyl ether contained in articles and review the continued need for this specific exemption. This specific exemption shall in any case expire at the latest in 2030.

Part VI

Technical endosulfan and its related isomers (endosulfan)

The production and use of endosulfan shall be eliminated except for Parties that have notified the Secretariat of their intention to produce and/or use it in accordance with Article 4 of the Convention. Specific exemptions may be available for the use of endosulfan for the following crop-pest complexes:

Crop	Pest
Apple	Aphids
Arhar, gram	Aphids, caterpillars, pea semilooper, pod borer
Bean, cowpea	Aphids, leaf miner, whiteflies
Chilli, onion, potato	Aphids, jassids
Coffee	Berry borer, stem borers
Cotton	Aphids, cotton bollworm, jassids, leaf rollers, pink bollworm, thrips, whiteflies
Eggplant, okra	Aphids, diamondback moth, jassids, shoot and fruit borer
Groundnut	Aphids
Jute	Bihar hairy caterpillar, yellow mite
Maize	Aphids, pink borer, stem borers
Mango	Fruit flies, hoppers
Mustard	Aphids, gall midges
Rice	Gall midges, rice hispa, stem borers, white jassid
Tea	Aphids, caterpillars, flushworm, mealybugs, scale insects, smaller green leafhopper, tea geometrid, tea mosquito bug, thrips
Tobacco	Aphids, oriental tobacco budworm
Tomato	Aphids, diamondback moth, jassids, leaf miner, shoot and fruit borer, whiteflies
Wheat	Aphids, pink borer, termites

Part VII

Hexabromocyclododecane

Each Party that has registered for the exemption pursuant to Article 4 for the production and use of hexabromocyclododecane for expanded polystyrene and extruded polystyrene in buildings shall take necessary measures to ensure that expanded polystyrene and extruded polystyrene containing hexabromocyclododecane can be easily identified by labelling or other means throughout its life cycle.

Part VIII

Pentachlorophenol and its salts and esters

Each Party that has registered for the exemption, pursuant to Article 4 for the production and use of pentachlorophenol for utility poles and cross-arms shall take the necessary measures to ensure that utility poles and cross-arms containing pentachlorophenol can be easily identified by labelling or other means throughout their life cycles. Articles treated with pentachlorophenol should not be reused for purposes other than those exempted.

Part IX

Decabromodiphenyl ether

1. The production and use of decabromodiphenyl ether shall be eliminated except for Parties that have notified the Secretariat of their intention to produce and/or use it in accordance with Article 4.
2. Specific exemptions for parts for use in vehicles may be available for the production and use of commercial decabromodiphenyl ether limited to the following:
 - (a) Parts for use in legacy vehicles, defined as vehicles that have ceased mass production, and with such parts falling into one or more of the following categories:
 - (i) Powertrain and under-hood applications such as battery mass wires, battery interconnection wires, mobile air-conditioning (MAC) pipes, powertrains, exhaust manifold bushings, under-hood insulation, wiring and harness under hood (engine wiring, etc.), speed sensors, hoses, fan modules and knock sensors;

- (ii) Fuel system applications such as fuel hoses, fuel tanks and fuel tanks under body;
 - (iii) Pyrotechnical devices and applications affected by pyrotechnical devices such as air bag ignition cables, seat covers/fabrics (only if airbag relevant) and airbags (front and side);
 - (iv) Suspension and interior applications such as trim components, acoustic material and seat belts.
- (b) Parts in vehicles specified in paragraphs 2 (a) (i)–(iv) above and those falling into one or more of the following categories:
- (i) Reinforced plastics (instrument panels and interior trim);
 - (ii) Under the hood or dash (terminal/fuse blocks, higher-amperage wires and cable jacketing (spark plug wires));
 - (iii) Electric and electronic equipment (battery cases and battery trays, engine control electrical connectors, components of radio disks, navigation satellite systems, global positioning systems and computer systems);
 - (iv) Fabric such as rear decks, upholstery, headliners, automobile seats, head rests, sun visors, trim panels, carpets.
3. The specific exemptions for parts specified in paragraph 2 (a) above shall expire at the end of the service life of legacy vehicles or in 2036, whichever comes earlier.
4. The specific exemptions for parts specified in paragraph 2 (b) above shall expire at the end of the service life of vehicles or in 2036, whichever comes earlier.
5. The specific exemptions for spare parts for aircraft for which type approval has been applied for before December 2018 and has been received before December 2022 shall expire at the end of the service life of those aircraft.

Part X

Perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds

1. The production and use of perfluorooctanoic acid (PFOA), its salts and PFOA related compounds shall be eliminated except for Parties that have notified the Secretariat of their intention to produce and/or use them in accordance with Article 4 of the Convention.
2. Each Party that has registered for a specific exemption pursuant to Article 4 for the use of PFOA, its salts and PFOA-related compounds for fire-fighting foam shall:
 - (a) Notwithstanding paragraph 2 of Article 3, ensure that fire-fighting foam that contains or may contain PFOA, its salts and PFOA-related compounds shall not be exported or imported except for the purpose of environmentally sound disposal as set forth in paragraph 1 (d) of Article 6;
 - (b) Not use fire-fighting foam that contains or may contain PFOA, its salts and PFOA-related compounds for training;
 - (c) Not use fire-fighting foam that contains or may contain PFOA, its salts and PFOA-related compounds for testing unless all releases are contained;
 - (d) By the end of 2022, if it has the capacity to do so, but no later than 2025, restrict uses of fire-fighting foam that contains or may contain PFOA, its salts and PFOA-related compounds to sites where all releases can be contained;
 - (e) Make determined efforts designed to lead to the environmentally sound management of fire-fighting foam stockpiles and wastes that contain or may contain PFOA, its salts and PFOA-related compounds, in accordance with paragraph 1 of Article 6, as soon as possible;
3. With regard to the specific exemption for the use of perfluorooctyl iodide for the production of perfluorooctyl bromide for the purpose of producing pharmaceutical products, at its thirteenth ordinary meeting and at every second ordinary meeting thereafter, the Conference of the Parties shall review the continued need for this specific exemption. This specific exemption shall in any case expire at the latest in 2036.

ANNEX B³

RESTRICTION

Part I

Chemical	Activity	Acceptable purpose or specific exemption ⁴
DDT (1,1,1-trichloro-2,2-bis (4-chlorophenyl)ethane) CAS No: 50-29-3	Production	<u>Acceptable purpose:</u> Disease vector control use in accordance with Part II of this Annex <u>Specific exemption:</u> Intermediate in production of dicofol Intermediate
	Use	<u>Acceptable purpose:</u> Disease vector control in accordance with Part II of this Annex <u>Specific exemption:</u> Production of dicofol Intermediate

³ As amended by decision SC-4/17 of 8 May 2009 and SC-9/4 of 10 May 2019

⁴ Please note that, in accordance with paragraph 9 of Article 4 of the Convention, when there are no longer any Parties registered for a particular type of specific exemption no new registrations may be made with respect to such exemptions, which appear in gray text in the table.

Chemical	Activity	Acceptable purpose or specific exemption ⁴
Perfluorooctane sulfonic acid (CAS No. 1763-23-1), its salts ^a and perfluorooctane sulfonyl fluoride (CAS No. 307-35-7) ^a For example: potassium perfluorooctane sulfonate (CAS No. 2795-39-3); lithium perfluorooctane sulfonate (CAS No. 29457-72-5); ammonium perfluorooctane sulfonate (CAS No. 29081-56-9); diethanolammonium perfluorooctane sulfonate (CAS No. 70225-14-8); tetraethylammonium perfluorooctane sulfonate (CAS No. 56773-42-3); dicycldimethylammonium perfluorooctane sulfonate (CAS No. 251099-16-8)	Production	<u>Acceptable purpose:</u> In accordance with Part III of this Annex, production of other chemicals to be used solely for the use below. Production for uses listed below. <u>Specific exemption:</u> None
	Use	<u>Acceptable purpose:</u> In accordance with Part III of this Annex for the following acceptable purpose, or as an intermediate in the production of chemicals with the following acceptable purpose: <ul style="list-style-type: none"> • Insect baits with sulfluramid (CAS No. 4151-50-2) as an active ingredient for control of leaf-cutting ants from <i>Atta</i> spp. and <i>Acromyrmex</i> spp. for agricultural use only <u>Specific exemption:</u> <ul style="list-style-type: none"> • Metal plating (hard-metal plating) only in closed-loop systems • Fire-fighting foam for liquid fuel vapour suppression and liquid fuel fires (Class B fires) in installed systems, including both mobile and fixed systems, in accordance with paragraph 10 of part III of this Annex

Notes:

- (i) Except as otherwise specified in this Convention, quantities of a chemical occurring as unintentional trace contaminants in products and articles shall not be considered to be listed in this Annex;
- (ii) This note shall not be considered as a production and use acceptable purpose or specific exemption for purposes of paragraph 2 of Article 3. Quantities of a chemical occurring as constituents of articles manufactured or already in use before or on the date of entry into force of the relevant obligation with respect to that chemical, shall not be considered as listed in this Annex, provided that a Party has notified the Secretariat that a particular type of article remains in use within that Party. The Secretariat shall make such notifications publicly available;
- (iii) This note shall not be considered as a production and use specific exemption for purposes of paragraph 2 of Article 3. Given that no significant quantities of the chemical are expected to reach humans and the environment during the production and use of a closed-system site-limited intermediate, a Party, upon notification to the Secretariat, may allow the production and use of quantities of a chemical listed in this Annex as a closed-system site-limited intermediate that is chemically transformed in the manufacture of other chemicals that, taking into consideration the criteria in paragraph 1 of Annex D, do not exhibit the characteristics of persistent organic pollutants. This notification shall include information on total production and use of such chemical or a reasonable estimate of such information and information regarding the nature of the closed-system site-limited process including the amount of any non-transformed and unintentional trace contamination of the persistent organic pollutant-starting material in the final product. This procedure applies except as otherwise specified in this Annex. The Secretariat shall make such notifications available to the Conference of the Parties and to the public. Such production or use shall not be considered a production or use specific exemption. Such production and use shall cease after a ten-year period, unless the Party concerned submits a new notification to the Secretariat, in which case the period will be extended for an additional ten years unless the Conference of the Parties, after a review of the production and use decides otherwise. The notification procedure can be repeated;

- (iv) All the specific exemptions in this Annex may be exercised by Parties that have registered in respect of them in accordance with Article 4.

Part II

DDT (1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane)

1. The production and use of DDT shall be eliminated except for Parties that have notified the Secretariat of their intention to produce and/or use it. A DDT Register is hereby established and shall be available to the public. The Secretariat shall maintain the DDT Register.
2. Each Party that produces and/or uses DDT shall restrict such production and/or use for disease vector control in accordance with the World Health Organization recommendations and guidelines on the use of DDT and when locally safe, effective and affordable alternatives are not available to the Party in question.
3. In the event that a Party not listed in the DDT Register determines that it requires DDT for disease vector control, it shall notify the Secretariat as soon as possible in order to have its name added forthwith to the DDT Register. It shall at the same time notify the World Health Organization.
4. Every three years, each Party that uses DDT shall provide to the Secretariat and the World Health Organization information on the amount used, the conditions of such use and its relevance to that Party's disease management strategy, in a format to be decided by the Conference of the Parties in consultation with the World Health Organization.
5. With the goal of reducing and ultimately eliminating the use of DDT, the Conference of the Parties shall encourage:
 - (a) Each Party using DDT to develop and implement an action plan as part of the implementation plan specified in Article 7. That action plan shall include:
 - (i) Development of regulatory and other mechanisms to ensure that DDT use is restricted to disease vector control;
 - (ii) Implementation of suitable alternative products, methods and strategies, including resistance management strategies to ensure the continuing effectiveness of these alternatives;

- (iii) Measures to strengthen health care and to reduce the incidence of the disease.
 - (b) The Parties, within their capabilities, to promote research and development of safe alternative chemical and non-chemical products, methods and strategies for Parties using DDT, relevant to the conditions of those countries and with the goal of decreasing the human and economic burden of disease. Factors to be promoted when considering alternatives or combinations of alternatives shall include the human health risks and environmental implications of such alternatives. Viable alternatives to DDT shall pose less risk to human health and the environment, be suitable for disease control based on conditions in the Parties in question and be supported with monitoring data.
6. Commencing at its first meeting, and at least every three years thereafter, the Conference of the Parties shall, in consultation with the World Health Organization, evaluate the continued need for DDT for disease vector control on the basis of available scientific, technical, environmental and economic information, including:
- (a) The production and use of DDT and the conditions set out in paragraph 2;
 - (b) The availability, suitability and implementation of the alternatives to DDT; and
 - (c) Progress in strengthening the capacity of countries to transfer safely to reliance on such alternatives.
7. A Party may, at any time, withdraw its name from the DDT Registry upon written notification to the Secretariat. The withdrawal shall take effect on the date specified in the notification.

Part III

Perfluorooctane sulfonic acid, its salts, and perfluorooctane sulfonyl fluoride

1. The production and use of perfluorooctane sulfonic acid (PFOS), its salts and perfluorooctane sulfonyl fluoride (PFOSF) shall be eliminated by all Parties except as provided in Part I of this Annex for Parties that have notified the Secretariat of their intention to produce and/or use them for acceptable purposes. A Register of

Acceptable Purposes is hereby established and shall be available to the public. The Secretariat shall maintain the Register of Acceptable Purposes. In the event that a Party not listed in the Register determines that it requires the use of PFOS, its salts or PFOSF for the acceptable purposes listed in Part I of this Annex it shall notify the Secretariat as soon as possible in order to have its name added forthwith to the Register.

2. Parties that produce and/or use these chemicals shall take into account, as appropriate, guidance such as that given in the relevant parts of the general guidance on best available techniques and best environmental practices given in Part V of Annex C of the Convention.

3. Every four years, each Party that uses and/or produces these chemicals shall report on progress made to eliminate PFOS, its salts and PFOSF and submit information on such progress to the Conference of the Parties pursuant to and in the process of reporting under Article 15 of the Convention.

4. With the goal of reducing and ultimately eliminating the production and/or use of these chemicals, the Conference of the Parties shall encourage:

- (a) Each Party using these chemicals to take action to phase out uses when suitable alternative substances or methods are available;
- (b) Each Party using and/or producing these chemicals to develop and implement an action plan as part of the implementation plan specified in Article 7 of the Convention;
- (c) The Parties, within their capabilities, to promote research on and development of safe alternative chemical and non-chemical products and processes, methods and strategies for Parties using these chemicals, relevant to the conditions of those Parties. Factors to be promoted when considering alternatives or combinations of alternatives shall include the human health risks and environmental implications of such alternatives.

5. The Conference of the Parties shall evaluate the continued need for these chemicals for the various acceptable purposes and specific exemptions on the basis of available scientific, technical, environmental and economic information, including:

- (a) Information provided in the reports described in paragraph 3;
- (b) Information on the production and use of these chemicals;

- (c) Information on the availability, suitability and implementation of alternatives to these chemicals;
 - (d) Information on progress in building the capacity of countries to transfer safely to reliance on such alternatives.
6. The evaluation referred to in the preceding paragraph shall take place no later than in 2015 and every four years thereafter, in conjunction with a regular meeting of the Conference of the Parties.
7. Due to the complexity of the use and the many sectors of society involved in the use of these chemicals, there might be other uses of these chemicals of which countries are not presently aware. Parties which become aware of other uses are encouraged to inform the Secretariat as soon as possible.
8. A Party may, at any time, withdraw its name from the Register of acceptable purposes upon written notification to the Secretariat. The withdrawal shall take effect on the date specified in the notification.
9. The provisions of note (iii) of Part I of Annex B shall not apply to these chemicals.
10. Each Party that has registered for an exemption pursuant to Article 4 for the use of PFOS, its salts and PFOSF for fire-fighting foam shall:
- (a) Notwithstanding paragraph 2 of Article 3, ensure that fire-fighting foam that contains or may contain PFOS, its salts and PFOSF shall not be exported or imported except for the purpose of environmentally sound disposal as set forth in paragraph 1 (d) of Article 6;
 - (b) Not use fire-fighting foam that contains or may contain PFOS, its salts and PFOSF for training;
 - (c) Not use fire-fighting foam that contains or may contain PFOS, its salts and PFOSF for testing unless all releases are contained;
 - (d) By the end of 2022, if it has the capacity to do so, restrict uses of fire-fighting foam that contains or may contain PFOS, its salts and PFOSF to sites where all releases can be contained;
 - (e) Make determined efforts designed to lead to the environmentally sound management of fire-fighting foam stockpiles and wastes that contain or may contain PFOS, its salts and PFOSF, in accordance with paragraph 1 of Article 6, as soon as possible.

ANNEX C⁵

UNINTENTIONAL PRODUCTION

Part I

Persistent organic pollutants subject to the requirements of Article 5

This Annex applies to the following persistent organic pollutants when formed and released unintentionally from anthropogenic sources:

Chemical

Hexachlorobenzene (HCB) [CAS No: 118-74-1]

Hexachlorobutadiene [CAS No: 87-68-3]

Pentachlorobenzene (PeCB) [CAS No: 608-93-5]

Polychlorinated biphenyls (PCB)

Polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/PCDF)

Polychlorinated naphthalenes, including dichlorinated naphthalenes, trichlorinated naphthalenes, tetrachlorinated naphthalenes, pentachlorinated naphthalenes, hexachlorinated naphthalenes, heptachlorinated naphthalenes, octachlorinated naphthalene

Part II

Source categories

Hexachlorobenzene, hexachlorobutadiene, pentachlorobenzene, polychlorinated biphenyls, polychlorinated dibenzo-*p*-dioxins and dibenzofurans, polychlorinated naphthalenes, including dichlorinated naphthalenes, trichlorinated naphthalenes, tetrachlorinated naphthalenes, pentachlorinated naphthalenes, hexachlorinated naphthalenes, heptachlorinated naphthalenes, octachlorinated naphthalene are unintentionally formed and released from thermal processes involving organic matter and chlorine as a result of incomplete combustion or chemical reactions.

⁵ As amended by decisions SC-4/16 and SC-4/18 of 8 May 2009; SC-7/14 of 15 May 2015; and SC-8/12 of 5 May 2017.

The following industrial source categories have the potential for comparatively high formation and release of these chemicals to the environment:

- (a) Waste incinerators, including co-incinerators of municipal, hazardous or medical waste or of sewage sludge;
- (b) Cement kilns firing hazardous waste;
- (c) Production of pulp using elemental chlorine or chemicals generating elemental chlorine for bleaching;
- (d) The following thermal processes in the metallurgical industry:
 - (i) Secondary copper production;
 - (ii) Sinter plants in the iron and steel industry;
 - (iii) Secondary aluminium production;
 - (iv) Secondary zinc production.

Part III

Source categories

Hexachlorobenzene, hexachlorobutadiene, pentachlorobenzene, polychlorinated biphenyls, polychlorinated dibenzo-*p*-dioxins and dibenzofurans, polychlorinated naphthalenes, including dichlorinated naphthalenes, trichlorinated naphthalenes, tetrachlorinated naphthalenes, pentachlorinated naphthalenes, hexachlorinated naphthalenes, heptachlorinated naphthalenes, octachlorinated naphthalene may also be unintentionally formed and released from the following source categories, including:

- (a) Open burning of waste, including burning of landfill sites;
- (b) Thermal processes in the metallurgical industry not mentioned in Part II;
- (c) Residential combustion sources;
- (d) Fossil fuel-fired utility and industrial boilers;
- (e) Firing installations for wood and other biomass fuels;

- (f) Specific chemical production processes releasing unintentionally formed persistent organic pollutants, especially production of chlorophenols and chloranil;
- (g) Crematoria;
- (h) Motor vehicles, particularly those burning leaded gasoline;
- (i) Destruction of animal carcasses;
- (j) Textile and leather dyeing (with chloranil) and finishing (with alkaline extraction);
- (k) Shredder plants for the treatment of end of life vehicles;
- (l) Smouldering of copper cables;
- (m) Waste oil refineries.

Part IV

Definitions

1. For the purposes of this Annex:
 - (a) “Polychlorinated biphenyls” means aromatic compounds formed in such a manner that the hydrogen atoms on the biphenyl molecule (two benzene rings bonded together by a single carbon-carbon bond) may be replaced by up to ten chlorine atoms; and
 - (b) “Polychlorinated dibenzo-p-dioxins” and “polychlorinated dibenzofurans” are tricyclic, aromatic compounds formed by two benzene rings connected by two oxygen atoms in polychlorinated dibenzo-p-dioxins and by one oxygen atom and one carbon-carbon bond in polychlorinated dibenzofurans and the hydrogen atoms of which may be replaced by up to eight chlorine atoms.
2. In this Annex, the toxicity of polychlorinated dibenzo-p-dioxins and dibenzofurans is expressed using the concept of toxic equivalency which measures the relative dioxin-like toxic activity of different congeners of polychlorinated dibenzo-p-dioxins and dibenzofurans and coplanar polychlorinated biphenyls in comparison to

2,3,7,8-tetrachlorodibenzo-p-dioxin. The toxic equivalent factor values to be used for the purposes of this Convention shall be consistent with accepted international standards, commencing with the World Health Organization 1998 mammalian toxic equivalent factor values for polychlorinated dibenzo-p-dioxins and dibenzofurans and coplanar polychlorinated biphenyls. Concentrations are expressed in toxic equivalents.

Part V

General guidance on best available techniques and best environmental practices

This Part provides general guidance to Parties on preventing or reducing releases of the chemicals listed in Part I.

A. General prevention measures relating to both best available techniques and best environmental practices

Priority should be given to the consideration of approaches to prevent the formation and release of the chemicals listed in Part I. Useful measures could include:

- (a) The use of low-waste technology;
- (b) The use of less hazardous substances;
- (c) The promotion of the recovery and recycling of waste and of substances generated and used in a process;
- (d) Replacement of feed materials which are persistent organic pollutants or where there is a direct link between the materials and releases of persistent organic pollutants from the source;
- (e) Good housekeeping and preventive maintenance programmes;
- (f) Improvements in waste management with the aim of the cessation of open and other uncontrolled burning of wastes, including the burning of landfill sites. When considering proposals to construct new waste disposal facilities, consideration should be given to alternatives such as activities to minimize the generation of municipal and medical waste, including resource recovery, reuse, recycling, waste separation and promoting products that generate less waste. Under this approach, public health concerns should be carefully considered;

- (g) Minimization of these chemicals as contaminants in products;
- (h) Avoiding elemental chlorine or chemicals generating elemental chlorine for bleaching.

B. Best available techniques

The concept of best available techniques is not aimed at the prescription of any specific technique or technology, but at taking into account the technical characteristics of the installation concerned, its geographical location and the local environmental conditions. Appropriate control techniques to reduce releases of the chemicals listed in Part I are in general the same. In determining best available techniques, special consideration should be given, generally or in specific cases, to the following factors, bearing in mind the likely costs and benefits of a measure and consideration of precaution and prevention:

- (a) General considerations:
 - (i) The nature, effects and mass of the releases concerned: techniques may vary depending on source size;
 - (ii) The commissioning dates for new or existing installations;
 - (iii) The time needed to introduce the best available technique;
 - (iv) The consumption and nature of raw materials used in the process and its energy efficiency;
 - (v) The need to prevent or reduce to a minimum the overall impact of the releases to the environment and the risks to it;
 - (vi) The need to prevent accidents and to minimize their consequences for the environment;
 - (vii) The need to ensure occupational health and safety at workplaces;
 - (viii) Comparable processes, facilities or methods of operation which have been tried with success on an industrial scale;
 - (ix) Technological advances and changes in scientific knowledge and understanding.

(b) General release reduction measures: When considering proposals to construct new facilities or significantly modify existing facilities using processes that release chemicals listed in this Annex, priority consideration should be given to alternative processes, techniques or practices that have similar usefulness but which avoid the formation and release of such chemicals. In cases where such facilities will be constructed or significantly modified, in addition to the prevention measures outlined in section A of Part V the following reduction measures could also be considered in determining best available techniques:

- (i) Use of improved methods for flue-gas cleaning such as thermal or catalytic oxidation, dust precipitation, or adsorption;
- (ii) Treatment of residuals, wastewater, wastes and sewage sludge by, for example, thermal treatment or rendering them inert or chemical processes that detoxify them;
- (iii) Process changes that lead to the reduction or elimination of releases, such as moving to closed systems;
- (iv) Modification of process designs to improve combustion and prevent formation of the chemicals listed in this Annex, through the control of parameters such as incineration temperature or residence time.

C. Best environmental practices

The Conference of the Parties may develop guidance with regard to best environmental practices.

ANNEX D

INFORMATION REQUIREMENTS AND SCREENING CRITERIA

1. A Party submitting a proposal to list a chemical in Annexes A, B and/or C shall identify the chemical in the manner described in subparagraph (a) and provide the information on the chemical, and its transformation products where relevant, relating to the screening criteria set out in subparagraphs (b) to (e):

(a) Chemical identity:

- (i) Names, including trade name or names, commercial name or names and synonyms, Chemical Abstracts Service (CAS) Registry number, International Union of Pure and Applied Chemistry (IUPAC) name; and
- (ii) Structure, including specification of isomers, where applicable, and the structure of the chemical class;

(b) Persistence:

- (i) Evidence that the half-life of the chemical in water is greater than two months, or that its half-life in soil is greater than six months, or that its half-life in sediment is greater than six months; or
- (ii) Evidence that the chemical is otherwise sufficiently persistent to justify its consideration within the scope of this Convention;

(c) Bio-accumulation:

- (i) Evidence that the bio-concentration factor or bio-accumulation factor in aquatic species for the chemical is greater than 5,000 or, in the absence of such data, that the log K_{ow} is greater than 5;
- (ii) Evidence that a chemical presents other reasons for concern, such as high bio-accumulation in other species, high toxicity or ecotoxicity; or
- (iii) Monitoring data in biota indicating that the bio-accumulation potential of the chemical is sufficient to justify its consideration within the scope of this Convention;

- (d) Potential for long-range environmental transport:
 - (i) Measured levels of the chemical in locations distant from the sources of its release that are of potential concern;
 - (ii) Monitoring data showing that long-range environmental transport of the chemical, with the potential for transfer to a receiving environment, may have occurred via air, water or migratory species; or
 - (iii) Environmental fate properties and/or model results that demonstrate that the chemical has a potential for long-range environmental transport through air, water or migratory species, with the potential for transfer to a receiving environment in locations distant from the sources of its release. For a chemical that migrates significantly through the air, its half-life in air should be greater than two days; and
- (e) Adverse effects:
 - (i) Evidence of adverse effects to human health or to the environment that justifies consideration of the chemical within the scope of this Convention; or
 - (ii) Toxicity or ecotoxicity data that indicate the potential for damage to human health or to the environment.

2. The proposing Party shall provide a statement of the reasons for concern including, where possible, a comparison of toxicity or ecotoxicity data with detected or predicted levels of a chemical resulting or anticipated from its long-range environmental transport, and a short statement indicating the need for global control.

3. The proposing Party shall, to the extent possible and taking into account its capabilities, provide additional information to support the review of the proposal referred to in paragraph 6 of Article 8. In developing such a proposal, a Party may draw on technical expertise from any source.

ANNEX E

INFORMATION REQUIREMENTS FOR THE RISK PROFILE

The purpose of the review is to evaluate whether the chemical is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted. For this purpose, a risk profile shall be developed that further elaborates on, and evaluates, the information referred to in Annex D and includes, as far as possible, the following types of information:

- (a) Sources, including as appropriate:
 - (i) Production data, including quantity and location;
 - (ii) Uses; and
 - (iii) Releases, such as discharges, losses and emissions;
- (b) Hazard assessment for the endpoint or endpoints of concern, including a consideration of toxicological interactions involving multiple chemicals;
- (c) Environmental fate, including data and information on the chemical and physical properties of a chemical as well as its persistence and how they are linked to its environmental transport, transfer within and between environmental compartments, degradation and transformation to other chemicals. A determination of the bio-concentration factor or bio-accumulation factor, based on measured values, shall be available, except when monitoring data are judged to meet this need;
- (d) Monitoring data;
- (e) Exposure in local areas and, in particular, as a result of long-range environmental transport, and including information regarding bio-availability;
- (f) National and international risk evaluations, assessments or profiles and labelling information and hazard classifications, as available; and
- (g) Status of the chemical under international conventions.

ANNEX F

INFORMATION ON SOCIO-ECONOMIC CONSIDERATIONS

An evaluation should be undertaken regarding possible control measures for chemicals under consideration for inclusion in this Convention, encompassing the full range of options, including management and elimination. For this purpose, relevant information should be provided relating to socio-economic considerations associated with possible control measures to enable a decision to be taken by the Conference of the Parties. Such information should reflect due regard for the differing capabilities and conditions among the Parties and should include consideration of the following indicative list of items:

- (a) Efficacy and efficiency of possible control measures in meeting risk reduction goals:
 - (i) Technical feasibility; and
 - (ii) Costs, including environmental and health costs;
- (b) Alternatives (products and processes):
 - (i) Technical feasibility;
 - (ii) Costs, including environmental and health costs;
 - (iii) Efficacy;
 - (iv) Risk;
 - (v) Availability; and
 - (vi) Accessibility;
- (c) Positive and/or negative impacts on society of implementing possible control measures:
 - (i) Health, including public, environmental and occupational health;
 - (ii) Agriculture, including aquaculture and forestry;
 - (iii) Biota (biodiversity);

- (iv) Economic aspects;
 - (v) Movement towards sustainable development; and
 - (vi) Social costs;
- (d) Waste and disposal implications (in particular, obsolete stocks of pesticides and clean-up of contaminated sites):
- (i) Technical feasibility; and
 - (ii) Cost;
- (e) Access to information and public education;
- (f) Status of control and monitoring capacity; and
- (g) Any national or regional control actions taken, including information on alternatives, and other relevant risk management information.

ANNEX G

ARBITRATION AND CONCILIATION PROCEDURES FOR SETTLEMENT OF DISPUTES⁶

Part I

Arbitration procedure

The arbitration procedure for purposes of paragraph 2 (a) of Article 18 of the Convention shall be as follows:

Article 1

1. A Party may initiate recourse to arbitration in accordance with Article 18 of the Convention by written notification addressed to the other party to the dispute. The notification shall be accompanied by a statement of the claim, together with any supporting documents, and state the subject-matter of arbitration and include, in particular, the articles of the Convention the interpretation or application of which are at issue.

2. The claimant party shall notify the Secretariat that the parties are referring a dispute to arbitration pursuant to Article 18. The notification shall be accompanied by the written notification of the claimant party, the statement of claim and the supporting documents referred to in paragraph 1 above. The Secretariat shall forward the information thus received to all Parties.

Article 2

1. If a dispute is referred to arbitration in accordance with Article 1 above, an arbitral tribunal shall be established. It shall consist of three members.

2. Each of the parties to the dispute shall appoint an arbitrator and the two arbitrators so appointed shall designate by common agreement the third arbitrator, who shall be the President of the tribunal. The President of the tribunal shall not be a national of one of the parties to the dispute, nor have his or her usual place of

⁶ Annex G was adopted by the first meeting of the Conference of the Parties in its decision SC-1/2

residence in the territory of one of those parties, nor be employed by any of them, nor have dealt with the case in any other capacity.

3. In disputes between more than two parties, parties in the same interest shall appoint one arbitrator jointly by agreement.

4. Any vacancy shall be filled in the manner prescribed for the initial appointment.

5. If the parties do not agree on the subject-matter of the dispute before the President of the arbitral tribunal is designated, the arbitral tribunal shall determine the subject-matter.

Article 3

1. If one of the parties to the dispute does not appoint an arbitrator within two months of the date on which the respondent party receives the notification of the arbitration, the other party may inform the Secretary-General of the United Nations, who shall make the designation within a further two-month period.

2. If the President of the arbitral tribunal has not been designated within two months of the date of the appointment of the second arbitrator, the Secretary-General of the United Nations shall, at the request of a party, designate the President within a further two-month period.

Article 4

The arbitral tribunal shall render its decisions in accordance with the provisions of the Convention and international law.

Article 5

Unless the parties to the dispute otherwise agree, the arbitral tribunal shall determine its own rules of procedure.

Article 6

The arbitral tribunal may, at the request of one of the parties, indicate essential interim measures of protection.

Article 7

The parties to the dispute shall facilitate the work of the arbitral tribunal and, in particular, using all means at their disposal, shall:

- (a) Provide it with all relevant documents, information and facilities; and
- (b) Enable it, when necessary, to call witnesses or experts and receive their evidence.

Article 8

The parties and the arbitrators are under an obligation to protect the confidentiality of any information they receive in confidence during the proceedings of the arbitral tribunal.

Article 9

Unless the arbitral tribunal determines otherwise because of the particular circumstances of the case, the costs of the tribunal shall be borne by the parties to the dispute in equal shares. The tribunal shall keep a record of all its costs, and shall furnish a final statement thereof to the parties.

Article 10

A party that has an interest of a legal nature in the subject matter of the dispute which may be affected by the decision in the case may intervene in the proceedings with the consent of the tribunal.

Article 11

The tribunal may hear and determine counterclaims arising directly out of the subject matter of the dispute.

Article 12

Decisions both on procedure and substance of the arbitral tribunal shall be taken by a majority vote of its members.

Article 13

1. If one of the parties to the dispute does not appear before the arbitral tribunal or fails to defend its case, the other party may request the tribunal to continue the proceedings and to make its award. Absence of a party or a failure of a party to defend its case shall not constitute a bar to the proceedings.

2. Before rendering its final decision, the arbitral tribunal must satisfy itself that the claim is well founded in fact and law.

Article 14

The tribunal shall render its final decision within five months of the date on which it is fully constituted unless it finds it necessary to extend the time limit for a period which should not exceed five more months.

Article 15

The final decision of the arbitral tribunal shall be confined to the subject matter of the dispute and shall state the reasons on which it is based. It shall contain the names of the members who have participated and the date of the final decision. Any member of the tribunal may attach a separate or dissenting opinion to the final decision.

Article 16

The award shall be binding on the parties to the dispute. The interpretation of the Convention given by the award shall also be binding upon a Party intervening under Article 10 above insofar as it relates to matters in respect of which that Party intervened. The award shall be without appeal unless the parties to the dispute have agreed in advance to an appellate procedure.

Article 17

Any controversy which may arise between those bound by the final decision in accordance with Article 16 above, as regards the interpretation or manner of implementation of that decision, may be submitted by any of them for decision to the arbitral tribunal which rendered it.

Part II

Conciliation procedure

The conciliation procedure for purposes of paragraph 6 of Article 18 of the Convention shall be as follows:

Article 1

1. A request by a party to a dispute to establish a conciliation commission in consequence of paragraph 6 of Article 18 shall be addressed in writing to the Secretariat. The Secretariat shall forthwith inform all Parties to the Convention accordingly.

2. The conciliation commission shall, unless the parties otherwise agree, be composed of three members, one appointed by each party concerned and a President chosen jointly by those members.

Article 2

In disputes between more than two parties, parties in the same interest shall appoint their members of the commission jointly by agreement.

Article 3

If any appointments by the parties are not made within two months of the date of receipt by the Secretariat of the written request referred to in Article 1, the Secretary-General of the United Nations shall, upon request by a party, make those appointments within a further two-month period.

Article 4

If the President of the conciliation commission has not been chosen within two months of the second member of the commission being appointed, the Secretary-General of the United Nations shall, upon request by a party, designate the President within a further two-month period.

Article 5

1. The conciliation commission shall, unless the parties to the dispute otherwise agree, determine its own rules of procedure.
2. The parties and members of the commission are under an obligation to protect the confidentiality of any information they receive in confidence during the proceedings of the commission.

Article 6

The conciliation commission shall take its decisions by a majority vote of its members.

Article 7

The conciliation commission shall render a report with recommendations for resolution of the dispute within twelve months of being established, which the parties shall consider in good faith.

Article 8

Any disagreement as to whether the conciliation commission has competence to consider a matter referred to it shall be decided by the commission.

Article 9

The costs of the commission shall be borne by the parties to the dispute in shares agreed by them. The commission shall keep the record of all its costs and shall furnish a final statement thereof to the parties.

www.pops.int

Secretariat of the Stockholm Convention

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This is **Exhibit “S”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Government
of Canada

Gouvernement
du Canada

[Canada.ca](#) > [Environment and Climate Change Canada](#)

> [International affairs and the environment](#)

> [Partnerships with international organizations](#)

Persistent organic pollutants: Stockholm Convention

Official title: Stockholm Convention on Persistent Organic Pollutants (POPs)

Subject category:

Chemicals & Wastes

Type of agreement / instrument:

Multilateral

Form:

Legally binding treaty

Status:

- Signed by Canada May 23, 2001
- Ratified by Canada May 23, 2001
- In force in Canada May 17, 2004
- In force internationally May 17, 2004

Lead & partner departments:

Lead:

Environment and Climate Change Canada

Partners:

Health Canada-Pest Management Regulatory Agency, Crown-Indigenous Relations and Northern Affairs Canada, Global Affairs Canada

For further information:**Web links:**

- [Stockholm Convention](#)
- [Text of the Convention](#)
- [Management of Toxic Substances in Canada](#)

Contacts:

[ECCC Inquiry Centre](#)

Compendium edition:

January 2020

Reference #:

A31/EN



[Stockholm Convention on Persistent Organic Pollutants \(POPs\)](#)

[\[PDF \(Portable Document Format\) - 614 KB \(Kilobyte\)\]](#)

Plain language summary

The Convention aims to reduce levels of POPs entering the environment over time; by eliminating or restricting releases of POP industrial chemicals and pesticides, unintentionally produced POP by-products and stockpiles and POP wastes. Due to the tendency of POPs to migrate long distances and accumulate in northern climates, Canada continues to be particularly impacted by POPs and inhabitants of Canada's North are at greater risk for POPs exposure. Canada has therefore played a major leadership role in efforts to control POPs and in the development of this

global treaty, and was the first country to sign and ratify the Convention in 2001.

Objective

The objective of the [Stockholm Convention](#) is to protect human health and the environment from Persistent Organic Pollutants (POPs).

Key elements

Effective implementation of the Stockholm Convention is of vital interest to Canada because it will reduce Canada's exposure to major foreign sources of POPs. Due to the tendency of POPs to migrate long distances and accumulate in northern climates, Canada continues to be particularly impacted by POPs and inhabitants of Canada's North are at greater risk for POPs exposure.

Each Party is required to develop a National Implementation Plan detailing measures taken to implement obligations under the Convention. In addition, national reporting every four years is also required, where each Party provides statistical data on total quantities of production, import and export of listed chemicals, the measures taken to implement the provisions of the Convention, as well as the effectiveness of such measures in meeting the objectives of the Convention.

The Convention has a financial mechanism, operated by the Global Environment Facility, to assist developing countries and countries with economies in transition to implement and meet their obligations. A regular effectiveness evaluation assesses whether the Convention is meeting its objective.

Expected results

The Convention aims to reduce levels of POPs entering the environment over time; as a result of eliminating or restricting releases of POP industrial chemicals and pesticides, unintentionally produced POP by-products and stockpiles and wastes containing POPs.

The effectiveness of the Convention is evaluated on the basis of available scientific, environmental, technical and economic information, including:

1. Reports and other monitoring information on the presence of POPs and their regional and global environmental transport;
2. National reports from Parties; and
3. Non-compliance information.

Canada's involvement

Effective implementation of the Stockholm Convention is of vital interest to Canada because it will reduce Canada's exposure to major foreign sources of POPs.

Canada takes a risk-based approach to chemical substances, using strong science, assessment, management and monitoring tools. The Chemicals Management Plan assesses chemicals used in Canada and takes action on chemicals found to be harmful, including POPs. The production, use and release of POPs are managed through a well-established regulatory and policy framework involving both federal and provincial/territorial agencies. At the federal level, key policies and legislation governing chemical substances in food, drugs, pesticides and products include the Canadian Environmental Protection Act, 1999, the Pest Control Products Act and the Toxic Substances Management Policy.

Results / progress

Activities

Canada played a major leadership role in early efforts to control POPs and to develop this global treaty, and was the first country to sign and ratify the Convention in 2001. Canada also championed inclusion of effectiveness evaluation provisions and provided a \$20 million Canada POPs Fund to assist developing countries build their capacities to address POPs.

The National Implementation Plan (NIP) is reviewed periodically and updated to address new obligations under the Convention. Canada submitted its initial and updated NIPs in 2006 and 2013 respectively.

Canada actively participates on the POPs Review Committee (POPRC), a subsidiary technical body to the Convention, assisting in efforts to scientifically assess candidate POPs for addition to the Convention. Canada has also contributed expertise to help develop technical guidelines on POP wastes and to establish a Global POPs Monitoring Group for evaluating the effectiveness of the Convention. Canada monitors and conducts research on the pathways and effects of POPs through a number of programs, most notably the Northern Contaminants Program (NCP). Canada also participates in POPs-related monitoring and assessment by the Arctic Council's Arctic Monitoring and Assessment Programme (AMAP). The NCP and AMAP provided much of the foundational science on which the Convention is based.

POPs in Canada are regulated through the Prohibition of Certain Toxic Substances Regulations, 2012, the PCB Regulations, 2008, and the Pest Control Products Act, which prohibit production and use of several POPs.

The *Export of Substances on the Export Control List Regulations* control the export of POPs.

Reports

National reports contain information on the measures taken by a Party in implementing the Stockholm Convention, provide quantitative information on the effectiveness of such measures in meeting the objectives of the Convention, and must be submitted every four years. Canada's national reports, from 2006 to 2018 are available at the Convention's [National Reports](#) website.

The [Global Monitoring Plan](#) (GMP) under the Convention provides a harmonized organizational framework for the collection of comparable monitoring data on the presence of POPs from all regions, in order to identify changes in their concentrations over time, as well as on regional and global environmental transport. Canada is a key contributor to this report, available at the Convention's [Monitoring Reports](#) website.

Progress: National actions by all Parties to implement the Convention are ongoing. The most important indication of whether the Convention is meeting its objective comes from the results of the first six-year cycle (between 2010 and 2017) of the Convention's [Effectiveness Evaluation](#). Two key data sources for this evaluation are the National Reports submitted by Parties and the GMP report.

Results

The Stockholm Convention currently includes 30 POPs for elimination or restriction. Canada has put in place regulatory measures for all POPs and has ratified the listing of 21 of these substances.

Date modified:

2020-04-27

This is **Exhibit “T”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Stockholm Convention on Persistent Organic Pollutants

Persistent Organic Pollutants Review Committee

Seventeenth meeting

Geneva, 24–28 January 2022*

Item 4 (c) (i) of the provisional agenda**

Technical work: consideration of chemicals proposed for listing in Annexes A, B and/or C to the Convention: chlorpyrifos

Proposal to list chlorpyrifos in Annex A to the Stockholm Convention on Persistent Organic Pollutants

Note by the Secretariat

I. Introduction

1. The European Union has submitted a proposal to list chlorpyrifos in Annex A to the Stockholm Convention on Persistent Organic Pollutants, pursuant to paragraph 1 of Article 8 of the Convention (see annex to the present note). The proposal is being circulated as submitted and has not been formally edited. Additional information relating to the proposal is set out in document UNEP/POPS/POPRC.17/INF/4, as submitted by the European Union. The Secretariat's verification of whether the proposal contains the information specified in Annex D to the Convention is set out in document UNEP/POPS/POPRC.17/INF/6.

II. Proposed action

2. The Committee may wish:

- (a) To consider the information provided in the present note;
- (b) To decide whether it is satisfied that the proposal fulfils the requirements of Article 8 of and Annex D to the Convention;
- (c) To develop and agree on, if it decides that the proposal fulfils the requirements referred to in subparagraph 2 (b) above, a workplan for preparing a draft risk profile pursuant to paragraph 6 of Article 8 of the Convention.

* Subject to a final decision by the Bureau of the Persistent Organic Pollutants Review Committee in October 2021, taking into account the situation regarding the coronavirus disease (COVID-19) pandemic.

** UNEP/POPS/POPRC.17/1.

Annex

Proposal to list chlorpyrifos in Annex A to the Stockholm Convention on Persistent Organic Pollutants

1. Introduction

1. Chlorpyrifos, which belongs to the group of organophosphate pesticides, is widely applied as an insecticide in agriculture and as a biocide to control non-agricultural pests. In 2008 chlorpyrifos products were authorised for use in more than 88 countries. Usage as a biocide was phased-out in the European Union by Commission Decision (2007/565/EC) by 2008 (European Union, 2007). A decision on phasing out most non-agricultural applications was adopted by the EPA in 2000 (US-EPA, 2006). However, usage as a biocide, e.g. for termite control in buildings, is still practiced in other countries. For example, termite control is still recommended by the Indian authorities (India, 2020).

2. In 2014 the human health risk assessment on chlorpyrifos was revised by the US-EPA (2014). Risks were identified for workers; also, potential risks were found for drinking water. According to the US-EPA (2017) exposure to chlorpyrifos is also linked to the delay of mental development of young children.

3. In 2019, the renewal of the approval of chlorpyrifos for use as active substance in plant protection products has been denied in the European Union (European Union, 2020), following the risk assessment carried out by Member States and the European Food Safety Authority (EFSA, 2019). EFSA concluded that the approval criteria, which are applicable to human health as laid down in Article 4 of Regulation (EC) No 1107/2009 are not met. The decision was based on uncertainty regarding genotoxic potential and potential neurodevelopmental toxicity of chlorpyrifos. Furthermore, chlorpyrifos is banned in Morocco (ONSSA, 2020), Saudi Arabia, Sri Lanka (PIC Database, 2021), Indonesia (Indonesia, 2019) and Switzerland (Switzerland, 2019).

4. The data presented in this dossier is considered relevant, unless noted otherwise. All other information, as well as most tables, can be found in document UNEP/POPS/POPRC.17/INF/4.

2. Identification of the chemical

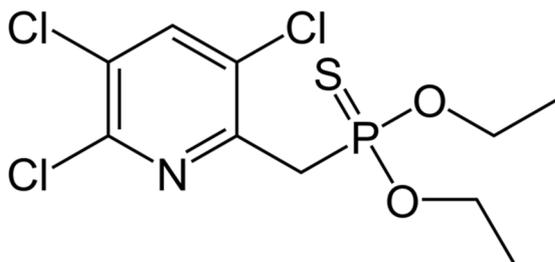
2.1 Names and identities

Table 1 Chemical identity of chlorpyrifos

CAS number:	2921-88-2
CAS chemical name:	O,O-diethyl O-(3,5,6-trichloro-2-pyridyl) phosphorothioate
IUPAC name:	O,O-Diethyl O-3,5,6-trichloro-2-pyridinyl phosphorothioate
EC number:	220-864-4
Smiles code	CCOP(=S)(OCC)Oc1nc(Cl)c(Cl)cc1Cl
Molecular formula:	C ₉ H ₁₁ Cl ₃ NO ₃ PS
Molecular weight:	350.59 g/mol
Synonyms:	chlorpyriphos; chlorpyrifos-ethyl; chlorpyriphos-ethyl; O,O-diethyl O-3,5,6-trichloro-2-pyridinyl phosphorothioate; phosphorothioic acid, O,O-diethyl O-(3,5,6 trichlor-2-pyridinyl) ester
Trade names:	Dursban, OMS 0971, Lorsban, Brodan, Killmaster, Pyrinex, Suscon, Coroban, Terial, Danusban, Durmet, Eradex

5. A table of physico-chemical properties of chlorpyrifos is included in document UNEP/POPS/POPRC.17/INF/4, table 1.

2.2 Structure



Credits: Andreas Buser, CH

2.3 Transformation products

6. Transformation products of chlorpyrifos are 3,5,6-trichloro-2-pyridinol (TCP), chlorpyrifos-oxon, des-ethyl chlorpyrifos, 3,6-dichloro-2-pyridinol (3,6-DCP) and 2,3,5-trichloro-6-methoxy pyridine (TMP). For information on chemical identity and physico-chemical properties please see table 1 of document UNEP/POPS/POPRC.17/INF/4.

7. TCP is the main degradation product of chlorpyrifos (Spain, 2017). It results from hydrolysis and photolysis of chlorpyrifos (Shemer et al., 2005), via degradation of chlorpyrifos-methyl (Racke, 1993) and triclopyr (US-EPA, 1998) and the metabolization of chlorpyrifos-oxon (Sultatos & Murphy, 1983). The estimated atmospheric half-life for TCP is 60.5 days (Spain, 2017a), which indicates potential for long range transport. The Half-lives in soil show moderate to high persistence with a DT50 of up to 150 days in European assessments (Spain, 2017a) and 360 days in US-EPA assessments (US-EPA, 1998). Acute toxicity of TCP is considered lower than that of the parent compound with an 96h LC50 value of 12.6 mg/L in rainbow trout and 48h LC50 of 10.4 mg/L for *Daphnia magna* (Spain, 2017a), although *Daphnia carinata* is the susceptible species with an 48h LC50 value of 0.20 ± 0.08 µg/L (Cáceres et al., 2007). Chronic toxicity testing produced 21d NOEC of 0.029 mg/L for reproduction in *Daphnia magna* and a NOEC of 0.0808 mg/L for reduction of length and weight in rainbow trout early life stages (Spain, 2017a). TCP has a log K_{ow} of 3.21 and an estimated log K_{oa} of 9.32 (see UNEP/POPS/POPRC.17/INF/4, table 1). These values trigger the screening criteria for bioaccumulation assessment in air-breathing organisms set by ECHA (ECHA, 2017). However, no data on TCP bioaccumulation via inhalation could be identified. Aquatic bioaccumulation has been evaluated in two studies, in which BCF have been below 22 for fish, macroinvertebrates and algae (Hedlund (1973) and Lu and Metcalf (1975) as described in Racke (1993)). More data on bioaccumulation is needed to conclude on the fulfilment of the Annex D criteria for TCP.

8. Of the transformation products only chlorpyrifos-oxon is considered more toxic than the parent compound (Spain, 2017). The metabolization of chlorpyrifos to chlorpyrifos-oxon increases toxicity as the oxon exhibits a higher degree of acetylcholinesterase (AChE) inhibition (Timchalk, 2001). For more details on this pathway, please view the human health chapter of document UNEP/POPS/POPRC.17/INF/4. With a half-life of 11 hours (Muñoz et al., 2012) chlorpyrifos-oxon is more stable in air than chlorpyrifos. In other compartments it is considered less stable with half-lives of up to 30 days in soil (Mackay et al., 2014) and 40 days in water (Tunink (2010) in Mackay et al. (2014)). Based on these half-lives chlorpyrifos-oxon does not meet the Annex D criteria for persistence and is therefore not a POP candidate.

3. Information on chlorpyrifos and how it fulfils the Annex D screening criteria

3.1 Persistence

9. According to the European draft renewal assessment report (RAR) (Spain, 2017) and US-EPA (2006), the major route of dissipation of chlorpyrifos appears to be aerobic and anaerobic biodegradation. Based on available data, chlorpyrifos appears to degrade slowly in soil under both aerobic and anaerobic conditions. It has a low water solubility and a high soil binding capacity. Information on leaching and adsorption/desorption indicate that parent chlorpyrifos in soil or sediment is largely immobile. The pesticide agent can contaminate surface water via spray drift at the time of application or as runoff up to several months after application. Available data indicate that most chlorpyrifos runoff is generally via adsorption to eroding soil rather than by dissolution in runoff

water. However, under some conditions, dissolution in runoff water may be significant. All half-lives mentioned in the following chapters are listed in tables 3-7 in document UNEP/POPS/POPRC.17/INF/4.

Route of degradation and transformation products

10. Various studies examining the route of degradation have been assessed in the European RAR for chlorpyrifos (Spain, 2017b). A new study by B. Clark (2013) on the route of degradation in soil was submitted for the purpose of renewal of the EU approval of chlorpyrifos. The study was conducted according to OECD TG 307 and was considered valid by the Rapporteur Member State (RMS). A total of five metabolites were identified: the major transformation product detected was 3,5,6-Trichloro-2-pyridinol (TCP), with maximum mean concentrations of 14.8% - 59.7% in soil. Other minor metabolites, 2-Methoxy-3,5,6-trichloropyridine (TMP, max 2.9 % AR), MTCP (max 3.9 % AR), 3,5 DCMP (max 2 % AR) and 5,6 DMCP (max 0.7 % AR) were identified. Additional minor metabolites were not fully characterised or identified in the report.

11. In summary, chlorpyrifos will degrade mainly to TCP and to various other minor metabolites in soil. TCP is eventually degraded to CO₂ and to unextractable residues.

3.1.1 Abiotic degradation

12. It is reported by the US-EPA (2006) that abiotic hydrolysis, photodegradation and volatilisation do not seem to play significant roles in the dissipation process. However, according to UNEP (2012) the substance may be volatile with regard to its vapour pressure and its Henry's Law constant (for values see UNEP/POPS/POPRC.17/INF/4, table 1). It is concluded that volatilisation plays a role in the overall dissipation process in the field, but to which quantities remains unknown. Using EPI Suite's Volatilization module entering the Henry's Law constant mentioned in the dossier, volatilisation half-lives of 10 and 112 days are estimated for rivers and lakes, respectively.

Soil photolysis

13. The RAR (Spain, 2017b) lists four studies on soil photolysis (Havens et al., 1992; Racke et al., 1994; Walia et al., 1988; Yackovich et al., 1985). In the study by Havens et al. (1992), the half-life of chlorpyrifos in soil was calculated to be 30 h ($r^2=0.94$) and 28.5 hours ($r^2=0.96$) for light and dark respectively indicating that photolysis is not a significant degradation process for chlorpyrifos. The half-life for the main metabolite TCP was calculated to be 17.7 days in light, and could not be calculated in the dark since levels increased throughout the study period.

14. Racke et al. (1994) determined the photodegradation rate and identified the photodegradates of the main metabolite (TCP) of both chlorpyrifos and chlorpyrifos-methyl on soil surface. Approximately 50% of the applied TCP degraded during the first 8 hours of sunlight exposure, the half-life was calculated to be 14.1 days ($R^2 = 0.820$). The major photoproduct of TCP was CO₂ (40% AR at 30 days) and small amounts of polar and non-extractable residues were also formed. The study author suggests that these polar residues may represent transient intermediates to CO₂.

Water: Hydrolytic degradation

15. The RAR for chlorpyrifos (Spain, 2017b) lists five studies on hydrolysis. The hydrolysis of chlorpyrifos has been found by P.J. McCall (1986) to be independent of pH below pH 7 with a half-life of approximately 72 days. At alkaline pH, hydrolysis is dependent on pH with a measured half-life for chlorpyrifos of 16 days at pH 9, 25°C in this study. Under conditions encountered in the environment, where other dissipative processes act on the chemical, hydrolysis will tend to be a minor route for dissipation of the chemical. For an overview of pH dependant degradation of chlorpyrifos please see document UNEP/POPS/POPRC.17/INF/4, table 2.

16. Meikle and Youngson (1978) conducted a study to evaluate the hydrolysis rates at different pH and temperature values, and the fate of chlorpyrifos in water. In buffered distilled water at 25°C and pH 8.1, 6.9 and 4.7, the half-life was 23.1, 35.3, and 62.7 days, respectively. A comparable aqueous hydrolysis half-life at 35 °C and pH 4.7 of 15.75 days has been reported.

17. Macalady and Wolfe (1985) determined the hydrolysis of various organophosphorothioate insecticides in sediment-water samples to define the role of hydrolysis in the sediment-sorbed state. For chlorpyrifos, the observed rate constants were the same in the sediment and aqueous phases and similar in magnitude to those found for natural water samples.

18. In spite of some shortcomings, the study by Hui et al. (2010) supports the conclusions of other studies that chlorpyrifos is relatively stable in an acidic medium, but the rate of degradation increases with increasing pH. The half-life is also influenced by temperature.

19. WHO (2009) provides hydrolysis characteristics of chlorpyrifos. The half-lives in buffers at 25°C were 72 d at pH 5 and pH 7, and 16 d at pH 9 (guideline EPA Sub. N 161-1; source: Dow). The half-lives in buffers at 30°C were 72 d at pH 4.0, 40 d at pH 7.0, and 24 d at pH 9.0 (guideline EPA test method CS5000; source: Makhteshim).

20. A comprehensive discussion on chlorpyrifos hydrolysis data may be found in an evaluation by Mackay et al. (2014). These authors compiled studies from different sources. One major source for that evaluation was a review by Racke (1993). Reported half-lives for hydrolysis in distilled and natural waters at pH values between 5 and 9 (environmentally relevant pH) were between 1.5 d and 142 d. Mackay et al. (2014) reported an overall mean hydrolysis half-life of 46 d and a geometric mean half-life of 29 d. Half-lives at pH <5 were generally longer (16 - 210 d) and at pH >9 shorter (0.1 - 10 d). The authors also report that the chlorpyrifos hydrolysis half-lives are influenced by the presence of copper ions (increased hydrolysis rate) and suspended solids (decreased hydrolysis rate).

Water: Direct and indirect photochemical degradation

21. The European Union RAR for chlorpyrifos (Spain, 2017b) lists eight studies on direct photochemical degradation, one of which (Adam (2015)) also deals with indirect photochemical degradation. The study by Batzer et al. (1990) was carried out according to US EPA 161-2, using a mercury lamp as irradiation. As chlorpyrifos is more stable toward hydrolysis in acid than in alkaline solution, the influence of hydrolysis in the irradiated samples was minimized by the use of buffered solutions at pH 7. The half-lives were estimated in Jackson (1994) and amounted to 14.6 days for mid-summer at 20°N, and to 29208 days (80 years) for midwinter at 60°N. It should be noted that the long half-lives calculated for winter at northerly latitudes are unrealistic since they do not account for seasonal changes and assume that sunlight intensity does not vary from mid-winter conditions.

22. Adam (2015) concluded that chlorpyrifos is degraded by direct and indirect photolysis with net half-lives of 7.2 and 2.9 days natural summer sunlight at latitudes 30 to 50°N. For irradiated samples, it was not possible to completely avoid volatilisation of the test item from the water phase. The review by Racke (1993) cites the study by P.J. McCall (1986) who investigated photolytic degradation (0.35 - 0.38 ppm) in an aqueous buffer (pH 5) and reported a photolysis half-life of 52 days upon exposure to an artificial light source (general Electric Chroma lamps). The RMS used this information only as additional information. In the study of Meikle et al. (1983), photolysis half-lives observed ranged from 9.4 to 15.6 days (corrected for hydrolysis) and 7.8 to 11.0 days (uncorrected for hydrolysis). This study also was used as additional information. Dilling (1984) estimated half-lives for chlorpyrifos of 31 - 43 d in summer and 345 d in winter in pure water. In river water, summer half-life was estimated at 980 d for average light attenuation coefficients for ten river water samples from south-east US. The studies by Kralj et al. (2007) and Hossain et al. (2013) do not fulfil the OECD 116 test guideline and are thus not suitable to establish a reliable rate of photodegradation.

23. Although photolysis can be a degradation pathway, this is limited to the upper centimetres of a water body, depending on turbidity.

3.1.2 Biotic degradation

Water

24. The European Union RAR for chlorpyrifos (Spain, 2017b) reports one study on ready degradability according to OECD test guideline 301 (Douglas & Pell, 1985). The percentage of biodegradation after 28 days was 22%, which implies that chlorpyrifos is not readily biodegradable. In a study by (Gassen, 2015) on aerobic mineralisation in surface water, conducted according to OECD TG 309, DT50 values of 21 and 46 d at 22°C were estimated. In all systems, up to 28.5% of unchanged parent was progressively lost from the test systems due to evaporation from the aqueous layer during the incubation period, thus the DT50 values do not refer to degradation alone, but rather to dissipation: loss through volatilisation as well as degradation. In Caviezel (2015) dissipation of chlorpyrifos was mainly caused by volatilisation from the surface water, reaching between 58.6% and 64.4% AR after 61 days of incubation, and to a lesser extent by biodegradation. Similarly, in another study on degradation in three static marine water systems Swales (2003) DT50s of 45 d in estuarine (15°C), 35 d in coastal (12°C) and 75 d in open sea water (8°C), respectively, were estimated, again with a rapidly declining ¹⁴C-mass balance which points to substantial volatilisation. With a Henry's law constant of 0.478 Pa m³mol⁻¹ at 20°C, these observations are plausible. All half-lives mentioned here are listed in document UNEP/POPS/POPRC.17/INF/4, table 3.

25. Daam et al. (2008) investigated the dissipation of chlorpyrifos in outdoor freshwater microcosms in Thailand. The application rate was 1 µg/L active ingredient. 7 d after application about 30% of the initial chlorpyrifos could be detected, and after 28 d 10%. This can only in part be

attributed to degradation, since the concentrations in sediment increased to about 10% of the applied active ingredient after 28 d. Volatilisation and adsorption to biomass were not measured but cannot be excluded. The dissipation of ^{14}C -chlorpyrifos in estuarine outdoor microcosms in Vietnam was studied by Nhan et al. (2002) and Pablo et al. (2008) found chlorpyrifos dissipation half-lives of < 1 d (probably due to dilution processes) and about 5 d, respectively. Mackay et al. (2014) summarised that the dissipation half-life of chlorpyrifos in natural waters under field conditions is about 4 - 10 d (geometric mean 5 d). Since in field studies or open test systems volatilisation contributes considerably to the overall dissipation, the results of these outdoor microcosm studies are considered less relevant.

26. The DT50 values listed here probably overestimate degradation in water, since volatilisation contributes considerably to dissipation. Thus, with a DT50 of 75 d at 8°C, the criterion of a half-life >2 months mentioned in Annex D, chlorpyrifos can be considered persistent in water, especially at lower temperatures.

Soil

27. For the assessment of route and rate of degradation of chlorpyrifos, numerous studies are available, both published papers and proprietary studies conducted for registration purposes. Many of these studies have been conducted according to the OECD test guideline 307 (OECD, 2002), which is the current mandatory standard in the EU, but also according to US guidelines and older guidelines such as the BBA guidelines. Summaries for the proprietary studies, with details on mass balances, recovery rates and losses as well as other information on validity criteria, are provided in the European RAR, which are written by the RMS, and published by the European Commission (Spain, 2017b).

Laboratory studies – rate of degradation

28. De Vette and Schoonmade (2000) and B. Clark (2013) have conducted studies on route and rate of degradation in four soils each. The degradation kinetics have been re-evaluated by Abu (2015) according to FOCUS degradation kinetics (FOCUS, 2006) which is the current standard guidance for kinetic evaluations. Degradation half-lives range from 5.96 d – 110.3 d at 20°C. Although the soil used by Bidlack (1979) was stored for several months, the DegT50 values are in the same range as other studies (11 – 141 days). All half-lives mentioned here are listed in document UNEP/POPS/POPRC.17/INF/4, table 4.

29. Degradation in soil is temperature-dependant (Getzin, 1981), with DegT50 values ranging from 6 weeks (42 d) at 35°C through 13 weeks (91 d) at 25°C to 25 weeks (175 d) at 15°C in one soil (silt loam), which is just below the trigger value in Annex D of the Stockholm Convention (SSC, 2018). At 5°C, the temperature associated with some Arctic environments, the DegT50 would be expected to be in the order of 50 weeks, given that Getzin's (1981) figures show an approximate doubling of the value for each 10 degrees lowering of temperature. Racke et al (1994) also reported that degradation rates doubled with each increase of 10 °C.

30. As observed degradation process, hydrolysis in alkaline soils and a combination of hydrolysis and biodegradation in acidic soils is assumed. Degradation decreases in soils with low water contents, and in experiments at lower temperatures. The major transformation product of chlorpyrifos in soil was TCP (up to 40% of the applied test substance).

31. Chai et al. (2013) studied the degradation of chlorpyrifos in three humid tropical soils from Malaysia and found that degradation was fastest in moist soils ($t_{1/2}$ 53.3 - 77.0 days), compared to dry ($t_{1/2}$ 49.5 - 120 days) and wet soils ($t_{1/2}$ 63.0 - 124 days). Degradation increased markedly with temperature and decreased with higher chlorpyrifos dosages (5-fold) which are often applied in the tropics due to severe insect infestations. Degradation and mineralization rates decreased 2-fold.

Field studies

32. In general, DT50 values in field studies are lower than in laboratory studies. However, it has to be kept in mind that in field studies, the DT50 refers to dissipation, not degradation, since the test is not done in a closed system and losses due to volatilisation etc. are not accounted for (Mackay et al., 2014). Dissipation half-lives were in the range < 2 - 120 d, with a mean of 32 d and geometric mean of 22 d. However, according to European Commission (2012) field dissipation studies are not relevant for the persistence assessment of chlorpyrifos because of expected high losses due to volatilisation of the compound (vapour pressure of chlorpyrifos $\geq 1 \cdot 10^{-3}$ Pa at 20°C and Henry's Law constant > 0.5 Pa m³/mol; UNEP/POPS/POPRC.17/INF/4, table 1).

33. The overall rate of decline in field studies is influenced by factors such as volatilization, soil surface photolysis, leaching out of the sampled soil layers and uptake into plants, which can significantly influence the disappearance of the applied substance from the sampled soil layers in

addition to degradation within the soil matrix. As a result, in many cases the initial decline of applied substance can be more rapid followed by a slower rate of decline. In addition, the influence of soil photolysis could affect the apparent formation and decline profile of any metabolites/degradation products formed, particularly if the depth of sampling is limited. Since chlorpyrifos can be classified as semi-volatile according to its vapour pressure (1.43 mPa), the potential for volatilization of chlorpyrifos in field conditions cannot be ruled out.

34. Various studies examining field degradation have been assessed in the European RAR. Fontaine (1987) investigated three soils (see UNEP/POPS/POPRC.17/INF/4, table 5), and Old (2002a, 2002b, 2002c) investigated four soils. All of these studies belong to legacy studies which were not tailored to obtain the $\text{DegT50}_{\text{matrix}}$ and therefore it is reasonable to assume that the effects of volatilization may influence the degradation rates obtained from these studies. Thus, the DT50 values obtained in these studies were recalculated by the RMS and are in the range of 5 to 89 days.

Use of chlorpyrifos for termite control

35. The use of chlorpyrifos as a termiticide was phased-out in the USA in the year 2000. Although several other countries also have phased out the use of chlorpyrifos in termite control, this is not the case everywhere. Chlorpyrifos is still used as a termiticide in India (India, 2020) and Australia (Australia, 2000), as well as in a number of African states such as Zambia and Zimbabwe (Rother). However, in Australia a review process for chlorpyrifos usage as termiticide is in progress (Australia, 2019).

36. In the review by Giesy et al. (2014) a large number of studies on soil degradation of chlorpyrifos was compiled and evaluated. The work relied mainly on a previous review by Racke (1993). Half-lives for dissipation from soils via all pathways ranged from 1.1 to 1576 d. The highest half-life values were reported for the highest application rates (up to 1000 mg/kg, for control of termites). They are based on investigations by Racke (1993) who observed that the increase in application rate from typical agricultural use (10 mg/kg) to that for urban termiticide application (1000 mg/kg) resulted in a dramatically decreased rate of dissipation. These results were confirmed by a study by Murray et al. (2001). These authors found that the degradation rate of chlorpyrifos was strongly retarded at an initial soil concentration of 1000 mg/kg as compared to lower soil concentrations of 100 and 10 mg/kg in the same soils. The degradation followed a logarithmic function. The derived average half-lives for the three concentrations in several Australian soils were 385 d, 155 d, and 41 d, respectively.

37. Baskaran et al. (1999) performed a test under standard laboratory conditions (25°C, soil moisture 60% of the maximum water holding capacity) to determine the half-life of chlorpyrifos. The authors used termiticide application rates (1000 mg/kg) and dark conditions for a test with an Australian red-brown soil. Part of the losses of chlorpyrifos during the incubation period may have been due to volatilisation, but no trapping system for volatile compounds was installed. The observed degradation of chlorpyrifos was biphasic. Initially a fast degradation was measured for a two-month period. Subsequently, chlorpyrifos degraded at a slower rate. The degradation during the slower phase followed first-order kinetics. Half-lives of 315 – 462 d were estimated. The authors report that the transformation product TCP was found in the soil at levels corresponding to 29 % of the applied parent compound after 24 months.

38. Baker and Bellamy (2006) investigated the dissipation of chlorpyrifos applied at termiticide application rates in field plots in Arizona (USA) over a period of 5 years. The degradation was slower in covered plots, which may point to losses due to volatilisation in the open plots, thus leading to an overestimation of degradation. During the first year, the chlorpyrifos concentration decreased from 1420 µg/kg to 315 µg/kg soil (> 75 % dissipation). The estimated DT50(field) was below 3 months. For the covered plots the chlorpyrifos concentration was 1601 µg/kg at the study start and 813 µg/kg after one year (around 49 % dissipation; DT50(field) around 365 d).

39. Sardar and Kole (2005) conducted a laboratory experiment to study the dissipation of chlorpyrifos in an Indian alluvial soil. Test concentration corresponded to 1 kg, 10 kg and 100 kg per ha. The dissipation followed first order kinetics and the calculated half-lives ranged from 20 to 37 d at 28 °C. TCP was identified as primary transformation product (detected after 3 d, maximum level after 30 d). At all application levels TCP concentrations decreased afterwards and could no longer detected after 120 d. TMP as secondary transformation product was detected during the study course, but also not after 120 d.

40. The reduced degradation of chlorpyrifos at high application rates may not be a result of persistence as such but rather an effect of toxicity to microorganisms.

Anaerobic degradation

41. An unpublished laboratory study (Bidlack, 1979) compared chlorpyrifos degradation in two soils used for rice growing held under anaerobic conditions (flooded) and under aerobic conditions (for 30 d) followed by anaerobic conditions. For a clayey soil an aerobic degradation half-life of 107 d was determined. The degradation under anaerobic and aerobic/anaerobic conditions yielded half-lives of 51 d and 58 d, respectively. For a loamy soil a half-life of 39 d was found under anaerobic and of 15 d for aerobic/anaerobic conditions as compared to 11 d under aerobic conditions.

Sediment

42. Reeves and Mackie (1993) in (Spain, 2017b) have conducted a water-sediment study according to BBA Part IV Section 5-1, which was used before adoption of the OECD test guideline 308. They used a sandy loam from Brown Carrick Sediment and a clay loam from Auchingilsie Sediment. Due to low recoveries, the study cannot be considered fully valid, but it does give an indication: Chlorpyrifos degraded under aerobic aquatic conditions with DegT50 values in the total system of 22 and 51 days in the sandy loam and clay loam systems respectively (DT90 values 72 and 168 days). Dissipation was more rapid in the water layer, with DT50 values of 3 and 6 days respectively, this may be due either to adsorption to sediment, to volatilisation or to degradation. Significant levels of radioactivity were lost from the system. It was only partially retained by the connecting PVC tubing. This radioactivity was identified as volatile chlorpyrifos. Low levels of $^{14}\text{CO}_2$, < 1% AR, were formed during the incubation period. The principal degradation product was TCP, accounting for a maximum of 16.86% AR at 0 h in Sandy loam Total system and 9.89% AR at 100 d in Clay Loam Total system. In the study by Kennard (1996), chlorpyrifos was applied to the sediment (silty clay loam), not to the water. Here, too, significant amounts of radioactivity were lost. The half-life for chlorpyrifos in the test system (sediment and water) was 30.5 days, and only minimal mineralization to $^{14}\text{CO}_2$ was observed. The major degradation product formed was TCP, which accounted for a maximum of 44% applied radioactivity in the total system at the end of the incubation period (36d). Another study was conducted by Kang (2015), with two sediment/water test systems. One was collected from Calwich Abbey Lake, the other from Swiss Lake, both in the UK. Samples were incubated for up to 150 days under aerobic conditions with associated overlying waters at a sediment/water ratio of 1:3 in the dark at 20 ± 2 C. [^{14}C] chlorpyrifos was applied at a nominal concentration of 0.50 mg/L. The raw data of this study was re-evaluated by Abu, 2015, who estimated DegT50 values of 30.7 and 58.3 d for the total system.

43. Bondarenko and Gan (2004) investigated the degradation of chlorpyrifos in urban sediments from two creeks in southern California, USA. Under aerobic conditions, chlorpyrifos showed half-lives of 20.3 and 23.7 d, and under anaerobic conditions of 223 and 57.6 d, respectively. Half-lives were calculated for first-order degradation kinetics and based on measured concentrations at several time points. In this study, natural sediment was not topped up with original water but deionised water, no mass balance was reported and potential losses by volatilisation were not considered.

44. A shake-flask screening test with chlorpyrifos was performed by Walker (1984). The test was designed to rapidly evaluate the relative degradation rates under diverse regimes of, e.g., salinity, pH, and microbial biomass. The experimental design for the screening test covered four treatments. For chlorpyrifos, the half-lives ($n = 2$) were 18 and 25 d in active sediment, 17 and 39 d in sterile sediment, 16 and 27 d in active water, and 24 and 29 d in sterile water, respectively. The experiments with sterilized samples showed mostly longer half-lives which may be interpreted as degradation of chlorpyrifos being increased in the presence of micro-organisms (biodegradation).

45. In a comparative marine water/sediment degradation study by Schimmel et al. (1983) the approximate half-life for chlorpyrifos was reported as 24 d (degradation was tested with 10 g of sediment and 100 mL of pesticide-seawater solution). No appreciable loss of chlorpyrifos was observed after 28 d in a control sample with formalin-treated (sterile) sediment. The authors therefore concluded that the degradation was caused by microorganisms. The chlorpyrifos half-life was lower in outdoor seawater solution exposures than in the indoor experiments (half-life of 4.6 d in systems exposed to sunlight). Although a high volatilisation rate was observed for chlorpyrifos from seawater (up to 63%), the loss was negligible in the presence of sediment in the test systems.

46. Budd et al. (2011) studied the fate of chlorpyrifos in a ditch and a constructed wetland in California (USA). The DT50 for chlorpyrifos in the ditch sediment under anaerobic (flooded) conditions was 144 d and in the constructed wetland sediment 44 d. Under aerobic conditions the DT50 was 58 d in the ditch. Due to low concentrations it was not determined for the constructed wetland. The test set-up is not comparable to laboratory studies conducted according to OECD TG 308, as the studies in aerobic sediment were conducted *in situ*, with changing environmental

conditions, the water samples are not directly associated with the sediment samples and losses due to volatilisation are not accounted for.

47. Laabs et al. (2007) conducted a semi-field study in microcosms to investigate the fate of chlorpyrifos in a Brazilian wetland and in parallel in a laboratory system for up to 50 d. The semi-field DT50 for chlorpyrifos in water microcosms was 7.0 d (laboratory test: 1.9 d) and the DT90 23.4 d (laboratory test: 6.2 d). The semi-field DT50 for chlorpyrifos in water/sediment microcosms was 36.9 d (laboratory test: 12.2 d) and the DT90 122 d (laboratory test: 40.5 d) for the total system. The respective semi-field DT50 for chlorpyrifos in the water phase of the water/sediment microcosms was 16.0 d (laboratory test: 3.2 d) and the DT90 53.2 d (laboratory test: 10.5 d) for the total system. An environmental fate review from Dow Chemical Company (Racke 1993) gives a DT50 of 150 to 200 days in anaerobic pond sediments.

48. Chlorpyrifos adsorbs fairly strongly to sediment and suspended solids (Dabrowski et al., 2002; Gebremariam et al., 2012; Readman et al., 1992). Depending on sediment characteristics, the extent of adsorption and desorption can vary. Adsorption processes can have a profound influence on degradation processes, apparently from reduced availability of sorbed substance to microorganisms. Adsorption of chlorpyrifos strongly correlates with organic carbon content of soils and sediments. Its adsorption coefficients span two orders of magnitude in soils. Mean and median values for chlorpyrifos partition coefficients normalized to organic carbon, K_{OC} , were 8,163 and 7,227 L/kg for soils and 13,439 and 15,500 L/kg for sediments (Gebremariam et al., 2012).

49. From ATSDR (1997): 'The amount of chlorpyrifos available to be volatilized from surface water is reduced by sediment adsorption. Chlorpyrifos has a strong affinity for soil colloids, as evidenced by its measured range of organic carbon-adjusted soil sorption coefficient (K_{oc}) of 973-31,000 (Felsot & Dahm, 1979; Kenaga, 1980; P. J. McCall et al., 1980) in (Racke, 1993)). This suggests that chlorpyrifos in natural water ecosystems adsorbs strongly to suspended solids and sediments, and that this process may transport considerable amounts of chlorpyrifos from water to particulate matter. Several studies have reported very low concentrations of chlorpyrifos in surface waters.

3.1.3 Other evidence of persistence

50. For chlorpyrifos data from several monitoring studies are available: According to US-EPA (2006) monitoring data indicated a widespread and persistent occurrence of chlorpyrifos in aquatic areas in the USA from the early 1990s on. In a 1992 EPA fish monitoring study, approximately 23 % of the fish nationwide had measurable levels of chlorpyrifos residues (US-EPA, 1992). The study revealed that few sites with relatively high concentrations (above 50 ng/g) were scattered throughout the East and Midwest USA and in California. Highest concentrations were detected at sites near agricultural areas. This reflects high usage of chlorpyrifos, not so much persistence.

51. The Draft Assessment Report for EU approval (Spain, 2017b) lists seven studies on soil leaching behaviour (column leaching studies). The results all show that chlorpyrifos is immobile in soil and is unlikely to leach to groundwater (Reeves & O'Connor, 1994a, 1994b) both in Spain (2017b); Pike and Getzin (1981);(Racke, 1993); Fenoll et al. (2011); Rani et al. (2014)). However, in several recent studies, chlorpyrifos has been detected in groundwater in spite of its high adsorptive capacity. Chlorpyrifos was detected in the majority of ground water and surface water samples collected along the Mediterranean coast of Turkey (Tuncel et al., 2008). The detection frequency of chlorpyrifos in drinking water well samples from the state of Rio Grande do Sul, Brazil, at times, exceeded that of surface water samples (Bortoluzzi et al., 2007). Chlorpyrifos was also detected in many samples taken from Australian water wells (Wightwick & Allinson, 2007). Gebremariam et al. (2012) found that desorption of chlorpyrifos from soils and sediments was low but not insignificant. His model predictions indicate that solid-phase chlorpyrifos will eventually partition to the aqueous phase if the soil or sediment is subjected to continuous desorption events in which they are exposed to water. Thus, although the leaching potential of chlorpyrifos is low due to high adsorptive potential, contaminated soils and sediments could be secondary long-term sources of pollution.

52. Dabrowski et al. (2002) found that the concentration of chlorpyrifos in the Lourens river, South Africa, increased from nondetectable to 0.19 µg/L after a rainfall event. Chlorpyrifos was only found in one of the water samples, but it was detected in a majority of the suspended sediment samples, with a maximum concentration of 152 µg/kg. The Lourens River site downstream of the farming area has been identified as a site where potential toxic conditions could arise.

53. The strong association of chlorpyrifos with suspended sediments presents a potential migration route unique to aquatic environments and may explain reported detections of chlorpyrifos in water

wells and marine sediments, also because sorbed chlorpyrifos is more persistent in sediments than in soils and water (Gebremariam et al., 2012; Readman et al., 1992; Tuncel et al., 2008).

54. Monitoring data from the Arctic demonstrate that chlorpyrifos can be transported over long distances to remote regions (see section 3.3). Since degradation of chlorpyrifos is temperature dependent, it is expected to persist in these regions for a considerable length of time. Frequent findings of chlorpyrifos in all media in the Arctic support this. In addition, chlorpyrifos is found in dated sediment cores in Arctic and sub-Arctic lakes (Landers, 2008). Although the concentrations in these sediments are low, they do not derive from local use of chlorpyrifos and can be dated back several decades. This also demonstrates the persistence of chlorpyrifos in sediments.

3.1.4 Conclusion on persistence according to the criteria in Annex D

55. In the water degradation studies evaluated here, DT50 values range from 21 to 75 days at varying temperatures. Normalised to 12°C to reflect environmental conditions in temperate areas, these values range from 6.8 to 124 d. Chlorpyrifos fulfils the criterion for persistence with half-lives in water greater than two months.

56. In soil, highest half-lives for the chlorpyrifos degradation were found at high application rates (100 - 1000 mg/kg). These are used for termite control, which is still an approved use in a number of countries. The reduced degradation of chlorpyrifos at high application rates may not be a result of persistence as such but rather an effect of toxicity to microorganisms. At application rates for agricultural uses (below 100 mg/kg), the half-lives found in literature and study summaries of proprietary studies span a wide range from 6 to 224 d, at varying temperatures. Normalised to 12°C, these values range from 12.7 to 483 days. Of the numerous soil studies evaluated here, around half the normalised DT50 values exceed the criterion for persistence in soil with half-lives greater than 6 months.

57. Half-lives reported for chlorpyrifos degradation in aerobic sediment degradation studies in the laboratory are below the Stockholm Convention threshold of 180 d (six months) for the total system. In most cases, an estimation of half-lives for the sediment alone cannot be done. For studies performed under anaerobic conditions, the half-life values reported were longer and the threshold was exceeded by some studies. Chlorpyrifos sorbs strongly to sediment and can remain there for a prolonged time. Thus, chlorpyrifos is frequently detected in run-off, associated with sediment (Dabrowski et al., 2002; Readman et al., 1992). The strong sorption of chlorpyrifos especially to sediments, where the adsorbed fraction may not be available to microorganisms, may explain the reported detections of chlorpyrifos in water wells and marine sediments. The frequent detection could be attributed in part to widespread use, but also to higher persistence where it is associated with sediment and where temperatures are lower.

58. Environmental degradation half-lives of chlorpyrifos range from a few days to several years, depending on application rate, ecosystem type, soil or sediment characteristics, and other environmental factors, including temperature (Gebremariam et al., 2012). Monitoring data from the Arctic demonstrate that chlorpyrifos can be transported over long distances to remote regions (see section 3.3). Since degradation of chlorpyrifos is temperature dependent, it is expected to persist in these regions for a considerable length of time. Frequent findings of chlorpyrifos in all media in the Arctic support this. In addition, chlorpyrifos is found in dated sediment cores in Arctic and sub-Arctic lakes (Landers, 2008). Thus, chlorpyrifos can be considered persistent in some environments according to the definition of the Stockholm Convention.

3.2 Bioaccumulation

59. Regulatory assessments conducted by the US, Canada, Australia and the EU have determined moderate bioaccumulation of $BCF < 5000$ for chlorpyrifos. This assessment comes to the same conclusion. Although the majority of fish studies conclude on a $BCF < 2000$, toxic effects occur during these experiments at very low doses. Toxicity is also observed for other aquatic organisms, birds and mammals and especially for humans.

3.2.1 Bioaccumulation in laboratory studies

60. For chlorpyrifos log K_{ow} values between 4.7 and 5.2 and log K_{oa} values between 8.3 and 8.9 have been reported (see UNEP/POPS/POPRC.17/INF/4, table 1). These values indicate potential bioaccumulation in aquatic and air-breathing organisms.

61. Bioaccumulation of chlorpyrifos in fish has been studied for many species, developmental stages and exposure scenarios. The available BCF values cover a broad range, but many studies cannot

be considered fully valid. For an overview of all bioconcentration studies assessed for this dossier, please see document UNEP/POPS/POPRC.17/INF/4, table 8.

62. The key BCF considered for the Draft Assessment Report for EU approval is 1374 ± 321 in rainbow trout (*Onchorhynchus mykiss*) (report no ES-928 (J42) as summarized in Spain (2017b)). After a 30-day exposure to $0.3 \mu\text{g/L}$ chlorpyrifos under flow through conditions, a depuration phase of 16 days followed. Steady state was reached. This study was conducted according to EPA Guideline No. 72-6 and 165-4. It is not considered fully valid as values were not normalized for lipid content or growth dilution. As the study was conducted with juvenile trout, growth dilution can lead to underestimation of the BCF.

63. High bioaccumulation is documented for eleuthero embryos with kinetic BCF of 3548 and 6918 for zebrafish (*Danio rerio*) (El-Amrani et al., 2012) and 2187 for medaka (*Oryzias latipes*) (Alharbi et al., 2017). Exposure concentrations were $1 \mu\text{g/L}$ and $10 \mu\text{g/L}$. The semi static exposure lasted 48 h, depuration lasted 24 h. Four pooled samples of 20 individuals were sampled for each concentration and the control at 0, 2, 6, 21, 29, 45, 48 h of exposure time and 2, 4 and 24 h of the depuration phase. Chlorpyrifos was analysed with high-performance liquid chromatography. Limit of detection (LOD) for chlorpyrifos in water samples was $0.5 \mu\text{g/L}$ and 3 ng/g for eleuthero embryos. The kinetic BCF was calculated, as steady state was not reached. BCF values were not normalized for lipid content in either experiment. The lipid content of eleuthero embryos is high with 11 – 20% average range (El-Amrani et al., 2012).

64. Other fish studies have produced BCF in a wide range, most studies however show toxic effects at low concentrations. Jarvinen et al. (1983) calculated a BCF of 1673 ± 423 for the fathead minnow (*Pimephales promelas*). Toxic effects occurred in all concentrations and included significant mortality at $2.68 \mu\text{g/L}$, growth reduction at $1.21 \mu\text{g/L}$ and reduced reproduction at $0.12 \mu\text{g/L}$. For the same species J. Eaton et al. (1985) produced a lipid normalized BCF of 1150 at concentrations between $0.12 \mu\text{g/L}$ and $0.83 \mu\text{g/L}$. Toxic effects included reduced reproduction and decreased body weight. Goodman, Hansen, Middaugh, et al. (1985) exposed early life stages of two silverside species to chlorpyrifos and determined a maximum BCF of 580. Significant mortality occurred at $1 \mu\text{g/L}$ and $2 \mu\text{g/L}$. Following the same experimental set-up Goodman, Hansen, Cripe, et al. (1985) produced a maximum BCF of 1000 using the california grunion (*Leuresthes tenuis*). Here significant mortality and decreased body weight occurred at concentrations of $0.63 \pm 0.11 \mu\text{g/L}$ to $2.8 \pm 0.48 \mu\text{g/L}$. In the sheepshead minnows (*Cyprinodon variegatus*) a maximum BCF of 1830 was determined (Cripe et al., 1986). Reduced body weight and increased mortality occurred at concentrations above $3.0 \mu\text{g/L}$. Hansen et al. (1986) reported a maximum BCF of 5100 for the gulf toadfish (*Opsanus beta*). A decrease in body weight occurred at $18 \mu\text{g/L}$ and significant mortality at $150 \mu\text{g/L}$. For details on these studies please reference the chapter on bioaccumulation in document UNEP/POPS/POPRC.17/INF/4.

65. As demonstrated in the studies described above, toxicity to fish occurs at doses as low as $1.21 \mu\text{g/L}$. These findings are supported by data from the EU RAR (Spain 2017) which gives a 96 h LC_{50} value of $8 \mu\text{g}$ active substance per litre (a.s./L) for rainbow trout in a test performed with Dursban. Additionally, Gisey et al. (2014) calculated a species sensitivity distribution (SSD) for chlorpyrifos of $0.812 \mu\text{g a.s./L}$. For more details see chapter 3.4.3 of this document.

66. Fish studies show moderate bioaccumulation with BCF in the range of 1000 to 2000 at concentrations linked to toxic effects. BCF above 2000 are observed in early life stages. Even moderate bioaccumulation in combination with high toxicity gives reason for serious concern.

67. Besides fish, other aquatic species are highly susceptible to chlorpyrifos. For *Daphnia magna* an EC_{50} of $0.1 \mu\text{g a.s./L}$ (Spain 2017) and for *Xenopus laevis* (African clawed frog) a 96-h LC_{50} of 0.564 mg a.s./L (Richards and Kendall (2002)) was determined.

68. Toxicity in terrestrial species has also been demonstrated. For honey bees contact toxicity was identified as LD_{50} of $0.068 \mu\text{g a.s./bee}$ for Drusban (Bell (1994)). A LD_{50} of $39.24 \text{ mg a.s./kg body weight (bw)}$ was set for the Bobwhite quail (Spain 2017). Acute oral LD_{50} ranging from 64 to 71 mg a.s./kg bw have been set for mice and ranging between 66 to $192 \text{ mg a.s./kg (bw)}$ for rats (European Commission 2005). For further information on toxicity see chapter 3.4 of this document.

69. Bioaccumulation in sediment dwelling organisms has been measured for the oligochaete *Lumbriculus variegatus* (A. Jantunen et al., 2008). Four different sediments were tested in a 10-day static exposure with concentrations ranging from 0.06 to $1.1 \mu\text{mol/kg dry weight}$. Steady state was not reached, which may lead to an underestimation of bioaccumulation potential. Bioaccumulation was measured as biota-sediment accumulation factors (BSAFs). BSAFs ranged from 6 to 99 depending on soil and chlorpyrifos concentration. This BSAF value indicates high bioaccumulation (ECHA, 2017).

70. In the earth worm species *Eisenia Andrei* Svobodová et al. (2018) measured BAF values at steady state following the experimental design of OECD 317. Both soil types were sterilized with gamma radiation and the nominal concentration was set to 5 mg kg⁻¹ soil dry weight to represent worst case scenarios. BAF under steady state were calculated as 6.34 ± 1.30 and 4.51 ± 0.76 for the different soils.

3.2.2 Monitoring data concerning bioaccumulation

71. Chlorpyrifos has been detected in various biota samples from around the world, including the Arctic.

72. During the Western Airborne Contaminant Assessment Project (WACAP), levels of chlorpyrifos were measured in national parks of the USA. Chlorpyrifos was detected in lichen ranging from 1.57 to 19.83 ng/g lipid weight (lw) at sampling sites in national and secondary parks situated in the Western USA. First- and second-year lodgepole pine (*Pinus contorta*) and white fir (*Abies concolor*) needles from Emerald Lake basin in Sequoia National Park showed a time-dependent increase of chlorpyrifos concentration. In the one-year white fir needles chlorpyrifos was not detected, while the mean concentration in the older needles amounted to 19.7 ng/g lw. The mean concentration in the pine needles was 11.6 ng/g lw in the first year and 20.5 ng/g lw in the second year (Landers, 2008).

73. Kurt-Karakus et al. (2011) detected chlorpyrifos in zooplankton collected from three remote inland lakes in Ontario in 2003 and 2004. Plankton were collected with a 250 µm net. With regard to lw the geometric mean of the overall BAF was 3300 while the corresponding medians were 270 to 16,200 for the individual lakes. The highest BAF found at the three lakes amounted to 117,000 referring to lw. The uncertainty for plankton-based bioaccumulation is based on the high surface to volume ratio. Adsorption may occur and could skew bioaccumulation values.

74. In the years 1997 and 1998 blood samples from sea otters (*Enhydra lutris* ssp.) in California and Alaska, USA were analysed for POP and other chemicals of concern (Jessup et al., 2010). Recovery rates were > 90% and the detection limit was 4 ng/g lw with capillary gas chromatography. The lipid percentage of serum ranged from 0.6 to 1%. No chlorpyrifos contamination was reported for Alaskan sea otters. For Californian sea otters, a range from below LOD to 342.6 ng/g lw chlorpyrifos was reported. 40 individuals were sampled. Significant differences were based on the three sampling locations.

75. In 2005 the liver of river otters (*Lontra canadensis*) from New Jersey, USA were sampled for POP and other contaminants (Stansley et al., 2010). Analysis was performed with mass spectrometry. The sample size was 32, of which 12 showed no contamination with chlorpyrifos. The remaining individuals showed a mean concentration of 0.78 ng/g wet weight with a 95% confidence interval of 0.62 – 1.50 and a maximum of 6.91 ng/g.

76. During the winter of 2011, feathers of 23 blackbrowed albatross (*Thalassarche melanophris*) and 19 Cape petrels (*Daption capense*) were collected on the Patagonian Shelf of Argentina (Adrogué et al., 2019). They were analysed for different POP and chlorpyrifos using gas chromatography. The recovery rate was > 90% and the detection limit was between 0.08 and 0.33 ng/mL for different substances. Chlorpyrifos showed the highest concentrations of all substances analysed with 58.64 ± 27.31 ng/g feather in male Albatross and 84.88 ± 50.57 for male petrels.

77. The bioaccumulation of chlorpyrifos was investigated in the vegetation-caribou-wolf food chain in the Bathurst region (Nunavut) in Canada by Morris et al. (2014). The analytical recovery of chlorpyrifos from biota was low at 52 ± 17%. The minimum detection limits (MDLs) were 0.18 ng/g lw for plants, 0.13 ng/g lw for caribou and 0.054 ng/g lw for wolves. The detection frequency for vegetation samples above the MDL was about 50% for lichen species and green plants and 80% for mushrooms. All concentrations were corrected for blanks and normalized to lipid-equivalents and reported as the geometric mean ± standard errors (ng/g lw). For lichen the concentrations were 0.25 ± 0.21 ng/g lw, for green plants including willow, mosses and grasses the concentrations were 0.24 ± 0.088 ng/g lw and for mushrooms the concentrations were 0.85 ± 0.52 ng/g lw. Chlorpyrifos was found in five caribou samples at 0.40 ± 0.16 ng/g lw specifically in muscle but not in the liver and in one wolf liver below the MDL.

78. Morris et al. (2016) examined the polar bear and ringed seal food chains in three marine locations of Arctic Canada in the region Nunavut. Sampling took place in the years 2007, 2008 and 2010 at the sites Barrow Strait, Rae Strait and Cumberland Sound. The analytical recovery of chlorpyrifos from biota was only 52 ± 17%. The MDL values for biota were not reported, the detection frequencies for samples above the MDL were reported. Concentrations were blank corrected and lipid

normalized and given as geometric mean concentrations (ng/g lw) with the 95% confidence intervals. Chlorpyrifos was found in plankton at all three sites. The detection frequency above MDL varied between the tree sites from 25% to 100% with mean concentrations of 0.41 ng/g lw (95%-CI 0.33–0.51), 0.33 ng/g lw (95%-CI 0.11–0.95) and 1.1 ng/g lw (95%-CI 0.010–131). Concentrations of chlorpyrifos were measured in Arctic char (*Salvelinus alpinus*) and capelin (*Mallotus villosus*) at Cumberland Sound with a detection frequency above MDL of 80% and 40% and concentrations of 0.11 ng/g lw (0.013–0.93) and 0.31 ng/g lw (0.017–5.5) respectively. Two samples of ringed seals at Barrow Strait showed concentrations above the MDL at 0.022 ng/g lw and 0.038 ng/g lw. Chlorpyrifos was most consistently detected in polar bear fat with detection frequencies above MDL of > 75% at all three sampling sites. Mean concentrations in polar bear fat were 0.022 ng/g lw (0.013–0.035), 0.032 ng/g lw (0.013–0.076) and 0.016 ng/g lw (0.0078–0.033) at the different sites.

79. During monitoring in Jaunpur, India, blood samples were taken from fish, chicken, goats and men near the river Gomti (Singh et al., 2008). Sample size was five. Chlorpyrifos, endosulfan, aldrin, and HCH and DDT isomers were analysed with gas liquid chromatography at recovery rates between 93.02 and 95.5% and a detection limit of 0.1 ppb. In fish, levels of chlorpyrifos in blood were 150 ppb similar to levels of lindane. For other species chlorpyrifos levels in blood were measured at 80 ppb in chicken, 70 ppb for goat and 40 ppb for men. These levels were comparable to the level of aldrin found in the blood of these species.

80. Chlorpyrifos and chlorpyrifos-methyl were found in breast milk sampled from women of agricultural and urban regions of California, USA (Weldon et al., 2011). Breast milk of 13 women from Salinas and 21 women from San Francisco was sampled between 2002 and 2007. Chlorpyrifos was detected in all samples with a mean of 40.5 pg/g milk, minimum of 12.9 and maximum of 223 pg/g milk in urban samples. In agricultural samples the mean was 139 pg/g milk, with a minimum of 12.8 pg/g milk and a maximum of 1070 pg/g milk.

81. In Pakistan, chlorpyrifos was detected in breast milk samples from 55% of women cotton pickers at 0.001 to 0.04 ppm, in 40% of chili workers at 0.0002 to 0.15 ppm, in 45% of okra pickers at 0 to 0.048 ppm, and in 30% of berseem and wheat harvesters at 0.001 to 0.005 ppm. 20 women were sampled per crop. Pesticide recovery rates were between 85 and 100%. No limit of detection was given (Sheikh et al., 2014).

82. 53 breast milk samples were analysed from women of the agricultural area of Punjab, India (Bedi et al., 2013). Samples were collected during November and December of 2011. Chlorpyrifos was found in 5.7% of samples at a median of 1664.2 ng/g lw. Authors stated this to be the first finding of chlorpyrifos in human breast milk in the area of Punjab, which could be explained by the current shift towards the extensive use of this pesticide in India. Three samples exceeded the acceptable daily intake for infants set by EFSA (2014) at 0.001 mg/kg bw.

83. Similar observations have been made for the region Bhopal (India), where the breast milk of 12 women was sampled (Sanghi et al., 2003). The detection limit was 0.01 mg/kg. Here, all samples tested positive for chlorpyrifos with a mean value \pm SE of 0.230 ± 0.024 mg/kg and a range between 0.085 and 0.355 mg/kg. The consumption of 500 mL milk daily was calculated to exceed the acceptable daily intake for an infant by the factor 41.

84. Chlorpyrifos exposure during pregnancy has been linked to severe adverse effects on neurodevelopment in children. As discussed in chapter 3.4.1 of this dossier, animal studies and epidemiological studies confirm the developmental neurotoxicity of chlorpyrifos. Therefore, the exposure of pregnant women and new-borns via breastmilk gives rise to serious concern.

3.2.3 Conclusion on bioaccumulation according to the criteria in Annex D

85. The log K_{ow} for chlorpyrifos indicates potential bioaccumulation. The combination of a log $K_{ow} > 2$ and a log $K_{oa} > 5$ indicates potential bioaccumulation in air-breathing organisms. Chlorpyrifos has been found in biota at different trophic levels in the remote regions, globally in apex predators and in human breast milk at levels concerning for offspring. Based on current data available, a BCF of > 5000 cannot be concluded. Numerous BCF in fish show moderate bioconcentration. However, in combination with high toxicity, even moderate bioaccumulation can lead to body concentrations that elicit adverse effects, thus it is a serious concern. Based on high toxicity in fish and other species such as invertebrates, amphibians, birds and mammals, together with a moderate BCF and a BSAF above 6 for soil organisms, chlorpyrifos meets the second criteria (ii) for bioaccumulation in other species, high toxicity and ecotoxicity of annex D. Based on the reasons stated above, we conclude that chlorpyrifos overall meets the criteria for bioaccumulation.

3.3 Long-range transport potential

86. The atmospheric half-life of chlorpyrifos is mainly determined by the OH radical concentration. Gaseous chlorpyrifos does not exceed a half-life of two days. Particulate chlorpyrifos, however, is more recalcitrant to degradation by OH radical reaction and shows an atmospheric half-life up to 66.5 days. Modelling results indicate air and water as main media for chlorpyrifos transport. Chlorpyrifos has been measured in abiotic and biotic compartments of remote regions.

3.3.1 Environmental fate properties and model results

87. The vapour pressure for chlorpyrifos has been estimated between 1.0×10^{-3} and 3.35×10^{-3} Pa (see UNEP/POPS/POPRC.17/INF/4, table 1). Based on these values, chlorpyrifos in the atmosphere will exist mostly in the vapour phase and to a lesser extent the particulate phase.

88. For the vapour phase the dominant mechanism of degradation is based on a reaction with OH radicals (Zhou et al., 2010).

89. Using the Atmospheric Oxidation Program (AOPWIN; ver.1.89; (US-EPA)), Simon (2001) calculated an OH radical reaction rate of 9.16×10^{-12} cm³/molecule-sec for chlorpyrifos. When applying atmospheric OH radical concentrations of 0.5×10^6 molecules/cm³ (European standard value) and 1.5×10^6 molecules/cm³ (US standard value) it becomes clear that the resulting atmospheric half-life depends on the atmospheric OH radical concentration used for calculation. For an OH radical concentration of 0.5×10^6 molecules/cm³, the corresponding half-life is 4.1 hours. For an OH radical concentration of 1.5×10^6 molecules/cm³ as used in AOPWIN, the corresponding half-life is 1.4 hours.

90. Muir et al. (2004) replicated these results using AOPWIN in Epi Suite to calculate the half-life of chlorpyrifos. Applying an OH radical concentration of 1.5×10^6 molecules/cm³ the predicted half-life of chlorpyrifos amounted to 1.4 hours while an OH concentration of 1.5×10^5 molecules/cm³ resulted in a half-life of 14 hours. The authors noted, that the later scenario was realistic for spring in the northern hemisphere when chlorpyrifos may be applied early in the growing season.

91. Modelling results are confirmed by degradation experiments. In Muñoz et al. (2012) the atmospheric degradation of gas phase chlorpyrifos was observed in the European Photoreactor (EUPHORE). EUPHORE is a reaction chamber with about 200 m³ volume covered with FEP foil which allows at least 80 % of outside radiation at wavelengths between 290–500 nm to penetrate the chamber. Over a period of five minutes 280 scans were conducted for FTIR spectroscopy. Additionally, solid-phase microextraction was used to monitor the reaction. The rate constant for the reaction of chlorpyrifos with OH radicals was determined as $(9.1 \pm 2.1) \times 10^{-11}$ cm³/ molecules-sec at 29 ± 5 °C. The atmospheric half-life of chlorpyrifos was approximately 2 hours.

92. In the particulate phase, the reaction of chlorpyrifos with OH radicals is significantly reduced (ATSDR, 1997; El Masri et al., 2014). El Masri et al. (2014) measured a heterogeneous OH radical reaction rate of 5.8×10^{-12} cm³/ molecules-sec at 25°C. For an OH radical concentration of 0.5×10^6 molecules/cm³, the corresponding half-life of particulate chlorpyrifos is 66.4 hours. For an OH radical concentration of 1.5×10^6 molecules/cm³, the corresponding half-life is 22.1 hours.

93. Socorro and co-workers showed that recalcitrance of particulate phase chemicals may lead to an overall atmospheric half-life that exceeds values relevant for long range transport (Socorro et al., 2016).

94. Particulate phase chlorpyrifos was detected during monitoring in air from Spain (Borras et al., 2011; Coscollà et al., 2014), Czech republic (Degrendele et al., 2016) and China (Li et al., 2014).

95. Zhong et al. (2012) assumed that the proportion of current-use pesticides including chlorpyrifos in the particulate phase is generally below 0.001 %. However, at several sites the authors measured distributions between vapour and particulate phase with a percentage of up to 4 % of chlorpyrifos in the particulate phase in oceanic air (see Zhong et al. (2012), supporting information).

96. As described earlier, chlorpyrifos binds strongly to soil and sediment (see chapter on persistence). Coscollà et al. (2014) hypothesize that chlorpyrifos adsorbed to soil particles could be transported by wind erosion as has been shown for other pesticides (Larney et al., 1999).

97. In summary, particulate chlorpyrifos appears to be more recalcitrant to atmospheric degradation. However, the percentage of particulate chlorpyrifos is below 10% in observed scenarios.

98. Once in the water compartment, chlorpyrifos bound to suspended solids and sediment is persistent (see chapter on persistence) and could be carried to remote regions in long range transport via oceanic currents (Ma et al., 2018). Chlorpyrifos bound to particles in the Arctic ocean have been measured by Bigot et al. (2017) and Morris et al. (2016).

99. The OECD Pov and LRTP Screening tool¹ was developed to screen and compare chemicals for potential long-range transport. This tool was used to model the characteristic travel distance and transfer efficiency of chlorpyrifos. The results do not indicate potential for environmental long-range transport.² However, these calculations show that transport via water is relevant and that transport via air is also relevant when assuming a prolonged atmospheric half-life due to lowered OH radical concentrations.

3.3.2 Presence in remote areas

100. von Waldow et al. (2010) proposed an index to characterize the remoteness of regions. The resulting remoteness index is based on calculations with a global atmospheric transport model, with two different emission scenarios for industrial chemicals and plant protection products, respectively. For the crop emission scenario, regions with farmland were used as source regions. It should be noted that this remoteness index was derived based on atmospheric transport modelling, while transport via water is potentially more relevant for chlorpyrifos. In absence of an index including both water and atmospheric transport, the index of von Waldow based on the crop emission scenario is used as an indication of remoteness. A map generated by von Waldow et al. (2010) showing the resulting remoteness indices is shown in figure 1 of document UNEP/POPS/POPRC.17/INF/4; findings of chlorpyrifos in remote sections were manually plotted by the dossier drafters.

Monitoring in abiotic compartments of remote regions

101. According to an AMAP report on Arctic Pollution (Nilsson & Huntington, 2009) chlorpyrifos has been found in fish samples in Alaskan parks, in surface water, ice and fog from the Bering and Chukchi seas, snow samples from Alaska, in air in the eastern Canadian archipelago, and in subarctic and Arctic lakes in Canada. In the following two sections results of monitoring studies published in scientific literature are compiled.

102. Chlorpyrifos was detected in Arctic marine fog, sea water and marine ice by Chernyak et al. (1996) (as cited in Hoferkamp et al. (2010)) who investigated current-use pesticides in the Bering and Chukchi marine ecosystems in the summer of 1993. The highest concentration found in fog condensates was 5 ng/L chlorpyrifos. Only chlorothalonil and metolachlor were found in higher concentrations at most sampling points. Among the five pesticides analysed, chlorpyrifos was the most frequently identified contaminant in sea water with levels ranging up to 67 pg/L. The highest concentration amounting to 170 pg/L was measured in melting ice, where only atrazine was found in higher concentrations. Chernyak et al. (1996) concluded that chlorpyrifos and other detected pesticides could accumulate at the ice surface either directly or as dry fall and snow accumulation. In this frozen condition the compounds would be stable in comparison with its behaviour in a dissolved state. The concentration in an interstitial air sample taken at the same expedition at Chukchi Sea near the Siberian coast amounted to 0.76 pg/m³ in the vapour phase and 0.08 pg/m³ bound to particles, while the level in the water phase of a corresponding fog sample was 0.08 ng/L ((Rice & Chernyak, 1997) as cited in (Watts, 2012)).

103. Garbarino et al. (2002) analysed current-use pesticides in snow cores that were collected over sea ice from four northwest Alaskan Arctic estuaries. The five sampling sites were situated at the Chukchi and Beaufort Seas. The samples represented the annual snowfall from the 1995/1996 cold season. Chlorpyrifos was detected in snow from three sites with concentrations estimated as 70 to 80 ng/L.

104. Hermanson et al. (2005) analysed the upper 40 m of an ice core from Austfonna (Svalbard Norway), the largest ice cap in Eurasia, for several current-use pesticides and others contaminants. Chlorpyrifos first appears at Austfonna in 1972, it is one of 8 current-use pesticides with continuous profiles in the core. Its highest concentration amounting to 16.2 ng/L was found in sections of the core corresponding to the early to mid-1980s. Levels began to decline in the 1990s. The compound was not found in the surface layer of the core representing the period 1992 - 1998. All reported concentrations were blank corrected. The authors attributed the occurrence of chlorpyrifos to long-term atmospheric

¹ OECD POV and LRTP Screening Tool, Version 2.2, 2009.

² Input physico-chemical properties: log K_{ow} 5.2, log K_{aw} -3.9.

Half-life data calculation 1: air 14 h, water 1800 h, soil 5376 h.

Results calculation 1: Pov = 320 d, CTD (air) = 276 km, CTD (water) = 171 km, TE = 7.86 · 10⁻²%.

Half-life data calculation 2: air 4.2 h, water 1080 h, soil 2640 h.

Results calculation 2: Pov = 158 x d, CTD (air) = 86 km, CTD (water) = 106 km, TE = 7.69 · 10⁻³%.

transport concluding that the actual OH radical reaction rate apparently is much slower than predicted from the literature because OH radical production is seasonal and often low in the Arctic.

105. Ruggirello et al. (2010) investigated the current use and legacy pesticide deposition to ice fields on Svalbard (Norway). Samples from a 125 m deep ice core drilled at Holtedahlfonna in 2005 were analysed. Chlorpyrifos was the only organophosphorus current-use pesticide that was detected continuously in the Holtedahlfonna ice core. It was first detected in 1971 - 1980 with a comparatively low input (64.8 pg/cm²/year) and decreasing trend until the mid-1990s. Then increasing rapidly reaching maximum concentrations in the time period of 1995 - 2005. During this period the flux peaked at 808 pg/cm²/year. The chlorpyrifos burden of the entire ice core accumulated between 1953 and 2005 amounted to 776 ng, higher than any other analysed compound. Chlorpyrifos made up about 34% of the total pesticide burden in the core. The method detection limit was 0.153 ng/L as calculated from three times the standard deviation of blanks. It was noted that evidence of chlorpyrifos at Holtedahlfonna is contrary to the short atmospheric half-life of the substance predicted for mid-latitude environments. Instead, results suggested that it is persistent in some Arctic conditions. The results of this study were compared with the results found by Hermanson et al. (2005). For this purpose, the concentration data determined at Austfonna were converted to core burdens. The comparative data showed that the chlorpyrifos as well as the alpha-endosulfan burden at Austfonna were much higher than that at Holtedahlfonna. The chlorpyrifos burdens differed by a factor of about 13. It was assumed that the general sources of these pesticides are different at least part of the time, and that Austfonna generally receives the greater input. Ten-year cumulative 5-day air mass trajectories confirmed the assumption that Austfonna had received more atmospheric flow from Eurasia than Holtedahlfonna. The greater Eurasian flow to Austfonna suggested that airflows over populated and agricultural regions in northern Eurasia might be the source of greater burdens of some pesticides used there.

106. Muir et al. (2004) investigated the levels of current-use pesticides in 30 North American lakes, of which six were located in the Canadian Arctic, between 1998 and 2001. The concentrations of chlorpyrifos in the six Arctic lakes ranged from < 0.017 ng/L to 1.6 ng/L with a mean value amounting to 0.27 ng/L. The difference between the mean chlorpyrifos level in arctic lakes and that in mid-latitude lakes was less than one order of magnitude (mean level in lakes receiving agricultural inputs: 0.65; mean level in lakes situated at least 50 km from agricultural areas: 0.82 ng/L). The levels in the seven sub-Arctic lakes were below detection limit.

107. In the Western Airborne Contaminants Assessment Program (WACAP) (Landers, 2008) levels of chlorpyrifos and its transformation product chlorpyrifos oxon (reported as total chlorpyrifos) were analysed in air, snow and lake sediments at several sites in the core parks covered by WACAP. In addition, air samples were collected in the secondary parks. 37 Passive air sampling devices were deployed in all parks in summer 2005 and retrieved one year later. Total chlorpyrifos (almost entirely as chlorpyrifos oxon) was detected in two parks situated in the temperate zone, but not at the sites in the Alaskan parks. Before the onset of spring snowmelt, beginning in 2003 and ending in 2005, snow samples were collected at 13 sites in seven core parks. Total chlorpyrifos was among the most frequently detected pesticides, being found in more than 90% of the samples. The mean concentrations of total chlorpyrifos in snow that were determined in spring 2003, ranged from 0.010 to 0.030 ng/L at the five sites in the three Alaskan core parks. Values below the limit of detection had been replaced by one-half of the detection limit to determine the mean levels. The deposition of total chlorpyrifos accumulated in snow in winter 2002/2003 amounted to 0.48 to 32 ng/m² (reported in Hageman et al. (2006)). WACAP also included an investigation on contaminations of lake sediment cores that provided information on the temporal changes of contaminant loadings in the eight core parks over about the last 150 years. Total chlorpyrifos was detected in lakes situated in the three Alaskan core parks. Results from Noatak National Preserve and Gates of the Arctic National Park and Preserve showed increasing contamination of lake sediments with chlorpyrifos until 2000, the most recent year represented by the sediment cores (Landers, 2008).

108. L. M. Jantunen et al. (2007) as cited in Hoferkamp et al. (2010) analysed samples from a 2007 cruise of the Labrador Sea. The measured concentrations of chlorpyrifos in air samples ranged from 0.36 to 30.4 pg/m³.

109. During a cruise in 2008 across the Beaufort Sea chlorpyrifos was measured in the air at 3.1 ± 1.9 pg/m³ and in the sea water at 31 ± 19 pg/L (Pučko et al., 2015). These values were used to model the input of chlorpyrifos and other chemicals to the Beaufort Sea via melt ponds. Melt ponds occur during summer months as sea ice melts and act as input pathway for chemicals into the Arctic sea. The model suggested that 16 kg chlorpyrifos was released via meltponds each year, in comparison to 6 kg of alpha-endosulfan. This was estimated to be 4% of total chlorpyrifos contained in the upper layer of

the Beauford Sea region. Authors hypothesized that this phenomenon would increase with climate change.

110. Air samples collected between 2006 and 2009 at the Canadian High Arctic station of Alert in the Canadian Arctic showed a detection frequency of 19% for chlorpyrifos of 68 samples with a mean concentration of 0.39 pg/m³ (Hung et al. as cited in Balmer et al. (2019)).

111. Marine boundary layer air and surface sea water samples were taken during an expedition of a Chinese research vessel from East China Sea to the high Arctic in 2010 (Zhong et al., 2012). Chlorpyrifos was also measured in blanks. The method detection limit was therefore set at mean blank value added to three times its standard deviation. Still chlorpyrifos was ubiquitously found in oceanic air and sea water with 100% detection frequencies. Along with alpha-endosulfan and dicofol it was the most abundant substance of the six current-use pesticides that were investigated in this study. Air concentrations ranged from 1 to 146 pg/m³ in the gas phase. The levels of chlorpyrifos dissolved in sea water ranged from 0.1 to 111 pg/L. The highest levels in air and sea water were measured in samples from the Sea of Japan. A significant decline of air and water concentrations from East Asia toward Bering and Chukchi Sea was observed. Air-sea gas exchange data suggested that there was net deposition of chlorpyrifos into the North Pacific and the Arctic. The authors assumed Asian countries as sources of Chlorpyrifos and other detected pesticides for their long-range transport to the Arctic.

112. In 2012 Pućko et al. (2017) collected air, snow, sea-ice, melt-pond water and seawater from the Resolute Passage of the Canadian Arctic. Chlorpyrifos was found in more than 50% of the samples in all media. Concentrations are reported as mean \pm SD with 4.8 \pm 1.3 pg/L in snow, 14.4 \pm 2.5 pg/L in melt-pond water, 14.1 \pm 6.0 pg/L at surface level sea water, 10.5 \pm 1.7 pg/L at sea water of five-meter depth and 0.10 \pm 0.04 pg/m³ for air.

113. L. M. Jantunen et al. (2015) conducted sampling cruises in the Canadian Arctic Archipelago in the years 2007, 2008, 2010, 2011 and 2013. The mean detection frequency across all years was 95% for chlorpyrifos in water with mean values \pm SD of 13 \pm 12 pg/L. In comparison other POP such as dieldrin and chlordane had 75%, endosulfan 97% mean detection frequency and concentrations in water of 20 \pm 20 pg/L, 0.82 \pm 0.53 pg/L and 3.1 \pm 1.9 pg/L respectively. For air the detection frequency was 85% with a mean value of 1.1 \pm 1.3 pg/m³. Temporal trends were derived from regression of the logarithmic concentration in the medium to the year. This was not significant for chlorpyrifos concentrations in water, but indicated that a 50% change in air concentration was reached in 1.5 years.

114. In the summer of 2015 seawater, sea ice and snow were collected from northern Greenland (Bigot et al., 2017). Chlorpyrifos was found in all media, at concentrations between 6.2 – 11.5 pg/L in snow, 5.2 – 12.0 pg/L in sea ice and at 0.74 – 1.0 pg/L in seawater. Chlorpyrifos was also found adsorbed to particles in sea ice and seawater, but at much lower concentrations. Bigot et al. (2017) also measured chlorpyrifos at the Davis Station in Antarctica at concentration exceeding the MDL in sea-ice meltwater at 7.3 pg/L and in air samples between 0.41 and 16.8 pg/m³ (Supporting Information of Bigot et al. (2017)).

115. Chlorpyrifos was monitored as part of the Swedish national monitoring program for pesticides from 2002 to 2018 on agricultural sites (Boström, 2020). In Sweden chlorpyrifos was never used as plant protection product, but as indoor biocide in products until 2009. Air samples from two sampling sites were collected with polyurethane foam between 2009 and 2018 and produced a detection frequency of over 90% for chlorpyrifos with median concentrations of 0.002 ng/m³. Precipitation was sampled between 2002 and 2018 at four sampling sites. The detection frequency ranged between 12% to 56% with maximum concentrations ranging between 0.0001 and 0.01015 μ g/L. Chlorpyrifos was not detected in surface water, groundwater or sediment. Based on these findings the authors hypothesised that the occurrence of chlorpyrifos in Sweden was based on long range transport.

Monitoring in biotic compartments of remote regions

116. Within the WACAP the contamination of the vegetation was investigated in the twenty parks during 2003 and 2005 (Landers, 2008). Levels of total chlorpyrifos (including chlorpyrifos-oxon) in lichen were below the limit of detection in all Alaskan core and secondary parks except the Stikine-LeConte Wilderness, Tomgass National Forest, the most southern park located at the southern end of Southeast Alaska. In this park, the mean concentration in lichen was 0.60 ng/g lipid. Two-year-old conifer needles from Sitka spruce were also analysed. However, needle samples were not collected in the largely treeless Noatak National Preserve and Gates of the Arctic National Park and Preserve. In these needles mean level of total chlorpyrifos in the Denali National Park was 0.86 ng/g lipid while the mean concentrations in the four Alaskan secondary parks ranged from 0.61 to 2.35 ng/g lipid (Hoferkamp et al., 2010; Landers, 2008).

117. Furthermore, WACAP reported levels in fish caught at overall 14 lake sites located at the eight core parks (Landers, 2008). A wide age distribution and an even sex ratio (with distributions roughly equal at the various sites) were intended to be achieved (Ackerman et al., 2008). The WACAP fish monitoring included inter alia the investigation of lake trouts (*Salvelinus namaycush*) from three lakes situated in the three Alaskan core parks and of whitefish (*Prosopium cylindraceum*) and burbot (*Lota lota*) from another lake in the Denali National Park. Since levels of current-use pesticides in fish were not reported in tabular form by Landers (2008) and Hoferkamp et al. (2010) the approximated mean contaminations from graphical illustrations is given here: total chlorpyrifos ranged from 0.041 to 0.1 ng/g wet weight among the four lakes.

118. A study from Norway included analyses of chlorpyrifos in several Arctic species like fish, seabirds and seals (Langford et al., 2012). The samples were collected in Svalbard during the autumn of 2011. The substance was detected in one of five seal blubber samples with a concentration of 1.4 ng/g. All other results were below the limit of detection. Vorkamp and Rig  t (2014) noted that the concentrations in fish reported by Landers (2008) were partly lower than the detection limit in the Norwegian study. The following studies on biomonitoring in remote areas are also described in chapter 3.2.2 of this dossier, for details please refer to chapter 3.2.2.

119. Feathers of blackbrowed albatross (*Thalassarche melanophris*) and Cape petrels (*Daption capense*) were sampled on the Patagonian Shelf of Argentina (Adrogu   et al., 2019). Chlorpyrifos showed the highest concentrations of all substances analysed with 58.64 ± 27.31 ng/g feather in male and 49.56 ± 18.45 ng/g in female Albatross and 84.88 ± 50.57 ng/g for male petrels and 75.98 ± 47.97 ng/g for female petrels.

120. Morris et al (2014) detected chlorpyrifos in the Canadian Arctic Archipelago in vegetation and mushrooms up to 0.85 ± 0.52 ng/g lw. Additionally, chlorpyrifos was detected above the MDL in five of six samples of caribou muscle tissue at a mean lipid normalized concentration of 0.40 ± 0.16 ng/g lw and in one of seven samples of wolf liver at 0.06 ± 0.033 ng/g lw (Supporting Information of Morris et al. (2014)).

121. Chlorpyrifos was detected in seals and polar bears in the same region by Morris et al. (2016). Concentrations in seals blubber were not reported as the number of samples showing values above MDL were below 20%. Chlorpyrifos was measured in polar bear fat at all three sites. Geometric mean concentrations of 0.022 (0.013–0.035) ng/g lw, 0.032 (0.013–0.076) ng/g lw and 0.016 (0.0078–0.033) ng/g lw were measured (all values were recovery corrected and lipid normalized) (Supporting Information of Morris et al. (2016)).

3.3.3 Discussion on long-range-transport potential according to the criteria in Annex D

122. While modelling results do not predict long-range transport, chlorpyrifos is widely detected in remote areas far away from point sources and/ or agricultural use. Potential routes of transport include atmospheric transport in the gas or particulate phase, transport via water in rivers and/ or ocean currents.

123. Chlorpyrifos in the vapour phase is susceptible to reaction with OH radicals. As described by Muir et al. (Muir et al. 2004), atmospheric half-life is impacted by seasonal variations of OH radical concentration. Calculations indicate that a reduced OH radical concentration would result in a higher contribution of atmospheric transport.

124. Particulate chlorpyrifos is more recalcitrant to atmospheric degradation and has been detected in several studies. However, the available data indicate that its percentage is low.

125. Based on physico-chemical properties and modelling results, transport in the water phase is expected to be relevant for chlorpyrifos. In the water compartment, the substance may also bind to suspended solids and sediment (Macalady & Wolfe, 1985), where it is persistent (see chapter on persistence). Chlorpyrifos bound to particles in the Arctic ocean has been measured by Bigot et al. (2017). Water-borne chlorpyrifos could be carried to remote regions by long range transport via oceanic currents (Ma et al., 2018).

126. The numerous detections of chlorpyrifos in water samples from remote areas as well as modelling results indicate that transport also occurs via water. A recent study of S  hring et al. (2020) found that the long-range transport of organophosphate esters is not adequately predicted by the OECD Tool. Uncertainty in gas-particle partitioning of non-chlorinated organophosphate esters and river-based transport in case of chlorinated organophosphate esters were discussed as potential reasons for the underestimation of long-range transport (S  hring et al., 2020). Chlorpyrifos is an organothiophosphate, but the respective modelling results could be subject to similar problems. Particularly, transport in water might be underestimated by the OECD Tool.

127. There is no straightforward, model-supported explanation for a long-range transport of chlorpyrifos. However, the available data show that chlorpyrifos is present in ambient abiotic and biotic compartments in remote areas as the Arctic and Antarctic. It was detected in various studies, at different remote regions. Both modelling data and detection of chlorpyrifos in water indicate that transport via water is an important, but probably not the only route of transport.

3.3.4 Conclusion on long-range transport potential according to the criteria in Annex D

128. Predicted half-lives of gaseous chlorpyrifos in air ranging from 1.4 to 14 hours are relatively low and significantly below the threshold for LRTP of two days set by the Stockholm Convention. Particulate chlorpyrifos shows half-lives up to 66.5 hours and can be transported in air and water, although it presents a lower proportion of atmospheric chlorpyrifos. Though long-range transport is not predicted by modelling results, the compound has been found far away from point sources, in various abiotic and biotic compartments of remote areas such as in caribou, seals and ice bears in the Arctic and sea-ice meltwater and air of Antarctica. Thus, chlorpyrifos is considered to meet the criterion of the Stockholm Convention on long-range environmental transport (SSC, 2018).

3.4 Adverse effects

3.4.1 Human health effects

129. Chlorpyrifos can cause cholinesterase inhibition in humans at high enough doses that leads to an overstimulation of the nervous system causing nausea, dizziness, confusion, and at very high exposures (e.g. accidents or major spills), respiratory paralysis and death. Chlorpyrifos is listed in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation) as Acute Tox. 3, with the hazard phrase "H301-Toxic if swallowed". Prospective cohort studies in humans evaluated pre- and post-natal exposure to chlorpyrifos in mother-infant pairs and birth and developmental outcomes in neonates, infants, and children. The results from these studies have shown associations of exposure to chlorpyrifos during pregnancy with adverse neurodevelopmental outcomes in children, including changes in brain morphology, delays in cognitive and motor functions, and problems with attention, and tremors.

130. It is acknowledged that there is no established uniform mode of action/adverse outcome pathway (MOA/AOP pathway), single epidemiological studies do not provide causal linkages, and the window(s) of susceptibility is currently unknown. However, these uncertainties do not undermine or reduce the confidence in the findings of the epidemiology studies.

131. Severe poisoning in humans causes neurotoxic effects such as slurred speech, tremors, ataxia, convulsions, depression of respiratory and circulatory centres. Coma and death may ensue as a direct result of respiratory failure due to the combination of bronchoconstriction, bronchorrhea, central respiratory depression, and weakness or paralysis of respiratory muscles. Together, these immediate symptoms are referred to as the cholinergic syndrome or the cholinergic toxidrome. At lower concentrations, there is no evidence of systemic repeated dose toxicity, apart from significant decrease of RBC cholinesterase activity in chronic studies in rats and dogs. No evidence for a carcinogenicity potential was found upon chlorpyrifos administration in guideline studies in rats or mice. In the public literature, induction of oxidative stress was suggested to result in tissue damage and point towards beginning of cancer incidence. There is no evidence of adverse effects on fertility or prenatal developmental toxicity, with the exception of developmental neurotoxicity (DNT). Developmental neurotoxicity has been observed in rats and mice at doses that elicit minimal or no fetal brain acetylcholinesterase (AChE) inhibition. The developmental neurotoxicity database for chlorpyrifos is evolving and contains several in vivo animal studies that permit the establishment of a critical oral NOEL. The neurodevelopmental effects in these studies were similar regardless of the exposure window or the duration of the exposure.

Developmental neurotoxicity

Human studies

132. Epidemiological evidence showing associations between chlorpyrifos exposure during neurodevelopment and adverse health effects is in particular derived from, three cohort studies conducted by the Columbia Center for Children's Environmental Health (CCCEH) study, the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) and Mt. Sinai study.

133. In 2011, researchers at CCCEH published the results of a study that reported an association between foetal cord blood levels of chlorpyrifos and neurodevelopmental outcomes (Rauh et al., 2011). A sample of pregnant non-smoking women between 18-35 years old was enrolled. The cohort

started in 1997 to evaluate effects of prenatal exposure to ambient and indoor pollutants on birth outcomes, neurocognitive development, and procarcinogenic damage among a cohort of mother and new-borns from minority communities in New York City. As a follow-up, the authors performed magnetic resonance imaging studies on 40 cohort children (5.9 – 11.2 years old) to see if chlorpyrifos exposure in utero affected brain morphology (Rauh et al., 2012). Numerous morphological differences were reported in the children in high chlorpyrifos group, including enlarged superior temporal lobe, posterior middle temporal lobe, and inferior postcentral gyri bilaterally, as well as enlarged superior frontal gyrus, gyrus rectus, cuneus, and praecuneus along the mesial wall of the right hemisphere. These children also showed frontal and parietal cortical thinning and an inverse dose–response relationship between chlorpyrifos in cord blood and cortical thickness. The CCCEH cohort study was initiated while chlorpyrifos use was allowed for indoor use, U.S. EPA subsequently cancelled all indoor uses of chlorpyrifos by the end of 2001 (US-EPA, 2001).

134. In a follow up study, cohort children (n=271) were assessed again at age 11 (Rauh et al., 2015). The children underwent a full battery of neurodevelopmental measures, including a test of motor function. chlorpyrifos exposure was significantly associated with tremor in the dominant arm ($p = 0.015$), tremor in either arm ($p = 0.028$), and tremor in both arms ($p = 0.027$), and marginally associated with tremor in the non-dominant arm ($p = 0.055$) (Rauh et al., 2015). The authors state that morphologic changes appear to be related to lower IQs in these children and that the results support the notion that in utero exposure to chlorpyrifos is associated with general cognitive deficits (Rauh et al., 2012) and potential central or peripheral nervous system effects later in life (Rauh et al., 2015). Limitations of the study include the small sample size, and the extent of the cognitive assessment.

135. The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) project within the UC Berkeley Center for Children’s Environmental Health Research is a longitudinal birth cohort study of the effects of pesticides and other environmental exposures on the health of pregnant women and their children living in the Salinas Valley of California (Eskenazi et al., 2004). Eligible women were 18 or older and were less than 20 weeks pregnant at the time of enrollment (Oct 1999 – Oct 2000). (Bouchard et al., 2011) reported that children 7 years old in the highest quintile of prenatal Dialkyl phosphate (DAP) concentrations have an average deficit of 7.0 IQ points compared to the lowest quintile of prenatal urinary DAP. Prenatal DAP concentrations were also associated with poorer scores for Working Memory Processing Speed, Verbal Comprehension, and Perceptual Reasoning. Stein and colleagues published findings investigating early childhood adversities and the impact they may have on the association between prenatal OP pesticide exposures and the decrements in Full Scale IQ noted in the CHAMACOS cohort children. Overall, there were stronger associations between prenatal OP exposures (as measured by nonspecific urinary metabolites) and IQ scores among children who are experiencing certain adversities (Stein et al., 2016). PON1 genetic polymorphisms were studied in the CHAMACOS cohort, with allele frequencies for many polymorphisms differing between ethnic groups. The authors noted that functional effects of PON1 genetic variability related to susceptibility to organophosphates and oxidative stress varied by age, and variability should be considered in protecting certain subpopulations.

136. From 1998 to 2002, the Mount Sinai Children’s Environmental Health Study enrolled more than 400 pregnant women into a prospective study to investigate linkages between environmental exposures and impaired child cognitive development. All mothers gave birth at Mount Sinai Hospital in New York City between May 1998 and July 2001. The overall results support the association of prenatal OP exposure and the presence of specific PON1 genotypes associated with slower catalytic activities with negative effects on cognitive development. The authors note that reconciling estimated effects when using nonspecific urinary metabolites add uncertainty as those metabolites can derive from multiple parent compounds (Engel et al., 2011).

137. In 2015 US EPA updated a literature review (US-EPA, 2016). In addition to the three main birth cohort studies (CCCEH, CHAMACOS, Mt. Sinai study), the update identified seven studies which were considered relevant (Bouchard et al., 2010; Fortenberry et al., 2014; Furlong et al., 2014; Guodong et al., 2012; Oulhote & Bouchard Maryse, 2013; Shelton et al., 2014; Zhang et al., 2014). Despite differences in study design, with the exception of two negative studies in the 2015 literature review (Guodong et al., 2012; Oulhote & Bouchard Maryse, 2013) and the results from the more recent (Engel et al., 2016) study, all other study authors have identified neurodevelopmental outcomes associated with OP exposure; these conclusions were across four cohorts and twelve study citations.

138. In July 2018, California EPA published their “Final Toxic Air Contaminant Evaluation of Chlorpyrifos” (CalEPA, 2018) Several additional epidemiological studies have been reviewed (Bielawski et al., 2005; Corrion et al., 2005; Fluegge et al., 2016; Enrique M. Ostrea, Jr. et al., 2012; E. M. Ostrea, Jr. et al., 2006; Posecion et al., 2006; Silver et al., 2015; Silver et al., 2017; Wickerham et al., 2012). CalEPA concluded associations of indoor and outdoor exposure to chlorpyrifos during

pregnancy with adverse neurodevelopmental outcomes in children, including changes in brain morphology, delays in cognitive and motor functions, and problems with attention, and tremors.

139. In July 2019, the European Food Safety Authority (EFSA, 2019), published a statement on the available outcomes of the human health assessment in the context of the pesticides peer review of chlorpyrifos. The experts discussed the epidemiological evidence showing associations between chlorpyrifos exposure during neurodevelopment. In particular, the same three main birth cohort studies were considered: (CCCEH, CHAMACOS, and Mt. Sinai study). It was concluded that using different biomarkers of exposure, the studies show that prenatal exposure to organophosphates (OPs) produces a consistent pattern of early cognitive and behavioural deficits. The experts discussed also other epidemiological evidence from the public literature and considered that the results from some of these studies (mainly from CCCEH study, (Engel et al., 2011; Rauh et al., 2012; Silver et al., 2017) contribute to the evidence of DNT effects in humans due to the exposure to chlorpyrifos and occurring at doses lower than that causing 20% inhibition of AChE.

140. In the literature search conducted by Ramboll GmbH to contribute to this dossier, additional 28 epidemiological studies have been identified subsequently to the CalEPA review since 2017. The studies add information related to exposure assessments and potential targets. The results are in line with the remaining body of evidence but do not provide significant new information. An exemption is the reevaluation of the statistics used in a 1972 Dow study by researchers at the Albany Medical College (report no #071392 as summarized in Spain (2019)). Sheppard et al. (2020) suggest that the statistical method for deriving a chronic no-observed-adverse-effect-level (NOAEL) of 0.03 mg/kg-day for chlorpyrifos in humans was not correct. In contrast, the authors suggest a lower NOAEL of 0.014 mg/kg-day, and that use of statistical methods first available in 1982 would have shown that even the lowest dose in the study had a significant treatment effect.

141. It is acknowledged that single epidemiological studies cannot determine causation. There is also the lack of established MOA/AOP pathway and uncertainty about the window(s) of susceptibility. Genetic polymorphisms have been shown to influence the rates of organophosphate metabolism in humans (Bouchard et al., 2011; Engel et al., 2011). Genotype data is not available for most epidemiological study. However, these uncertainties do not undermine confidence in the results of the majority of epidemiological studies.

Animal experiments

142. The developmental neurotoxicity database for chlorpyrifos is evolving and currently contains several *in vivo* animal studies that might permit the establishment of an oral NOEL below the reported threshold of 1 mg/kg/day established for RBC AChE inhibition. Silva et al. (2017) investigated the effects on complex behaviors (particularly anxiety and depression) in Wistar rats exposed to chlorpyrifos *in utero*. Pregnant dams (11-14/dose) received 7 consecutive daily doses (0.01, 0.1, 1 and 10 mg/kg/day) by oral gavage on gestation days 14–20. Behavioral parameters in male offspring were evaluated during the infant-juvenile period (postnatal day [PND] 21) and in adulthood (PND70). Male pups were separated into 4 groups (8-10 pups/group) comprised of those tested on PND 21 or PND70. The elevated plus-maze test was used to assess anxiety levels. The open field test was used to evaluate locomotor activity. The modified forced swimming test was used to assess depressive behavior. Neither RBC nor brain AChE levels were determined in dams or pups. The authors concluded that chlorpyrifos treatment during pregnancy induced anxiogenic behavior in pups at the end of lactation (PND21). It should be emphasized that the use of maze-based behaviours as the method for discerning cognitive deficits may not cover the more complex neurological functions in humans. Therefore, its direct relevancy is unknown. As a result, the authors set the LOEL for neurodevelopmental effects at 0.1 mg/kg/day. The lowest tested dose 0.01 mg/kg/day was the NOEL. The apparent absence of a dose-related exacerbation of this response above 0.1 mg/kg/day was unexplained but was considered plausibly due to saturation of one or more of the neural pathways involved in regulation of complex behaviors such as these. The data were presented without reporting individual data, means, or standard deviations.

143. Gómez-Giménez et al. (2017) conducted a study to determine if spatial learning was affected in either sex after developmental exposure and if hippocampal inflammation was associated with effects on spatial learning. Pregnant Wistar rats (6/dose) were fed chlorpyrifos mixed in sweet jelly at GD 7-GD20 (0, 0.1, 0.3 and 1.0 mg/kg/d). Pups were weaned PND 21 and were tested for Cognitive Impairment in the Morris water maze (Escape latency, Reference errors, Working memory). Escape latency in males increased at 0.1 mg/kg/day and above. Time spent in right quadrant on day 3 of testing was decreased in males at 1.0 mg/kg/day and unaffected in females. Spatial reference errors (first visits to unbaited arms) on testing day 4 were increased in males at >0.3 mg/kg/day. Working errors (visits to arms already visited in the same trial when seeking the baited arm) over the 5 days of

testing increased in males at 0.3 mg/kg/day; females were not statistically significantly affected. Learning index at day 4 decreased in males at >0.3 mg/kg. There was no apparent dose response in any of the effects. The authors conclude that chlorpyrifos impaired learning in males but not in females. The LOEL for decreased spatial learning in males was 0.1 mg/kg/day. After the behavioral tests, rats were terminated and the hippocampus was for proteins indicative of neuroinflammation. Neuroinflammation was also equivocal since only one parameter (IL10) was positive out of 13 tested in both sexes. Effects to IL10 in females at 0.3 mg/kg/d lead to a LOEL for neuroinflammation was 0.1 mg/kg/d for both males and females.

144. In 2018, Gómez-Giménez et al. (2018) tested for potential gender-related effects of chlorpyrifos on spontaneous motor activity and motor coordination. As in the previous study, pregnant Wistar rats were fed chlorpyrifos mixed in sweet jelly at 0, 0.1, 0.3 and 1.0 mg/kg/day at GD 7 through PND 21. The pups, weaned on PND 21, were tested at age 2-3 months for impacts on motor activity. Spontaneous motor activity was measured in an open-field activity chamber (novel environment) using an actimeter (infrared motion detection). Motor coordination was measured by rotarod. Females at 0.3 mg/kg/day exhibited decreased motor coordination on the rotarod. There was a statistically significant increase in spontaneous motor activity in males and females at 0.1 mg/kg/day, but not at 0.3 or 1 mg/kg/day. The LOEL was established at 0.1 mg/kg/d based on increased spontaneous motor activity in both sexes at that dose.

145. Similar motor effects were observed by Lee et al. (2015) in PND 60 mouse pups both at doses of 0.1 mg/kg. Male NMRI mice were treated by gavage with chlorpyrifos during rapid brain growth and maturation to investigate whether an acute perinatal exposure could be associated with behavioral effects in adulthood. Testing included motor activity assessment, brain AChE inhibition analysis and neuroprotein analysis. Results indicated 8-12% brain AChE inhibition at 5.0 mg/kg (only dose tested: inhibition peaked at 3 h post-dose) which was reversed by 6 hours post-dose. The spontaneous motor behavior tests at 2 or 4 months after exposure showed statistically significant decreases in locomotion, rearing and total activity at 5.0 mg/kg. Total activity was statistically significantly increased at 0.1 and 1 mg/kg/day at 2 months and remained increased for the rats at 1 mg/kg/day at 4 months. The LOEL for increased total activity was 0.1 mg/kg/day. The authors suggested that homeostatic disturbances during BGS of CaMKII may lead to irreversible behavioral effects lasting into adulthood.

146. Mohammed et al. (2015) showed that male and female rat pups treated by oral gavage with chlorpyrifos at 0.5 mg/kg/day during PND 10-16 exhibited behavioral anomalies when tested on PND 25. Decreased anxiety was evident through increases in number and percent of open arm entries, time and percent time spent in open arm of a plus maze, occurrences of crawling over/under, motor activity, play-fighting and time spent playing. In a subsequent study, pups were treated by gavage on PND 10-15 with 0, 0.5, 0.75 or 1 mg/kg/day chlorpyrifos (6-8/sex/dose) (Carr et al., 2017). Forebrain AChE inhibition was noted at the high dose, setting the LOEL for brain AChE inhibition at 1.0 mg/kg/day. Behavioral testing showed decreased times to emergence from a dark container into a novel environment at 0.5 mg/kg/day in both sexes. This behavior was associated with decreased anxiety. The data confirm earlier findings from this group showing that chlorpyrifos treatment generated behavioral effects at doses lower than those inhibiting brain AChE. The LOEL for decreased anxiety in PND 25 pups was 0.5 mg/kg/day.

147. Effect on developmental neurotoxicity (DNT) was examined by daily oral gavage of chlorpyrifos in pregnant rats (25/dose) during gestation and the perinatal period (GD 6 - PND 11) at doses of 0, 0.3, 1, and 5 mg/kg/d (Hoberman, 1998). Evident maternal effects were observed at 5 mg/kg bw/day, with decreased bodyweight gain, food consumption, brain, RBC and plasma cholinesterase inhibition, and manifestation of clinical signs (fasciculations, hyperpnea and hyperactivity). The critical maternal effect was a decrease in the RBC Cholinesterase at all dose levels (maternal LOAEL: 0.3 mg/kg bw/day). The offspring showed signs of toxicity at the same dose, such as decreased viability index (day 1-5), bodyweight and food consumption. Developmental landmarks were also delayed. On the contrary, brain AChE was not altered. Developmental neurotoxicity was transiently manifested with changes in the brain weight, decreased layer thickness in brain areas (PND 12), and increased latency of the auditory startle response at PND 23. All effects were resolved in the adult period (PND 60-71). Morphometric measurements for nine brain regions in PND 12 pups revealed statistically reduced cerebellar dimensions in high dose males. As high dose male brain weights were 11.5% lower than concurrent controls, a chlorpyrifos-mediated impact on cerebellar growth in these males was considered to be possible. Similar morphometric measurements were conducted in PND 66-71 adults, revealing statistically reduced parietal cortex dimensions in 1 and 5 mg/kg females (4% and 5%, respectively; $p < 0.05$). Because control and 1 mg/kg/day female brain weights were unaffected, these changes were consistent with the possibility of a chlorpyrifos-mediated effect. A developmental lowest observed effect level (LOEL) of 1 mg/kg/day was suggested based on reduced parietal cortex and hippocampal dimensions in PND 66-71. Morphometric observations were

not made at 0.3 mg/kg/day; consequently, a discrete no-observed effect level (NOEL) could not be determined.

148. In October 2000, Hoberman et al. provided a Report Supplement to Hoberman 1998 (# supplement: 304-001) (Hoberman, 2000). Brain morphometric data from the original report were re-tabulated alongside historical control data from 4 or 5 studies per parameter. Only one measurement having a high dose value statistically significantly different from concurrent controls was outside the range of the historical controls: the cerebellar anterior/posterior dimension in 5 mg/kg/d male 12-day pups was significantly below concurrent control dimension, and also outside the range of the available historical controls. Females did not suggest such a relationship at 12 days, and neither sex showed altered cerebellar anterior/posterior distance after 66 days. In the context of the demonstrated high maternal and neonatal toxicity of this dose, the supplemental data reinforce the conclusion that study findings are not of sufficient magnitude or persistence to be considered as “adverse” even at gestational / postnatal doses as high as 5 mg/kg/day. This was surprising in light of the observations in later studies of effects at 0.1 mg/kg.

149. Both anxiogenic and anti-anxiogenic responses were observed in the DNT studies (Carr et al., 2017; Silva et al., 2017), highlighting the possibility that the effects were mutable and possibly toxicologically insignificant. However, CalEPA notes that the anxiogenic behavior observed by Silva et al. (2017) resulted from gestational exposure, while the anti-anxiogenic behavior observed by Carr et al. (2017) resulted from postnatal exposure (CalEPA, 2018). As the developmental status of the very young organism changes with time, the precise staging of chlorpyrifos exposures likely affects the nature of the response.

150. Several *in vitro* studies have observed negative effects of chlorpyrifos and chlorpyrifos-oxon on neuronal growth in tissue culture, including decreased axonal length and inhibition of neurite outgrowth (D. L. Eaton et al., 2008) These *in vitro* effects occurred at concentrations orders of magnitude less than what would result in AChE inhibition and add to the body of evidence, that effects other than AChE inhibition might trigger the risk assessment of chlorpyrifos.

3.4.2 Ecotoxicological effects

151. As mentioned earlier in this dossier, chlorpyrifos is an organophosphorus insecticide with a broad-spectrum pest-control. Because chlorpyrifos induces irreversible inhibition of acetylcholinesterase in the central and peripheral nervous system (Colovic et al., 2013; K. R. Solomon et al., 2014; WHO, 1987), severe toxic effects in non-target organisms are also expected. This was confirmed by the US EPA Registration Review of chlorpyrifos from 2009 (US-EPA, 2006), which identified concerns about acute and chronic risks to birds, mammals, fish, aquatic invertebrates and terrestrial invertebrates. Similar concerns to birds and mammals were identified by EFSA (2005) and EFSA (2014). Additionally, marine and semi-aquatic mammals such as manatees, whales, dolphins, sea otters and sea lions lack the Paraoxonase 1 enzyme needed to further metabolize chlorpyrifos and other organophosphate pesticides (Meyer et al., 2018).

Adverse effects on aquatic organisms

152. Chlorpyrifos displays high acute and chronic toxicity to aquatic organisms. According to the Globally Harmonised System of Classification and Labelling, the EU has classified chlorpyrifos in 2005 as Aquatic Acute Tox 1, with the hazard phrase “H400 – very toxic to aquatic life”; and Aquatic Chronic Tox 1, with the hazard phrase “H410 – very toxic to aquatic life with long lasting effects” (EFSA, 2014).

153. Standard laboratory studies performed with the active ingredient chlorpyrifos according to the OECD 203 guideline for acute effects (i.e. lethality) identify *Oncorhynchus mykiss* as the most sensitive fish species tested. Spain (2017b) reports a 96 h LC₅₀ value of 8 µg active substance per litre (a.s./L) for a test performed with “Dursban” (trade name of DOW, 99.9% purity). For fish, based on data available in Spain (2017b) there is no evidence for higher toxicity of the active ingredient when formulated, although no test with EC formulations (Emulsified Concentrate), the most common formulations in agriculture, are available. When considering studies from the literature not strictly following the OECD 203 but performed under similar conditions, lower 96 h LC₅₀ values are reported. Accordingly, 96 h LC₅₀ values ranging from 0.53 to 520 µg a.s./L are reported in J. R. Clark et al. (1985). The authors identified the estuarine fishes *Menidia menidia*, *M. peninsulae*, *M. beryllina* and *Leuresthes tenuis* as the most sensitive species, with 96 h LC₅₀ values ranging from 0.53 to 4.2 µg a.s./L. However, there is no strict evidence in sensitivity differences between saline and/or freshwater fish species. Based on data ranging from 0.53 to > 860 µg a.s./L collected for 25 fish species, Giesy et al. (2014) used species sensitivity distribution (SSD) to calculate a hazardous concentration for 5% of species (HC₅-LC₅₀) of 0.812 µg a.s./L. This means that at the concentration of 0.812 µg a.s./L already

5% of the fish species included in the SSD reach their LC₅₀, which clearly demonstrates the acute toxicity of Chlorpyrifos to fish.

154. Studies looking at chronic toxicity usually expose animals to sub-lethal concentrations. However, in the case of Chlorpyrifos, because of its high toxicity, lethality often remains the most sensitive endpoint recorded in chronic tests, despite the low concentrations tested in such studies. Only few studies performed in laboratory conditions similar to those of the OECD 210 guideline, i.e. focusing on sub-lethal effects and on the early life stages of the species tested, record effects at concentrations slightly lower but still in the same range as lethality. For the estuarine fish *Leuresthes tenuis*, Goodman, Hansen, Cripe, et al. (1985) reported NOEC values of 0.14 and 0.3 µg a.s./L for embryo weight and lethality respectively. Jarvinen and Tanner (1982) determined NOEC values of 1.6 and 3.2 µg a.s./L for weight and lethality of *Pimephales promelas* fry exposed to Dursban technical grade for 35 days. The lowest NOEC estimated for chronic mortality is 0.3 µg a.s./L. This endpoint was assessed for embryo lethality in *Leuresthes tenuis* in a 35-days exposure design (Goodman, Hansen, Cripe, et al., 1985).

155. Substantial quantity of data is available for aquatic exposure of amphibians to chlorpyrifos. Fryday and Thompson (2012) report 96-h LC₅₀ < 1 mg/L for the *Xenopus laevis* and *Bufo bufo Gargarizans* (0.564 from Richards and Kendall (2002) and 0.800 mg a.s./L from Yin et al. (2009), respectively).

156. Invertebrates, especially crustaceans and insects, are the most sensitive taxa among aquatic organisms. Considering only tests performed in an OECD 202 design, European Commission (2005) and Spain (2017b) identified *Daphnia magna* as the most sensitive species with an EC₅₀ of 0.1 µg a.s./L. This endpoint is in the same range as the EC₅₀ of 0.138 µg a.s./L determined for the macroinvertebrate *Hyaella azteca* (Brown et al., 1997). When referring to non-OECD tests with similar set ups, Giddings et al. (2014) identified *Daphnia ambigua* as the most sensitive species with an EC₅₀ of 0.035 µg a.s./L. Using an SSD approach, the authors calculate HC5 values of 0.034 µg a.s./L for crustacea and 0.087 µg a.s./L for insects, based on EC₅₀ values collected for 23 and 17 species, respectively. These hazardous concentrations are a factor 10 below the HC₅-LC₅₀ calculated for the fish.

157. Reproductive studies following the OECD 202 test design with *Daphnia magna* found no effect on reproduction or mortality at the concentration of 0.056 µg/L. However, 100% mortality occurred within 21 days for the next tested concentration of 0.1 µg/L (Adema and DeRuiter, 1990). Similar studies performed on the marine shrimp *Mysidopsis bahia*, reported a NOEC of 4.6 ng a.s./L. based on mortality and growth impairment occurring at concentrations of 10 ng a.s./L and above (Sved, 1993).

Adverse effects on terrestrial organisms

158. Chlorpyrifos shows high acute toxicity to terrestrial vertebrates, especially to birds (Solomon et al., 2014). Considering the current state of science and technology, the rapporteur member state Spain proposed in the RAR (Spain (2017b) to revise the LD₅₀ of 13.3 mg a.s./kg bw initially recorded in a Peer Review study (Schafer et al., 1983) on the Japanese Quail (*Coturnix coturnix*) to the LD₅₀ of 39.24 mg a.s./kg bw calculated according to the OECD 223 guideline for the Bobwhite quail (*Colinus virginianus*). Both tests were performed with chlorpyrifos as technical grade. When tested as product, chlorpyrifos indicates a slightly higher toxicity for Emulsified Concentrate (EC) or Capsule Suspension (CS) formulations. Spain (2017b) reports LD₅₀ values of 19.92 and 17.5 mg a.s./kg bw for *Colinus virginianus* in EC and CS formulations, respectively. High toxicity for birds is confirmed in dietary studies, which represent a more realistic exposure scenario. Dietary studies (i.e. 5 days feeding followed by 3 days observation) performed on the mallard duck *Anas platyrhynchos* calculated a LD₅₀ of 71 mg a.s./kg bw (European Commission, 2005).

159. When the substance is administrated by gavage in mammals, European Commission (2005) reports acute oral LD₅₀ ranging from 66 to 192 mg a.s./kg body weight (bw) in rats and from 64 to 71 mg a.s./kg bw in mice. The LD₅₀ of 64 mg a.s./kg bw was confirmed by EFSA (2011) to assess the acute toxicity of chlorpyrifos for wild mammals.

160. Long-term reproduction toxicity studies identified various effects on nervous system, depression of erythrocyte (RBC) and acetylcholinesterase (AChE) in mammals. Considering a two-generation reproductive study in rats performed in an OECD 416 design, European Commission (2005) reported a parental and neonatal NOAEL of 1 mg a.s./kg bw/day based on brain cholinesterase depression, histopathologic alteration for parents and decreased growth and survival for offspring. However, lower NOAEL of 0.1 mg/kg bw/day due to a decreased body weight gains and brain

cholinesterase depression was also observed in a 2-year dietary study in rats (European Commission, 2005).

161. For birds, no reproductive impairment (NOAEL) was reported in a study of DOW for the mallard duck (*Anas platyrhynchos*) at a dose level of 2.885 mg/kg bw/day (European Commission, 2005). Additionally, to these classical reproductive endpoints usually recorded in OECD test designs, Eng et al. (2017) recently demonstrated that sub-lethal endpoints such as migratory activity and orientation are highly relevant to describe the risk to granivorous birds. In their paper, the authors focused on a granular formulation and reported that wild songbirds consuming the equivalent of eight chlorpyrifos granules per day over 3 days could suffer impaired condition, migration delays and improper migratory direction, which could lead to increased risk of mortality or loss of breeding opportunity.

162. Chlorpyrifos has been designed to control a wide variety of foliage- and soil-borne insects. It is a broad-spectrum insecticide and thus toxic effects on non-target arthropods, especially pollinators, exist. Chlorpyrifos is highly acutely toxic to the honey bee *Apis mellifera*. The highest toxicity is identified when the substance is administered via contact. Bell (1994) measured an acute LD₅₀ of 0.068 µg a.s./bee in a test performed with Dursban F (97.4% purity). For comparison, the lowest LD₅₀ estimated for oral toxicity is 0.15 µg a.s./bee (Bell, 1993).

163. In addition to acute toxicity, Spain (2017b) reports recent studies on chronic toxicity of chlorpyrifos for bees and bee brood. These tests follow the recommendations of Decourtye et al. (2005) and EFSA (2013) to evaluate among others the chronic mortality following a 10-day exposure at very low concentrations, or they follow the OECD 237 guideline to assess potential lethal or sublethal effects affecting the bee brood and development. Accordingly, for chlorpyrifos technical Noël (2015) calculated a 10 d-LC₅₀ of 0.002 µg a.s./bee/day. For bee brood development, Deslandes (2014) determined a NOED of 0.018 µg a.i./bee for larvae.

164. Chlorpyrifos has been extensively tested on non-target arthropods. Laboratory tests reported in Spain (2017b) indicate that Chlorpyrifos is very harmful for beneficial arthropods. When exposed to fresh dry residues of an EC formulation (EF-1042) on glass plates, the 24h-LR₅₀ of the beneficial aphid parasite *Aphidius colemani* (Hymenoptera: Braconidae) was determined to be < 1ppm (Mead-Briggs, 1997). The high acute toxicity of Chlorpyrifos to Braconidae is confirmed by tests performed in a topical (i.e. contact) design (e.g. 24h-LR₅₀ values of 3.21 and 3.62 ppm for *Bracon brevicornis* and *Chelonus blackburni*, respectively). Acute LR₅₀ values < 1ppm were also reported for the beneficial aphids *Acyrtosiphon kondoi*, *A. Pisum* (Homoptera: Aphididae) as well as for the brown lacewings *Austromicromus tasmaniae* (Neuroptera: Hemerobiidae). Further acute LR₅₀ values of 1 ppm or less are reported in Spain (2017b) for the damselflies *Enallagma* spp. and *Ischmura* spp. (Odonata: Coenagrionidae) and larvae of Trichopteran species *Hydropsyche* and *Chematopsyche* spp. (Trichoptera: Hydropsychidae).

165. Among Coleoptera, the lady beetle *Coccinella undecimpunctata* was the most sensitive species tested (LR₅₀ = 1.9 ppm). A LR₅₀ of 24 ppm is reported by Siegfried (1993) for the European corn borer pest *Ostrinia nubilalis* (Lepidoptera: Crambidae).

166. The acute toxicity of chlorpyrifos tested as EC formulation (EF 1042 = Dursban 480) on the redworm *Eisenia foetida* in an artificial soil (OECD 207) delivers a 7-days LC₅₀ of 313 ppm corresponding to about 137 mg a.s./kg soil (European Commission (2005)). However, additionally to acute effects, chlorpyrifos appears to be highly chronically toxic to earthworms. In a 56 days study following the OECD 222 design (earthworm reproduction test), De Silva et al. (2009) detected effects of the technical chlorpyrifos on the reproduction of *E. foetida* at concentration around and lower than 1 mg a.s./kg soil. Compared to the earthworms, chlorpyrifos is more chronically toxic to soil macro-organisms such as collembola and mites. A test on the springtail *Folsomia candida* (Collembola) conducted with technical chlorpyrifos following an OECD 232 design reports a 28-d NOEC mortality of 0.075 mg a.s./kg soil (Witte, 2014). When looking at sub-lethal effects, the NOEC is 0.024 mg a.s./kg soil for effects on reproduction of the animals. These effects observed at laboratory level were confirmed by field data.

3.4.3 Conclusion on adverse effects concerning human health and the environment according to the criteria in Annex D

167. Laboratory studies clearly demonstrate that chlorpyrifos is highly toxic to aquatic communities at concentrations around 0.1 µg a.s./L and below for aquatic invertebrates. Chlorpyrifos also shows high acute toxicity to terrestrial vertebrates, especially to birds, with an LD₅₀ value of 13.3 mg a.s./kg bw for Japanese quail. For mammals, LD₅₀ values from 64 to 71 mg a.s./kg bw in mice are reported. Values for chronic toxicity are lower, with e.g. a NOAEL of 0.1 mg/kg bw/day observed

in a 2-year dietary study in rats. Based on these studies, the available data on ecotoxicity of chlorpyrifos indicates the potential for damage to the environment.

168. *In vivo* animal studies provide evidence of developmental neurotoxicity (DNT) at chlorpyrifos doses below those causing cholinesterase inhibition. Effects on the developing nervous system include altered cognition, motor control, and behaviour in rats and mice. Based on these studies, along with epidemiological evidence, chlorpyrifos is considered toxic to the developing nervous system.

4. Statement of the reasons for concern and need for global action

169. Environmental degradation half-lives of chlorpyrifos range from a few days to several years, depending on application rate, ecosystem type, soil or sediment characteristics, and other environmental factors (Gebremariam et al., 2012). Chlorpyrifos can be persistent in marine water, in some soils and deeper sediment layers. Monitoring data from the Arctic and Antarctic demonstrate that chlorpyrifos can be transported over long distances to remote regions. Since degradation of chlorpyrifos is temperature dependent, it is expected to persist in these regions for a considerable length of time. Frequent findings of chlorpyrifos in all media in the Arctic support this. In addition, chlorpyrifos is found in dated sediment cores in Arctic and sub-Arctic lakes (Landers, 2008). Thus, it can be concluded that chlorpyrifos is sufficiently persistent to justify its consideration within the Convention.

170. Although numerous studies show moderate bioconcentration, this in combination with high toxicity gives reason for serious concern. As chlorpyrifos has been found in biota at different trophic levels in the Arctic regions, globally in apex predators and in human breast milk at levels concerning for offspring, we conclude that the bioaccumulation potential of chlorpyrifos is sufficient to justify its consideration within the Convention.

171. The predicted half-lives of chlorpyrifos in air ranging from 1.4 to 14 hours are relatively low, but it has been found in various abiotic compartments of remote areas in the Arctic and Antarctic, as well as in apex predators of the Arctic including polar bears, demonstrating its ability to undergo long-range transboundary transport. Potential routes of transport include atmospheric transport in the gas or particulate phase, transport via water in rivers and/ or ocean currents.

172. Epidemiological evidence in combination with animal studies are evidence for developmental neurotoxicity (DNT) of chlorpyrifos in humans. Additionally, chlorpyrifos exhibits acute and chronic effects at very low and environmentally relevant concentrations. It is highly toxic to aquatic communities, early life stages of fish and aquatic invertebrates, bees, birds and mammals. The ecotoxicological and toxic properties of chlorpyrifos lead to adverse effects for human health and the environment.

173. Based on the persistence, potential for bioaccumulation, toxicity to aquatic organisms and terrestrial animals (including humans) and the widespread occurrence in environmental compartments including remote regions, it is concluded that the use of chlorpyrifos is likely to lead to significant adverse human health and environmental effects such that global action is warranted.

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This is **Exhibit “U”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)

Laura Bowman

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February 15, 2021

Andrea Bourke / Karen Lovell / Elizabeth Koudys / Andrew Law
Department of Justice Canada
Ontario Regional Office
sent by email: andrea.bourke@justice.gc.ca

Dear Counsel:

Re: Safe Food Matters et al v AGC (T-956-21), (T-121-22) and (T-1412-21)

Thank you for delivering the public version of the certified tribunal record (CTR) in T-121-22. We are writing to follow up on some aspects of the CTR which appear to be incomplete.

The record does not provide any clarity regarding the existence (or lack thereof) of scientific evaluations supporting the recommendations in the Briefing Note (CTR Doc 79) or final decision in REV2021-04. In particular, there does not appear to be a scientific analysis document for the conclusions referenced in REV2021-04. For example, we would expect to see a monograph completed by PMRA technical staff and peer reviewed on each scientific issue, as is PMRA practice. It is not clear if scientific staff involved in the re-evaluation prepared any technical analysis in support of the conclusions in REV2021-04, and if so, what that analysis was. This information has heightened relevance because there are no detailed minutes provided of the SMC meeting where the decision in REV2021-04 was approved, and the Briefing Note does not disclose how the scientific conclusions were reached.

In contrast to the CTR provided in T-956-21, your clients have not provided any draft Briefing Notes or emails from technical staff discussing the preparation of the Briefing Note. In further contrast to the CTR provided in T-956-21 your clients have not provided monographs, science memos or analyses. These documents, if they exist, would shed light on the considerations the PMRA engaged in when making its decision in REV2021-04.

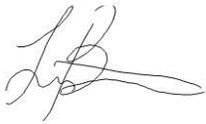
This information is relevant to whether the decision in REV2021-04 was reasonable. It would demonstrate whether the PMRA considered available information in reaching the conclusions in REV2021-04, whether it followed the prescribed methodology in the *Pest Control Products Act* and PMRA policies, and whether the PMRA addressed the concerns of the applicants in assessing whether the phase-out period was appropriate.

If these materials exist, we request that they be provided as part of the CTR. For clarity the materials include:

- (1) scientific evaluations (including monographs, science memos, or analyses);
- (2) draft Briefing Notes and revision history;
- (3) emails from technical staff providing background and context to the Briefing Note;
- (4) any other materials relevant for the conclusions and recommendations in the final Briefing Note, or that support the SMC decision on December 16, 2021.

We note that our clients' Rule 317 request included these materials. Please advise us as soon as is possible whether your client intends to disclose this documentation and if not, why not.

Sincerely,

A handwritten signature in black ink, appearing to read 'LB', with a long horizontal flourish extending to the right.

Laura Bowman
Counsel

cc: co counsel

This is **Exhibit “V”** referred to in the affidavit of
Dr. Elaine MacDonald affirmed remotely before
me in accordance with O. Reg 431/20,
Administering Oath or Declaration Remotely
this 7th day of March, 2022.



Commissioner for Taking Affidavits
(or as may be)



Department of Justice
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Via Email

Our File Number: LEX-500078416

February 18, 2022

Laura Bowman and Daniel Cheater
Ecojustice
1910 – 777 Bay Street, PO Box 106
Toronto, ON M5G 2C8
Fax: 416-363-2746
Tel: 416-368-7533 ext 522

Dear Ms. Bowman and Mr. Cheater:

Re: Safe Food Matters et al v AGC et al (T-121-22)

I write further to Ms. Bowman's letter of February 15, 2022, concerning the Certified Tribunal Record ("CTR") that the Attorney General of Canada delivered in response to your request in Court File T-122-22. I confirm that the Pest Management Regulatory Agency ("PMRA") has produced all documents that it considered in making the challenged decision that are not already in your clients' possession as a result of the delivery of the CTR in Court File T-956-21, subject only to solicitor-client and litigation privilege, which documents PMRA objects to producing.

We remind you that the challenged decision at issue was not a decision to register or re-evaluate a product, but the communication to the public about the cancellation of certain products pursuant to paragraph 20(1)(a) as a result of failures to respond to data call in requests by PMRA, and the corresponding conditions of cancellation pursuant to subsection 21(5). PMRA already had in its possession significant information on which to determine the appropriate phase out period having regard to the factors set out in PMRA policy documents.

Sincerely,

Andrea Bourke
Senior Counsel
Litigation, Extradition and Advisory Division