

# Additional information relating to the draft risk profile for chlorpyrifos

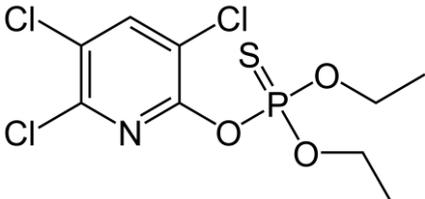
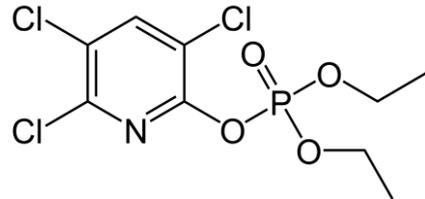
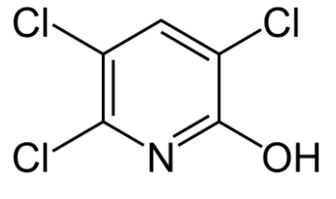
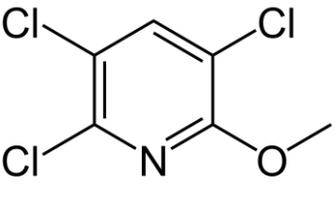
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## 1. Physico-chemical properties

Table 1. Physico-chemical properties of chlorpyrifos and its degradation and transformation products

	Chlorpyrifos	Chlorpyrifos-oxon (CPYO)	3,5,6-Trichloro-2-pyridinol (TCP)	2-Methoxy-3,5,6-trichloro-pyridine (TMP)
<b>Structure</b>				
<b>Property</b>	Value and source	Value and source	Value and source	Value and source
<b>CAS no.</b>	2921-88-2	5598-15-2	6515-38-4	31557-34-3
<b>Molecular weight [g/mol]</b>	350.59	334.52	198.44	212.46
<b>Form</b>	Tan, crystalline solid (94 % purity) (EC, 2005) Colourless to white crystalline solid (ILO & WHO, 2014)	No data	No data	No data
<b>Odour</b>	Mild mercaptan (experimental, 99.6 % purity) (EC, 2005)	No data	No data	No data
<b>Melting point [°C]</b>	41–42 (experimental at 97–99 % purity) (EC, 2005) 42 at 99.9 % purity (Spain, 2017)	83.44 (estimated) (US-EPA, 2012)	82.30 (estimated) (US-EPA, 2012)	58.75 (estimated) (US-EPA, 2012)
<b>Thermal decomposition point [°C] (decomposition before boiling)</b>	170–180 Experimental data (EC, 2005; Spain, 2017)	No data	No data	No data
<b>Vapour pressure [Pa]</b>	$3.35 \times 10^{-3}$ 25°C (purity 99.8%) (EC, 2005) $1.43 \times 10^{-3}$ 20°C (purity 99.8%) (EC, 2005) $1.0 \times 10^{-3}$ Experimental, 25°C (purity 98%) (WHO, 2009) $2.3 \times 10^{-3}$ Compiled by Mackay et al. (2014)	$8.87 \times 10^{-4}$ (estimated) (US EPA, 2012)	0.138 (estimated) (US EPA, 2012) $3.57 \times 10^{-3}$ at 25°C $1.79 \times 10^{-3}$ at 20°C (purity 99.6%) (Spain, 2017)	1.43 (estimated) (US EPA, 2012) 1.27 at 25°C 0.9 at 20°C (purity 100%) (Spain, 2017)

	<b>Chlorpyrifos</b>	<b>Chlorpyrifos-oxon (CPYO)</b>	<b>3,5,6-Trichloro-2-pyridinol (TCP)</b>	<b>2-Methoxy-3,5,6-trichloro-pyridine (TMP)</b>
<b>Water solubility [mg/L]</b>	1.05 at 20°C, in unbuffered solution, no pH dependency reported (EC, 2005) 0.39 at 19.5°C, pH not cited (98 % purity) (WHO, 2009) 0.73 Cited by Mackay et al. (2014) 0.941 (20°C, pH unknown, guideline EEC Method A6/OECD 105) Dow, as cited in WHO (2009) 0.588 (20°C, pH not stated, guideline OECD 105 flask method) Makhteshim, as cited in WHO (2009)	25.97 (25°C, estimated from log $K_{ow}$ ) (US EPA, 2012) 2623.4 (25°C, estimated from fragments) (US EPA, 2012)	80.85 (25°C, estimated from log $K_{ow}$ ) (US EPA, 2012) 125.09 (25°C, estimated from fragments) (US EPA, 2012)	60.36 (25°C, estimated from log $K_{ow}$ ) (US EPA, 2012) 750.88 (25°C, estimated from fragments) (US EPA, 2012)
<b>Henry's Law constant [Pa m<sup>3</sup>/mol]</b>	1.09 (25°C) Cited by Mackay et al. (2014) 0.478, estimated (EC, 2005) 1.11 Cited by Mackay et al. (2014)	$5.53 \times 10^{-4}$ (25°C, QSAR estimated) (US EPA 2012) $1.142 \times 10^{-2}$ (estimated from estimated vapour pressure and estimated water solubility) (US EPA 2012)	$1.91 \times 10^{-3}$ (25°C, QSAR estimated) (US EPA 2012) $3.370 \times 10^{-1}$ (estimated from estimated vapour pressure and estimated water solubility) (US EPA 2012)	9.89 (25°C, QSAR estimated) (US EPA 2012) 5.021 (estimated from estimated vapour pressure and estimated water solubility) (US EPA 2012)
<b>n-Octanol/water partition coefficient (log <math>K_{ow}</math>)</b>	5.11 ( $K_{ow}$ WIN v1.68 estimate) 4.7 at 20°C, neutral pH, (EC 2005) 5.0 at 24.5°C (purity 98%), (WHO 2009) 4.96–5.11 at 20°C (Gebremariam et al., 2012) 5.2–5.267 at 25°C (Gebremariam et al., 2012)	2.89 (estimated) (US EPA 2012)	3.21 (experimental) (US EPA 2012)	No data
<b>n-Octanol/air partition coefficient (log <math>K_{OA}</math>)</b>	8.882 (estimated) (US EPA 2012) 8.34 Cited by Mackay et al. (2014)	9.541 (estimated) (US EPA 2012)	9.324 (estimated) (US EPA 2012)	5.669 (estimated) (US EPA 2012)
<b>Air/water partition coefficient (log <math>K_{AW}</math>)</b>	-3.922 Experimental database (US EPA 2012) -3.35 Cited by Mackay et al. (2014)	-6.651 (estimated) (US EPA 2012)	-6.114 (estimated) (US EPA 2012)	-2.399 (estimated) (US EPA 2012)
<b>Soil organic carbon/water partition coefficient (log <math>K_{oc}</math>)</b>	3.4–4.5 (mean: 3.9) (EC 2005) 3.7 Experimental database (US EPA 2012) 3.93 cited by Mackay et al. (2014)	2.597 (estimated) (US EPA 2012) 2.618 (estimated) (US EPA 2012)	2.942 (estimated) (US EPA 2012) 3.188 (estimated) (US EPA 2012) 2.173 (PPDB 2020)	2.640 (estimated) (US EPA 2012) 3.111 (estimated) (US EPA 2012)

## 2. Status of the chemical under national regulations and international forums

Table 2. Status of the chemical under national legislations and international forums

Country/Organisation	Regulatory process
Argentina	The information on the human health and environmental effects of chlorpyrifos was reviewed in 2021, concluding that the risks posed by its use are unacceptable (Argentina, 2021). Furthermore, the National Food Health and Quality Service (Senasa) highlighted that by resolution 414/2021 the commercialisation and import of chlorpyrifos or products containing chlorpyrifos is prohibited with a 1-year phase-out, meaning use should cease by November 2022.
Australia	Chlorpyrifos is currently being reviewed on the basis of concerns related to toxicology, work health and safety, chemistry, residues and environment. In 2019 the Australian Pesticides and Veterinary Medicines Authority (APVMA) cancelled the registration of chlorpyrifos products for domestic and home garden use and in certain public spaces such as parks and footpaths. A proposed regulatory action on agricultural uses is expected to be published in late 2022.
Belarus	Chlorpyrifos is registered in accordance with the Law of the Republic of Belarus on Quarantine and Plant Protection (December 25, 2005 No. 77-Z) and is included in the State Register of Plant Protection Products and Fertilizers Permitted for Use on the Territory of the Republic of Belarus. As a result of a toxico-ecological assessment of insecticides based on chlorpyrifos it has been classified as highly hazardous (Belarus, 2022).
Brazil	In Brazil, the Brazilian Health Regulatory Agency (Anvisa) is currently reviewing chlorpyrifos based on concerns related to toxicology, mutagenicity, and developmental toxicity.
Canada	Health Canada's Pest Management Regulatory Agency requested additional health data for the re-evaluation of chlorpyrifos. As the registrants of chlorpyrifos products were unable to fulfil these data requirements, Health Canada cancelled the remaining pest control products containing chlorpyrifos in 2021, phased out sale by registrants on 10 December 2021, and will complete the phase out of sale by retailers on 10 December 2022. The last date of use for all chlorpyrifos products is by 10 December 2023 (Health Canada Pest Management Regulatory Agency, 2021).
China	The Ministry of Agriculture and Rural Affairs has issued measures to restrict the use of chlorpyrifos: it was prohibited from being used on vegetables since December 31, 2016 (Comment CCPIA on 1 <sup>st</sup> draft).
Colombia	Resolution 2906 of 2007 is enforced in which maximum residues limits (MRL) are defined for foods and feedstock. It includes limits for chlorpyrifos for several products including bananas, coffee, meat, onions, strawberries and beans, among many others.
Dominican Republic	Since 2009, this product has been identified as a pesticide that affects the production of vegetables indicated in resolution 0050/2009. It is not permitted to be used on cundeamor, chili peppers, green beans, eggplant, bangaña, mango, tomato and crops under a protected environment.
Egypt	Chlorpyrifos will be restricted to use in cotton and against termites and locusts at the end of 2022 (Egypt, 2022).
European Union	In the European Union chlorpyrifos has been prohibited to be placed on the market and used as an active substance in plant protection products since 2020 and in biocidal products since 2008 (Regulation (EC) No 1107/2009, Regulation (EU) No 528/2012). Overall, no reference values could be set because of the unclear genotoxicity potential of chlorpyrifos; moreover, significant uncertainties were linked to the neurodevelopmental toxicity study, where effects were observed at the lowest dose tested in rats (decrease in cerebellum height corrected by brain weight). These concerns were supported by the available epidemiological evidence related to developmental neurological outcomes in children. In the absence of toxicological reference values, a risk assessment for consumers, operators, workers, bystanders and residents cannot be conducted. This issue represents a critical area of concern for chlorpyrifos. According to harmonised classification in the EU (Regulation (EC) No 1272/2008), chlorpyrifos is classified as Acute Tox 3* H301 (toxic if swallowed), Aquatic acute 1 H400 (very toxic to aquatic life) and Aquatic chronic 1 H410 (very toxic to aquatic life with long

Country/Organisation	Regulatory process
	lasting effects), M-factor reflecting high aquatic toxicity: 10000 (Regulation (EC) No 1272/2008, Annex VI).
Guatemala	Chlorpyrifos is formulated and used in Guatemala in residential uses against cockroaches, fleas and termites. It is also used as active ingredient in anti-flea collars for domestic pets. In agriculture, it is used against cattle ticks and as spray on cultures. It is one of the leading molecules in the control of locusts. Chlorpyrifos in solo and combination formulations is widely used by farmers as a cost-effective tool in multiple crops.
India	Chlorpyrifos has been registered under the Insecticides Act of 1968 since 1977. Labelling of chlorpyrifos follows the Insecticides Rules 1971, where chlorpyrifos falls under Category II with a yellow colour code and caution as “POISON” to represent the level of toxicity as Highly toxic (PFMAI, 2022). Seven formulations are registered for use in India under the Insecticides Act, 1968. In addition, it is also approved to be used for desert locust control on crops, acacia and other trees in concentrations of 240 grams active substances per hectare.
Madagascar	The Plant Protection Directorate with the committee for the approval of phytopharmaceutical products has started in 2021 a process towards the non-use (import, distribution and use) of chlorpyrifos. However, in the field of locust control, it is still widely used.
Mauritius	Chlorpyrifos is not recommended for use in agriculture in Mauritius and no import permit has been issued by the Dangerous Chemicals Control Board since 2004.
New Zealand	The New Zealand <u>Environment Protection Agency</u> (EPA) has assigned the following GHS hazard classifications to chlorpyrifos <sup>III</sup> : Acute toxicity cat.2 (H310), acute toxicity cat.3 (H301), acute toxicity cat.4 (H332), Eye irritation cat.2 (H319), Reproductive toxicity Cat.2 (H361), STOT single exp. cat.1 (H370), STOT repeat exp. cat.1 (H372) Aquatic acute cat.1 (H400), Aquatic chronic cat.1 (H410). The classification of Reproductive toxicity Cat.2 has been legally applied to formulated products but not yet to the active ingredient and will be applied during the current reassessment. Chlorpyrifos is used in New Zealand specifically formulated as wettable powder, liquid and granulates (17 products) in different crops such as grasses, orchard fruits and vegetables. Currently, chlorpyrifos and chlorpyrifos-methyl are being reassessed as plant protection products by the EPA. Non-plant protection uses, such as veterinary medicines and use in urban pest management, were reassessed in 2016 and the <u>approvals were revoked</u> (New Zealand, 2022).
Norway	Chlorpyrifos has never been authorised for use as a plant protection product. For use as a biocide, it was phased out in 2008.
Saudi-Arabia	Chlorpyrifos is widely used in the Kingdom of Saudi Arabia to control agricultural pests.
Thailand	Chlorpyrifos is regulated under the Hazardous Substance Act. Household and public health pesticides containing chlorpyrifos as active ingredient are classified as type 4 hazardous substances (under the responsibility of Thai Food and Drug Administration), which have high degrees of hazard or risks arising either from their applications or intrinsic properties. Thus, their manufacturing, import, export or possession is prohibited (Thailand, 2022).
Trinidad and Tobago	The Republic of Trinidad and Tobago through the Ministry of Health’s Pesticides and Toxic Chemicals Control Board have deregistered all pesticide formulations containing chlorpyrifos as its active ingredient in 2009, as a result of the adverse health effects posed by this pesticide to pregnant women and young children.
United Kingdom of Great Britain and Northern Ireland (UK)	Chlorpyrifos is not authorised for use as a plant protection product. Additionally, in the UK there are no products containing chlorpyrifos as the active ingredient registered for use as a biocide (UK, 2022).
United States of America (USA)	The US EPA has performed numerous human health risk assessments over the years, as well as an ecological risk assessment and released a biological evaluation for chlorpyrifos in 2021. Chlorpyrifos has been used as a pesticide since 1965 in both agricultural and non-agricultural areas. However, in 2000 residential uses (except for ant and roach baits in child resistant packaging and fire ant mound drenches for public health purposes), all indoor non-residential non-agricultural uses (with exemptions), and most outdoor non-residential uses were eliminated (US EPA, 2006). All chlorpyrifos tolerances expired on 28 February 2022 pursuant to the final rule. The non-food uses will remain registered as chlorpyrifos undergoes registration review, a program that re-evaluates all pesticides on a 15-year cycle. Non-food

Country/Organisation	Regulatory process
	uses of chlorpyrifos in the US include nursery/greenhouse, turf farms, golf courses, and wide area treatments such as mosquito control and recreational areas, among others. Use of chlorpyrifos on exported food crops can still take place as long as it is not in conflict with the laws of the country to which it is intended for export ((21 USC 381 (e)(1) (USA, 2022; US EPA, 2022).
Uzbekistan	According to the Agency for Quarantine and Plant Protection, chlorpyrifos and preparations containing chlorpyrifos are included in the "List of chemical and biological means of combating pests, plant diseases and weeds, defoliants and plant growth regulators approved for use in agriculture of the Republic of Uzbekistan". In the same list chlorpyrifos is categorized as hazard class III (moderately hazardous) for humans and preparations based on it belong to classes II and III. The Ministry of Health of the Republic of Uzbekistan plans to take measures for the phased restriction and decommissioning of chlorpyrifos. (Uzbekistan, 2022)
Vietnam	The Ministry of Agriculture and Rural Development issued a decision in 2019 removing the approval for chlorpyrifos containing products sold and used within the country. The decision included a phase-out period which meant all remaining use of chlorpyrifos should have ceased by 2021 (Eurofins, 2019).

<sup>[1]</sup> <https://www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/F20DCF7B-634B-4FF3-B3C8-015E4C2E7FA7>

### 3. Uses

**Table 3. Overview of the specific products, crops and target pests approved for use in India**

Product	Crop	Pest	Dose (g a.i./ha)	Formulation dose (ml or g/ha)	Dilution in water (L/ha)
Chlorpyrifos 10.00% G	Rice (Paddy)	Yellow stem borer, Leaf folder, Gall midge	1000	10000	-
Chlorpyrifos 20.00% EC	Rice (Paddy)	Hispa	250-375	1250-1875	500 – 1000
Chlorpyrifos 50.00% EC	Rice (Paddy)	Yellow stem borer, Leaf roller	375-400	750-800	500-1000
	Cotton	Bollworms	500-600	1000-1200	500-1000
Chlorpyrifos 01.50% DP	Rice (Paddy)	Yellow stem borer, Green leaf hopper, Brown plant hopper, Leaf folder, Gall midge, Grass hopper	Not given	Not given	Not given
	Bengal gram	Pod borer ( <i>Helicoverpa armigera</i> )	Not given	Not given	Not given
Acetamiprid 00.40%+Chlorpyrifos 20.00% EC	Rice (Paddy)	Stem borer, Brown plant hopper, White backed plant hopper	10 + 500	2.50	500 - 800
Bifenthrin 03.00%+Chlorpyrifos 30.00% w/w EC	Rice (Paddy)	Stem borer, Leaf folder	24 + 240-30 + 300	800 - 1000	500
Chlorpyrifos 50.00%+Cypermethrin 05.00% EC	Cotton	Aphid, Jassids, Thrips, Whitefly, <i>Spodoptera litura</i> , Spotted bollworm, Pink bollworm, American bollworm	500 + 50	1000	500 - 1000
	Rice (Paddy)	Yellow stem borer, Leaf folder	312 + 32-	625 - 750	500 - 700

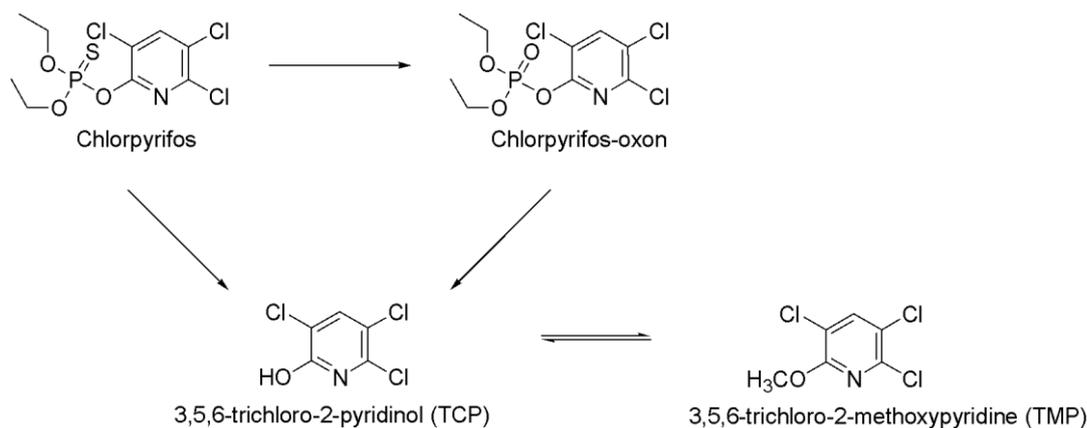
			375 + 38		
Chlorpyrifos 16.00%+Alphacypermethrin 01.00% EC	Cotton	Spotted bollworm, Pink bollworm, American bollworm	425	2500	500 - 750

Source: PMFAI (2022).

#### 4. Transformation products

1. 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-methoxypyridine (TMP). For information on chemical identity and physico-chemical properties please see table 1.

Figure 1: Environmental transformation pathways of chlorpyrifos



(US EPA's biological evaluation <https://www.epa.gov/endangered-species/biological-evaluation-chapters-chlorpyrifos-esa-assessment>)

2. 3,5,6-trichloro-2-pyridinol (TCP; CASRN 6515-38-4) is a metabolite of chlorpyrifos and chlorpyrifos-methyl, both organophosphate insecticides, and triclopyr, a carboxylic acid herbicide (Health Canada, 2016). TCP is the major chlorpyrifos metabolic product. TCP can be found in blood and urine (ATSDR, 1997). Urine is the principal route of excretion for TCP and levels in urine are correlated with the degree of recent (within 48 hours) exposure to chlorpyrifos (ATSDR, 1997). The presence of TCP in urine may also be the result of exposure to chlorpyrifos-methyl. In the environment, TCP can also be found as a result of the breakdown of parent compounds. As TCP is more persistent than its parent compounds in the environment, urinary levels may also reflect direct environmental exposure to the metabolite (EPA, 2006b). The estimated atmospheric half-life for TCP is 60.5 days (Spain, 2017), which indicates potential for long range transport. The water solubility is high and the log  $K_{OC}$  (2-3) indicates that the substance is mobile. The half-lives in soil show moderate to high persistence with a DT50 of up to 150 days in European assessments (Spain, 2017) and 360 days in US-EPA assessments (US-EPA, 1998). Acute toxicity of TCP is considered lower than that of the parent compound with a 96h LC50 value of 12.6 mg/L in rainbow trout and 48h LC50 of 10.4 mg/L for *Daphnia magna* (Spain, 2017), although *Daphnia carinata* is the susceptible species with a 48h LC50 value of  $0.20 \pm 0.08$  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, 2017). TCP has a log  $K_{OW}$  of 3.21 and an estimated log  $K_{OA}$  of 9.32 (see table 1 INF-document). 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 bioconcentration factor (BCF) values 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 would be needed to conclude on the fulfilment of the Annex D criteria for TCP. Minor metabolites include diethylphosphate (DEP) and diethylthiophosphate (DETP), are also produced by other OP pesticides (that is, coumaphos, diazinon, phorate and terbufos). (Health Canada, 2013)

3. 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). 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.

## 5. Persistence

### 5.1 Abiotic degradation

#### 5.1.1 Soil photolysis

4. The RAR (Spain, 2017) 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 h ( $r^2=0.96$ ) 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 d in light, and could not be calculated in the dark since levels increased throughout the study period.

5. Racke et al. (1994) determined the photodegradation rate and identified the photodegradates of the main metabolite (TCP) of chlorpyrifos on soil surface. Approximately 50% of the applied TCP degraded during the first 8 h of sunlight exposure, the half-life was calculated to be 14.1 d ( $r^2=0.820$ ). The major photoproduct of TCP was CO<sub>2</sub> (40% AR at 30 days), small amounts of polar and non-extractable residues were also formed. The study author suggests that these polar residues may represent transient intermediates to CO<sub>2</sub>.

6. In the study by Yackovich et al. (1985), the degradation of chlorpyrifos also did not differ significantly in light or dark. Since the study was not conducted according to current guidelines and a mercury lamp was used as the irradiation source, the study is only considered as additional information. Walia et al. (1988) irradiated chlorpyrifos under different photochemical conditions and showed that chlorpyrifos gives various photoproducts mainly by oxidative desulfuration, dehalogenation and hydrolytic processes under laboratory conditions. The study is also considered as additional information.

#### 5.1.2 Hydrolytic degradation

7. The European Union RAR for chlorpyrifos (Spain, 2017) lists five studies on hydrolysis in pure water. 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 d. At alkaline pH, hydrolysis occurs more quickly with a measured half-life for chlorpyrifos of 16 d 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 including primary degradation. For an overview of pH dependant hydrolytic degradation of chlorpyrifos see table 3 in this document.

8. 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 d, respectively. A comparable aqueous hydrolysis half-life at 35 °C and pH 4.7 of 15.75 d was also reported.

9. 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 rate of neutral hydrolysis was unaltered when sorbed to sediment. The observed rate constants were the same in the sediment and aqueous phases and similar in magnitude to those found for natural water samples. On the other hand, alkaline hydrolysis rates in the sediment-sorbed phase were approximately ten times slower than in the bulk solution.

10. Although it is unclear from the details in the report whether the test vessel were protected from light, 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 in aqueous solution increases with increasing pH. The half-life is also influenced by temperature.

11. A comprehensive discussion on chlorpyrifos hydrolysis data may be found in an evaluation by Mackay et al. (2014). They 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).

**Table 4. Dependency on pH for abiotic degradation (hydrolysis) of chlorpyrifos**

Reference	pH	Temperature	Half-lives
McCall (1986)	pH 5	25°C	73 d
	pH 7	25°C	72 d
	pH 9	25°C	16 d
Meikle and Youngson (1978)	pH 4.7	25°C	62.7 d
	pH 6.9	25°C	35.3 d
	pH 8.1	25°C	23.1 d

Reference	pH	Temperature	Half-lives
Chandorkar (2019) <sup>1</sup>	pH 4	25°C	341.7 h (=14.2 d)
	pH 7	25°C	301.4 h (=12.6 d)
	pH 9	25°C	258.5 h (=10.8 d)
Hui (2010)	pH 4 (distilled water)	29°C	14 d
	pH 7 (distilled water)	16°C	12.3 d
	pH 7 (distilled water)	29°C	11.3 d
	pH 7 (distilled water)	40°C	8.12 d
	pH 7 (reverse osmosis water)	29°C	11.9 d
	pH 10 (distilled water)	29°C	4.57 d

### 5.1.3 Direct and indirect photochemical degradation in water

12. The European Union RAR for chlorpyrifos (Spain, 2017b) lists eight studies on direct photochemical degradation in water, 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 FIFRA Guideline 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 d for mid-summer at 20°North.

13. Adam (2015) concluded that chlorpyrifos is degraded by direct and indirect photolysis with net half-lives of 7.2 and 2.9 d in 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 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 d upon exposure to an artificial light source (General Electric Chroma lamps). In the study of Meikle et al. (1983), photolysis half-lives observed ranged from 9.4 to 15.6 d (corrected for hydrolysis) and 7.8 to 11.0 d (uncorrected for hydrolysis). This study is considered 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.

14. Although photolysis can be a degradation pathway, this is limited to the upper centimetres of a water body, depending on turbidity.

15. 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.

### 5.1.4 Volatilisation

16. The Henry's Law constant of 1.11 Pa.m<sup>3</sup>/mole (Mackay, 2014) is high enough that volatilisation from water should occur. Early laboratory half-lives of 8-24 h in open beakers of distilled water are too short for hydrolysis and thought to reflect volatilisation. Aeration of 10 L of a 50 ppb solution at 80 mL/minute left less than 15% of the applied dose after 24 h. In (Schimmel et al., 1983, cited in Racke 1993 and Australia, 2000a), 63% of applied chlorpyrifos were recovered from resin traps attached to jars holding aerated seawater solutions. Please also refer to para 67 for further information on volatilisation.

<sup>1</sup> PMFAI information, study summary not available.

## 5.2 Biotic degradation

### Rate of degradation in water

17. The European Union RAR for chlorpyrifos (Spain, 2017b) reports several studies on degradation in water. 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 refer to dissipation rather than to degradation. In a follow-up test conducted to investigate the reasons for the low recovery in the main test, on day 40 up to 95.7% of the radioactivity were found in the foam plugs of the volatile organic carbon trap. This was shown to be 100% unchanged chlorpyrifos. Also, in the study conducted by Caviezel (2015), dissipation of chlorpyrifos was mainly caused by volatilisation from the surface water. This amounted to 58.6% and 64.4% of applied radioactivity (AR) after 61 d of incubation. Minimal mineralization of < 1.7% CO<sub>2</sub> was observed at the end of the study. Similarly, in another study on degradation in three static marine water systems by Swales (2003), dissipation half lives 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 <sup>14</sup>C-mass balance which points to substantial volatilisation, and not to biotic degradation in water. No traps were used. With a Henry's law constant of 1.1 Pa m<sup>3</sup>/mol at 20°C, these observations are plausible. Early laboratory half-lives of 8-24 h in open beakers of distilled water (Schimmel et al., 1983) are too short for hydrolysis and thought to reflect volatilisation. Aeration of 10 L of a 50 ppb solution at 80 mL/minute left less than 15% of the applied dose after 24 h. The most compelling evidence is the recovery of 63% of applied chlorpyrifos from resin traps attached to jars holding aerated seawater solutions (Schimmel et al., 1983, cited in Racke 1993 and Australia, 2000a). All dissipation half-lives mentioned here are listed in Table 4 of document UNEP/POPS/POPRC.18/INF/8.

18. 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, as detailed above, the results of these outdoor microcosm studies are considered less relevant.

19. No reliable degradation half lives in water could be secured, since in all of the studies that were reviewed, volatilisation contributed considerably to dissipation. Thus, if the remaining chlorpyrifos in the test system permits the estimation of a DT50 of 75 d at 8°C, which exceeds the criterion of a half-life >2 months in water mentioned in Annex D, chlorpyrifos can be considered persistent in open sea water, at 8°C. In aquatic systems, the primary routes of dissipation of chlorpyrifos from the water phase is volatilisation and partitioning to the sediment (10–52%) (Australia, 2022).

Table 5. Rate of degradation in water, laboratory studies

Water source	Water	Half-life or DT <sub>50</sub> (d)	Method of calculation	DT50 normalised to 12°C <sup>2</sup>	χ <sup>2</sup> -error	r <sup>2</sup>	Application (µg/L)	Temperature (°C)	pH	Salinity (%)	Oxygen content (%)	Total organic Carbon (mg/L)	Reference	Remarks
Fröschweiher pond, Möhlin AG, Switzerland	Pond	46 d	SFO	124.4 d	5.84	0.8851	12.1	22.5°C	7.89	-/-	7.62	13.60	Gassen, 2015	High losses due to volatilisation, underestimation of DT50 values
Fröschweiher pond, Möhlin AG, Switzerland	Pond	21 d	SFO	56.8 d	7.51	0.9468	126	22.5°C	7.89	-/-	7.62	13.60		
Biederthal, France	Pond	2.78	FOMC	6.8 d	-	0.9804	100.0	21.5 ± 0.2 °C.	8.08	-/-	9.70	10.64	Caviezel, 2015	58.6 % AR to 64.5 % AR, lost from the test system due to volatilisation, Dissipation of chlorpyrifos due to volatilisation and hydrolysis, not biotic degradation, minimal mineralisation (max CO <sub>2</sub> <1.7 %) observed, not accepted for regulatory risk assessment in the EU
	Pond, sterile	2.92	FOMC	7.2 d	-	0.9783	100.0	21.5 ± 0.2 °C.	8.08	-/-	9.70	10.64		
	Pond	2.98	FOMC	7.3 d	-	0.9510	10.0	21.5 ± 0.2 °C.	8.08	-/-	9.70	10.64		
Ynys Tachwedd, nr, Borth, Ceredigion, Wales	Estuarine	45 d	SFO	59.8 d	-	0.935	40	15 °C	7.79	17	110	589.5	Swales, 2003	

<sup>2</sup> Temperature normalised using the Arrhenius equation.

Water source	Water	Half-life or DT <sub>50</sub> (d)	Method of calculation	DT50 normalised to 12°C <sup>2</sup>	χ <sup>2</sup> -error	r <sup>2</sup>	Application (µg/L)	Temperature (°C)	pH	Salinity (%)	Oxygen content (%)	Total organic Carbon (mg/L)	Reference	Remarks
Borth Sands, Ceredigion, Wales	Coastal	35 d	SFO	35 d	-	0.883	40	12°C	7.83	36	114	812.9		High losses due to volatilisation (mass balance declining to 75.8 % AR (15°C water), 81 % AR (12°C water) and 89 % AR (8°C water)), no traps used, no information on mineralisation. DT50 values refer to dissipation, not degradation. Study was not accepted for regulatory risk assessment in the EU
> 5 miles off shore from Plymouth, Devon, England	Open Sea water	75 d	SFO	51.3 d	-	0.850	40	8°C	8.06	38	112	645.3		
Range Point, Santa Rosa Island, Escambia County, Florida, USA	Sea water	<2 d	1 <sup>st</sup> order	-/-			<water solubility of cpy	25°C					Schimmel, 1983	Volatilisation of 63% of applied chlorpyrifos, which was recovered as parent substance in air traps, thus DT 50 refers to dissipation only
India	Normal water	5.77 d 5.67 d 6.64 d	Not reported				48% EC 0.5 ppm 1.0 ppm 1.5 ppm	Not reported					Balasubramaniam M. and Ramesh A. (1995a)	Proprietary study, only basic information available
India	Acidic water	8.83 d 8.61 d 7.55 d	Not reported				48% EC 0.5 ppm 1.0 ppm 1.5 ppm	Not reported					Vijyalakshmi A. and Ramesh A. (1995)	Proprietary study, only basic information available

Water source	Water	Half-life or DT <sub>50</sub> (d)	Method of calculation	DT50 normalised to 12°C <sup>2</sup>	χ <sup>2</sup> -error	r <sup>2</sup>	Application (µg/L)	Temperature (°C)	pH	Salinity (%)	Oxygen content (%)	Total organic Carbon (mg/L)	Reference	Remarks
India	Basic water	3.94 d 3.55 d 3.86 d	Not reported				48% EC 0.5 ppm 1.0 ppm 1.5 ppm	Not reported					Vijyalakshmi A. and Ramesh A. (1996a)	Proprietary study, only basic information available
India	Saline water	11.58 d 14.90 d 14.82 d 17.02 d 19.70 d	Not reported				Analytical grade CPY			0.03 dSm <sup>-1</sup> 23.11 dSm <sup>-1</sup> 5.97 dSm <sup>-1</sup> 10.80 dSm <sup>-1</sup> 19.80 dSm <sup>-1</sup>			Awasthi and Prakash (1998)	Proprietary study, only basic information available
<b>Range</b>		<2–75 d		6.8–124.4										

### 5.3 Rate of degradation in soil

20. 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 Biologische Bundesanstalt für Land- und Forstwirtschaft (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 Union RAR (Spain, 2017b) and PMFAI, 2022.

#### *Laboratory studies—rate of degradation*

21. De Vette and Schoonmade (2001) 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)<sup>3</sup>. Degradation half-lives (DegT50) 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 d). All half-lives are listed in table 6 below. There, one column is included with DT50 values normalised to 12°C for comparability and to reflect degradation expected in more temperate regions.

22. Degradation in soil is temperature-dependant (Getzin, 1981), with DegT50 values ranging from 6 weeks (42 d) at 35°C, 13 weeks (91 d) at 25°C, and 25 weeks (175 d) at 15°C in a previously air-dried soil (silt loam), which is just below the trigger value in Annex D of the Stockholm Convention (SSC, 2018). The study authors hypothesized that “it is possible that air-drying soils prior to the addition of insecticides disrupted the activity of those species (microbial communities) with the capacity to degrade the insecticide and prevented them from metabolizing the insecticide during the early stages of the 16-week incubation period. (Getzin 1981)”. In microbially active soils, the DT50s were 4 and 12 weeks in the clay loam and silt loam soils, respectively, whereas, in sterilized soils the DT50s were 25 weeks for both soils. 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 in the range of 15–35 °C. However, the extrapolation to 5°C in the real circumstance has some uncertainties since the temperature range in original literature is 15–35 °C.

23. 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 d, at field moisture content), compared to dry ( $t_{1/2}$  49.5–120 d) and wet ( $t_{1/2}$  63.0–124 d, at 61–68% gravimetric water content) soils. Degradation increased markedly with higher temperatures and decreased with higher chlorpyrifos dosages (at 25 µg/g versus 5 µg/g) which are often applied in the tropics due to severe insect infestations.

24. Chlorpyrifos is strongly bound to soil and immobile to slightly mobile in soils with KOC values ranging from 2,785–31,000 (Canadian Proposed Re-Evaluation Decision (PRVD2019-05)). The major metabolite TCP (a weak acid) is weakly bound to soil and highly mobile (KOC 27–389), with increasing mobility as the pH increases. 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).

25. The reasoning for a temperature normalisation to 12°C is given in the REACH guidance R.7b, Endpoint specific guidance: “New kinetic simulation studies should be conducted at environmentally relevant temperatures, by default at 12°C, which is regarded as a reasonable alleged average temperature for the European Union. If information on degradation half-life is already available from existing simulation degradation tests performed at a higher temperature, they should be normalised to a half-life corresponding to 12°C by using the Arrhenius equation .... In every case, kinetic results such as the degradation rates and degradation half-lives should correspond to an environmentally relevant temperature, i.e., by default 12°C. For the purpose of identifying degradation products, a higher test temperature (but within the frame provided by the study guideline) could be used to overcome potential analytical limitations for the identification and quantification of those degradation products.” (ECHA, 2017).

26. An unpublished laboratory study (Bidlack, 1979), in Spain, 2017, 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 clay 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.

<sup>3</sup> FOCUS is a tool for the estimation of half-lives used for the evaluation of pesticides in the EU.

**Table 6. Rate of degradation in soil, laboratory studies**

Soil source	Soil texture	Half-life or DT <sub>50</sub> (d)	Method of calculation	DT50 normalised to 12°C <sup>4</sup>	χ <sup>2</sup> -error	r <sup>2</sup>	Application (ppm)	Temperature (°C)	Soil moisture	pH	Organic Carbon (%)	Reference	remarks
Boone County, Missouri, USA	Silt Loam	21.43 9.55 (fast phase) 60.70 (slow phase)	DFOP	45.7 d 20.4 d (fast phase) 129.6 d (slow phase)	4.49	-	1.5 µg/g=1000 g a.i./ha	20±2°C	50% MWHC	5.2/4.7 <sup>+</sup>	1.6	Clark, 2013	
Raymondville, Texas, USA	Sandy Clay Loam	5.964	SFO	12.7 d	10.39	-	1.5 µg/g=1000 g a.i./ha	20 ± 2	50% MWHC	8.0/7.6	0.65		
MSL-PF, North Dakota, USA	Sandy Loam	9.6	FOMC	20.5 d	2.622	-	1.5 µg/g=1000 g a.i./ha	20 ± 2	50% MWHC	6.4/6.2	1.7		
Tehama County, California, USA	Clay Loam	36.87 5.3 (fast phase) 49.19 (slow phase)	DFOP	78.7 d 11.3 d (fast phase) 105.0 d (slow phase)	1.174	-	1.5 µg/g=1000 g a.i./ha	20 ± 2	50% MWHC	6.7/6.4	1.3		
Marcham, UK	Sandy clay loam	22.25	FOMC	47.5 d	2.48	-	1.28 mg/kg=960 g as/ha	20±2°C	40% MWHC	7.7/8.3	1.7	De Vette and Schoonmade, 2001a	
Charentilly, France	Silty clay loam	94.1	SFO	200.9 d	3.59	-	1.28 mg/kg=960 g as/ha	20±2°C	40% MWHC	6.1/8.0	1.0		
Cuckney, UK	Sand	110.3	SFO	235.4 d	3.974	-	1.28 mg/kg=960 g as/ha	20±2°C	40% MWHC	6.0/6.8	1.2		
Thessaloniki, Greece	Sandy silt loam	56.59	FOMC	120.8 d	2.505	-	1.28 mg/kg=960 g as/ha	20±2°C	40% MWHC	7.9/8.2	0.8		
Commerce, MS, USA	Loam	11	Not reported	37.7 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	7.4	0.68	Bidlack, H.D., 1979	Except for Stockton clay, soils were stored for longer than the recommended 3 months with no measurement of microbial activity
Barnes, ND, USD	Loam	22	Not reported	75.4 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	7.1	3.60		
Norfolk, VA, USA	Loamy sand	102	Not reported	349.7 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	6.6	0.29		
Miami, IND, USA	Silt loam	24	Not reported	82.3 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	6.6	1.12		

<sup>4</sup> Temperature normalised using the Arrhenius equation.

Soil source	Soil texture	Half-life or DT <sub>50</sub> (d)	Method of calculation	DT50 normalised to 12°C <sup>4</sup>	χ <sup>2</sup> -error	r <sup>2</sup>	Application (ppm)	Temperature (°C)	Soil moisture	pH	Organic Carbon (%)	Reference	remarks
Catlin, ILL, USA	Silty clay loam	34	Not reported	116.6 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	6.1	2.01		
German 2.3, Germany	Sandy loam	141	Not reported	483.4 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	5.4	1.01		
Stockton, CA, USA	Clay	107	Not reported	366.9 d	-	-	6.7 ppm, 7.6 kg/ha	25°C	75% 1/3 Bar	5.9	1.15		
Sultan, Washington, USA	Silt loam	25 weeks =175 d	Not reported	232.6 d	-	-	18 mg	15°C	20%	6.3	3.1	Getzin, 1981	
		13 weeks =91 d	Not reported	312.0 d	-	-		25°C					
		6 weeks =42 d	Not reported	371.5 d	-	-		35°C					
Chehalis, Washington, USA	Clay loam	4 weeks =28 d	Not reported	96.0 d	-	-	18 mg	25°C	30%	5.7	7.0		
Semongok	Clayey red yellow podzolic	77.0	1st order	264.0			5 µg/g	25°C	33%	4.8	2.2	Chai, 2013	
		84.5	1st order	289.7			25 µg/g	25°C	33%	4.8	2.2		
Semongok, moisture dependence	Clayey red yellow podzolic	120	1st order	411.4			5 µg/g	25°C	Air-dry soil	4.8	2.2		
		77.0	1st order	264.0			5 µg/g	25°C	Field moisture content	4.8	2.2		
		124	1st order	425.1			5 µg/g	25°C	Wet (61–68%)	4.8	2.2		
Semongok, temperature dependence	Clayey red yellow podzolic	224	1st order	297.7			5 µg/g	15°C	33%	4.8	2.2		
		77.0	1st order	264.0			5 µg/g	25°C	33%	4.8	2.2		
		37.5	1st order	331.7			5 µg/g	35°C	33%	4.8	2.2		
Tarat	Alluvial	53.3	1st order	182.7			5 µg/g	25°C	32%	5.6	1.8		
		76.2	1st order	261.3			25 µg/g	25°C	32%	5.6	1.8		
Tarat, moisture dependence	Alluvial	49.5	1st order	169.7			5 µg/g	25°C	Air-dry soil	5.6	1.8		

Soil source	Soil texture	Half-life or DT <sub>50</sub> (d)	Method of calculation	DT50 normalised to 12°C <sup>4</sup>	χ <sup>2</sup> -error	r <sup>2</sup>	Application (ppm)	Temperature (°C)	Soil moisture	pH	Organic Carbon (%)	Reference	remarks
		53.3	1st order	182.7			5 µg/g	25°C	Field moisture content (32%)	5.6	1.8		Degradation of chlorpyrifos is slowest in the absence of soil microbial activity and at low soil temperatures. Degradation of chlorpyrifos is slower for waterlogged soils, acidic soils, soils with high clay, soils at low temperatures and at high application rates. The study was not performed in accordance with the OECD 307 TG, but does provide supporting evidence of abiotic and biotic degradation pathways of chlorpyrifos in soil, however 50% degradation was not achieved in the test.
		63	1st order	216.0			5 µg/g	25°C	Wet (61–68%)	5.6	1.8		
Tarat, temperature dependence	Alluvial	83.5	1st order	111.0			5 µg/g	15°C	32%	5.6	1.8		
		53.3	1st order	182.7			5 µg/g	25°C	32%	5.6	1.8		
		36.5	1st order	322.9			5 µg/g	35°C	32%	5.6	1.8		
Balai Ringin	Red Yellow Podzolic soil	69.3	1st order	237.6			5 µg/g	25°C	22%	5.6	1.4		
		120	1st order	411.4			25 µg/g	25°C	22%	5.6	1.4		
Balai Ringin, moisture dependence	Red Yellow Podzolic soil	84.5	1st order	289.7			5 µg/g	25°C	Air-dry soil	5.6	1.4		
		69.3	1st order	237.6			5 µg/g	25°C	field moisture content (22%)	5.6	1.4		
		63	1st order	216.0			5 µg/g	25°C	Wet (61–68%)	5.6	1.4		
Balai Ringin, temperature dependence	Red Yellow Podzolic soil	193	1st order	256.5			5 µg/g	15°C	22%	5.6	1.4		
		69.3	1st order	237.6			5 µg/g	25°C	22%	5.6	1.4		
		23.1	1st order	204.3			5 µg/g	35°C	22%	5.6	1.4		
Nadia District, West Bengal, India	Gangetic alluvial soil	20.1	1st order				0.1 kg a.i. ha <sup>-1</sup>	28°C	50 % MWHC	7.5	0.49	Sardar & Kole 2005	No air traps.
		23.2	1st order				10 kg a.i. ha <sup>-1</sup>						
		36.7	1st order				100 kg a.i. ha <sup>-1</sup>						
<b>Range</b>		6–224		12.7–483.4									

## 5.4 Rate of degradation in soil: termite control application rates

27. In Racke, 1994, half-lives for degradation in soils ranged from 175 to 1576 d for five U.S. soils at 25°C for application rates of 1000 mg/kg, replicating those used for control of termites. The application rates are given as 392 kg/ha in soil trench applications for termite applications, as opposed to 0.28–2.24 kg/ha for agricultural broadcast applications. Also, two of these soils were incubated at three temperatures (15°C, 25°C and 35°C), three application rates (10, 100 and 1000 mg/kg) and at 3 moisture levels (air dry, 1.5 MPa and field moisture capacity) each. The resulting half-lives range from <1 to >24 months (<30 d to > 720 d) (Racke, 1994) and are listed in UNEP/POPS/POPRC.18/INF/8. These results were confirmed by a study by Murray et al., (2001) who obtained half-lives of 385, 155 and 41 d, at 1000, 100 and 10 mg/kg application rates. Further information can be found in document UNEP/POPS/POPRC.18/INF/8.

28. 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. Chlorpyrifos showed a major loss (75–90%) of residue during the 24-month incubation period. 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.

29. 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).

30. 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 the primary transformation product (detected after 3 d, maximum level after 30 d). At all application levels TCP concentrations decreased afterwards and were no longer detected after 120 d. TMP as secondary transformation product was detected during the study course, but also not after 120 d.

31. Although Wright et al., 1994 do not give a half-life, they do report that chlorpyrifos was detected in the soil of all houses investigated 8 years after application, at 1.8–396 ppm near exterior walls, and 1.3–439 ppm near interior walls. The initial application rate is not given.

32. The reduced degradation of chlorpyrifos at high application rates may be a result of toxicity to the microorganisms responsible for biotic degradation.

**Table 7. Rate of degradation in soil, termite control application rates**

Soil source	Soil texture	Half-life or DT <sub>50</sub> (d)	Method of calculation	Application (ppm)	Temperature (°C)	Soil moisture	pH	Organic Carbon (%)	Reference
Tampa, Florida, USA	sand	205.5	Not given	100 ppm	25°C	75% FC	6.40	0.66	Racke 1993, Murray 2001
Tampa, Florida, USA	sand	1575.5	Not given	1000 ppm	25°C	75% FC	6.40	0.66	
Hawaii, USA	Sandy loam	335.2	Not given	1000 ppm	25°C	75% FC	5.70	5.70	
Phoenix, Arizona, USA	Sandy loam	229.8	Not given	1000 ppm	25°C	75% FC	8.30	0.88	
Medina, Texas, USA	Clay loam	115.7	Not given	1000 ppm	25°C	75% FC	8.00	1.20	
St. Petersburg, Florida, USA	sand	213.8	Not given	1000 ppm	25°C	75% FC	7.50	1.92	
Seaford Rise, Australia	Red brown earth	462	Not given	1000 mg/kg	25°C	60% MWHC	7.1	1.2	Baskaran, 1999
Bedding material	Quarry sand	330	Not given	1000 mg/kg	25°C	60% MWHC	9.2	0.1	
Bedding material	Reidmix/sand-dolomite	315	Not given	1000 mg/kg	25°C	60% MWHC	9.6	0.2	

## 5.5 Rate of degradation in soil: field studies

33. In general, DT50 values in field studies are lower than in laboratory studies. However, it must be kept in mind that in field studies, the DT50 refers to dissipation, not degradation, since the test is not performed in a closed system and losses due to volatilisation etc. are not accounted for (Mackay et al., 2014). In PMRA (2019), DT50 values for field studies ranging from 2–56 d are described. Fontaine (1987) investigated three soils (see document UNEP/POPS/POPRC.18/INF/8, Table 6), and Old (2002a, 2002b, 2002c) investigated four soils. Dissipation half-lives were in the range 0.3 to 89 d. In India, various field studies were conducted, both proprietary and published studies, with dissipation half-lives ranging from 0.44 - 16 d (Menon et al., 2004; Vijyalakshmi et al., 1996; Balasubriam et al., 1995 and 1996, Sardar et al., 2005 and Upendra Kumar et al., 2017). Following application, volatilisation is expected to contribute significantly to early losses of chlorpyrifos from soil surfaces (up to 25% within 24–48 h) and plant surfaces (80% within 24–48 h) (Australia 2022). This is confirmed by Leistra et al., (2006), who investigated the volatilisation of chlorpyrifos in a field experiment on a potato crop with the characterization of meteorological conditions. Cumulative volatilization of chlorpyrifos was estimated to be about 65% of the applied substance. In a proprietary study from DOW cited in the US biological evaluation<sup>5</sup> of chlorpyrifos, approximately 28% of the applied chlorpyrifos were observed to volatilize within the first 24 h.

**Table 8. Rate of degradation in soil, field studies**

Soil source	Soil texture	Half-life or DisT <sub>50</sub> (d)	Method of calculation	Application (kg a.i./ha)	Depth	Soil moisture	pH	Organic Carbon (%)	Reference
Geneseo, Illinois, USA, cropped soil	Silt loam	88.89	SFO	3.36 kg a.i./ha	0–15 cm	45.89 % w/w	5.9	1.6	Fontaine, D.D et al. (1987)
Midland, Michigan, USA, cropped soil	Sandy Loam	30.04	SFO	3.36 kg a.i./ha	0–15 cm	23.10 % w/w	7.7	1.3	
Davis, California, USA, cropped soil	Loam	29.18	SFO	3.36 kg a.i./ha	0–15 cm	42.04 % w/w	7.9	0.75	
Tranent, Scotland, bare soil	Sandy clay loam	7.86 d	SFO	0.960 kg a.i./ha	0–10, 10–20 cm	Not reported	6.7	1.9	Old, J. (2002a)
Charentilly, Tours, France, bare soil	Clay loam	11 d		0.960 kg a.i./ha	0–10, 10–20 cm	Not reported	7.1	1.1	Old, J. (2002b)
Valtohor, Thessaloniki, Greece, bare soil	Sandy silt loam	9.022 2.24 (fast) 61.67 (slow)	DFOP	0.960 kg a.i./ha	0–10, 10–20 cm	Not reported	8.0	0.9	Old, J. (2002c)

<sup>5</sup> <https://www.epa.gov/endangered-species/biological-evaluation-chapters-chlorpyrifos-esa-assessment>.

Soil source	Soil texture	Half-life or DisT <sub>50</sub> (d)	Method of calculation	Application (kg a.i./ha)	Depth	Soil moisture	pH	Organic Carbon (%)	Reference
Tivenys, Tarragona, Spain, bare soil	Clay loam	0.323 0.09 (fast) 5.42 (slow)	DFOP	0.960 kg a.i./ha	0–10, 10–20 cm	Not reported	8.2	1.4	Old, J. (2002d)
India	Black soil	2.79 d 2.93 d 2.86 d 2.82 d	Not reported	500 g a.i. ha 750 g a.i. ha 1000 g a.i. ha 1500 g a.i. ha	Not reported	Not reported	Not reported	Not reported	Vijyalakshmi and Ramesh (1996)
Jaipur, semi-arid India	Loamy sand	12.3 d	Not reported	5 g ai kg <sup>-1</sup> seed and 800 g ai ha <sup>-1</sup> on day 14	0–15 cm	13 % WHC	8.2	0.3	Menon et al, 2004
Delhi, semi-arid India	Sandy loam	16.4 d	Not reported	5 g ai kg <sup>-1</sup> seed and 800 g ai ha <sup>-1</sup> on day 40	0–15 cm	24 % WHC	7.7	1.02	
India, region unspecified	red soil	0.44 d 1.13 d 2.66 d 2.64 d	Not reported	48% EC at 500 g a.i./ha 750 g a.i./ha 1000 g a.i./ha 1500 g a.i./ha	Not reported	Not reported	Not reported	Not reported	Balasubramanium and Ramesh, 1995
India, region unspecified	clay soil	3.88 d 5.04 d 5.60 d 5.03 d.	Not reported	48% EC at 500 g a.i./ha 750 g a.i./ha 1000 g a.i./ha 1500 g a.i./ha	Not reported	Not reported	Not reported	Not reported	Balasubramanium and Ramesh, 1996
ICAR-National Rice Research Institute (NRRRI), Cuttack, India	sandy clay loam	4.02 d	half-life calculated as per Hoskin, 1961	chlorpyrifos: 0.5 kg a.i./ha; cartap hydrochloride: 1 kg a.i./ha carbendazim: 0.1% and pretilachlor: 0.75 kg a.i./ha	0–15 cm	Rice paddy	6.6	0.66%	Upendra Kumar et al., 2017
Kenya, Nzoia Sugar Company estate	sandy loam	21 d 24 d 30 d 21 d	soil amended with filter mud compost soil amended with <i>Tithonia diversifolia</i> leaves non-amended soil with prior exposure	936 g a.i./ha, test carried out in PVC pipes in pre-exposed and non-exposed fields	Not reported	Not reported	Not reported	C 2.8 % N 0.14 %	Mutua et al., 2015
<b>Range</b>		0.44-88.89 d							

## 5.6 Rate of degradation in water-sediment studies

34. 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. Significant levels of radioactivity were lost from the system by volatilisation, which were 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. Chlorpyrifos dissipated under aerobic aquatic conditions with DT50 values in the total system of 22 and 51 d in the sandy loam and clay loam systems respectively (DT90 values 72 and 168 d). Dissipation was more rapid in the water layer, with DT50 values of 3 and 6 d respectively, this may be due either to adsorption to sediment, to volatilisation or to degradation. The principal degradation product was TCP, accounting for a maximum of 17.94 % AR at 100 d in sandy loam total system and 9.89% AR at 100 d in clay loam total system. 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 d under aerobic conditions with associated overlying waters at a sediment/water ratio of 1:3 in the dark at  $20 \pm 2$  °C. ( $^{14}\text{C}$ ) 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.
35. 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 d 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, compromising the reliability of the study.
36. 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 shorter 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.
37. In a study on the persistence of chlorpyrifos in seawater relative to fresh water, Bondarenko et al (2004) determined that it was approximately 3 times more persistent in seawater (half-life of 49.4 vs 18.7 at 10°C). The half-life in seawater was 15.2 at 21 °C; and 49.4 at 10 °C, so half-life tripled as the temperatures halved.
38. Daam et al. (2008) investigated the dissipation of chlorpyrifos in outdoor freshwater microcosms in Thailand. The application rate was 1 µg/L active ingredient. Seven days 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 and losses due to volatilisation and adsorption to biomass were not accounted for. The dissipation of  $^{14}\text{C}$ -chlorpyrifos in estuarine outdoor microcosms in Vietnam 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.
39. 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 (McCall et al., 1994, in Racke, 1993) gives a DT50 of 150 to 200 d in anaerobic pond sediments. No further details are available.
40. The Australian government review (APVMA 2000) refers to pond studies that give a half-life in sediment of 200 days, but no further details or reference were given.
41. 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).

42. 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.

43. 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, KOC, were 8,163 and 7,227 L/kg for soils and 13,439 and 15,500 L/kg for sediments (Gebremariam et al., 2012). Mackay (2014) lists a mean KOC of 8,500.

44. According to 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 (KOC) 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 such as suspended sediment.

**Table 9. Rate of degradation in water-sediment studies, laboratory studies**

Sediment source	Sediment texture	Half-life or DegT <sub>50</sub> total system (d)	DT50 total system normalised to 12°C <sup>6</sup>	DisT50 water (d)	DisT50 sediment (d)	Application (ppm)	Temperature (water) (°C)	pH sediment	pH water	Organic Carbon (%) sediment	Organic Carbon (%) water	Reference
Brown Carrick, sediment	Sandy loam	22 d	-/-	3 d		960 g a.i./ha	Not given	5.2	7.4	2.5	0.0016	Reeves, G.L. and Mackie, J.A., 1993
Auchingilsie sediment	Clay loam	51 d	-/-	6 d		960 g a.i./ha	Not given	6.3	6.7	3.2	0.00172	
Range Point, Santa Rosa Island, Escambia County, Florida, USA	Salt marsh	24 d		Not given	Not given	< water solubility	25°C	Not given	Not given	48%	Not given	Schimmel, 1983
Pond, sediment	Silty Clay Loam	30.5	104.6	Not given	Not given		25°C	7.7	8.1	3.1	Not given	Kennard, 1996
Calwich Abbey Lake,	Silt loam	30.67 (SFO)	65.5	3.075 (SFO)	3.007 (HS)	0.54 mg a.i./L	20 ± 2°C	7.5	7.71	5.8	Not given	

<sup>6</sup> Temperature normalised using the Arrhenius equation.

Sediment source	Sediment texture	Half-life or DegT <sub>50</sub> total system (d)	DT50 total system normalised to 12°C <sup>6</sup>	DisT50 water (d)	DisT50 sediment (d)	Application (ppm)	Temperature (water) (°C)	pH sediment	pH water	Organic Carbon (%) sediment	Organic Carbon (%) water	Reference
Staffordshire, UK												Kang, 2015, kinetics calculated by Abu, A., 2015d
Swiss Lake, Chatsworth, Derbyshire, UK	Sand	58.25 (SFO)	124.3	5.063 (SFO)	34.49 (SFO)	0.54 mg a.i./L	20 ± 2°C	7.0	7.84	0.7	Not given	
<b>Range</b>		22–58.25 d	65.5–124.3 d									

## 5.7 Other evidence of persistence

45. According to a 10-year water quality assessment study performed by the United States Geological Survey, chlorpyrifos was the most heavily used and frequently detected insecticide; it was found at concentrations exceeding an aquatic-life benchmark of 0.04 mg/L for water in 37% samples collected from water bodies with diverse land-use settings throughout the USA (Gilliom et al., 2006). Chlorpyrifos was detected frequently in both urban and rural streams and major rivers in the USA, but less frequently in groundwater samples (Kolpin et al., 2000).

## 6. Bioaccumulation

### 6.1 Bioaccumulation in laboratory studies

46. The EU RAR (Spain 2017) lists several fish bioconcentration studies, yet only one was conducted according to an accepted guideline: this was conducted according to EPA Guideline No. 72-6 and 165-4, and a BCF of  $1,374 \pm 321$  in rainbow trout (*Onchorhynchus mykiss*) was estimated. This BCF value was calculated after a 30-day exposure to 0.3 µg/L chlorpyrifos under flow through conditions, followed by a depuration phase of 16 days. Steady state was reached. This study was conducted according to EPA Guideline No. 72-6 and 165-4. Values were not normalized for lipid content or growth dilution. As the study was conducted with juvenile trout, growth dilution can lead to some underestimation of the BCF.

47. High bioconcentration is documented for eleuthero embryos with kinetic BCF of 3,548 and 6,918 for zebrafish (*Danio rerio*) (El-Amrani et al., 2012) and 2,187 for medaka (*Oryzias latipes*) (Alharbi et al., 2017). Exposure concentrations were 1 µg/L and 10 µg/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. 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).

48. Various studies, including Eaton et al., (1985) and others described in Table 10 and accompanying text in document UNEP/POPS/POPRC.18/INF/8, show toxicity to fish at very low concentrations. These findings are supported by data from the EU RAR (Spain 2017b) which gives a 96 h lethal concentration 50 (LC50) value of 8 µg active substance per litre (a.s./L) for rainbow trout (*Oncorhynchus mykiss*) in a test performed with Dursban. For the estuarine fish *Leuresthes tenuis*, Goodman, Hansen, Cripe, et al., (1985b) reported no observed effect concentration (NOEC) values of 0.14 and 0.3 µg a.s./L for embryo weight and lethality respectively. Additionally, Giesy et al., (2014) calculated a species sensitivity distribution (SSD) for chlorpyrifos of 0.812 µg a.s./L. The concern of moderate bioaccumulation is that body concentrations may be reached that could lead to toxic effects, due to high toxicity. Chlorpyrifos' high toxicity means that even moderate bioaccumulation may have a similar effect as high bioaccumulation of less toxic chemicals, reflected in criterion [c][ii] of Annex D.

49. Deneer (1994), compared lab and mesocosm BCF for three-spined stickleback (*Gasterosteus aculeatus*) to investigate the feasibility of predicting the concentration of chlorpyrifos in fish in outdoor mesocosms, using uptake and elimination rate constants determined in the laboratory. In the laboratory experiments, he found a lipid-based BCF of 21,000, or 1057 normalized to 5% lipid. Also, a decrease of the elimination rate upon increasing exposure concentrations was found, which leads to an increase of the BCF with increasing exposure concentrations. The predicted values were all lower than the levels of chlorpyrifos actually found in fish from the outdoor mesocosms.

50. Other fish studies have produced BCF values in a wide range, most studies however show toxic effects even at low concentrations. Generally speaking for BCF studies, no toxic effects should be observed in the study since these could affect the resulting BCF. Jarvinen et al. (1983) calculated a BCF of  $1673 \pm 423$  for the fathead minnow (*Pimephales promelas*) in a chronic toxicity study, not stating for which concentration this value was calculated. Toxic effects occurred in all concentrations and included significant mortality at 2.68 µg/L, growth reduction at 1.21 µg/L and reduced reproduction at 0.12 µg/L. For the same species Eaton et al. (1985) produced a lipid normalized BCF of 1150 at concentrations between 0.12 µg/L and 0.83 µg/L. Toxic effects included reduced reproduction and decreased body weight. Goodman et al. (1985a) exposed early life stages of two silverside species to chlorpyrifos and determined a maximum BCF of 580 at 0.38 µg/L. At 0.093 µg/L, no toxic effects were found, the corresponding BCF was 410. Significant mortality occurred at 1 µg/L and 2 µg/L. Following the same experimental set-up Goodman et al. (1985b) produced a maximum BCF of 1000 using the California grunion (*Leuresthes tenuis*) at 0.25 µg/L. Here significant mortality and decreased body weight occurred at concentrations of  $0.63 \pm 0.11$  µg/L to  $2.8 \pm 0.48$  µg/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 µg/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 µg/L and significant mortality at 150 µg/L.

51. Besides fish, other aquatic species are highly susceptible to chlorpyrifos. For *Daphnia magna* an EC50 of 0.1 µg a.s./L (Spain, 2017a) and for *Xenopus laevis* (African clawed frog) a 96-h LC50 of 0.564 mg a.s./L (Richards and Kendall, 2002) was determined.

52. Toxicity in terrestrial species has also been demonstrated. For honey bees contact toxicity was identified as LD50 of 0.068 µg a.s./bee for Dursban (Bell (1994)). A LD50 of 39.24 mg a.s./kg body weight (bw) was set for the Bobwhite quail (Spain, 2017b). Acute oral LD50 ranging 64 to 71 mg a.s./kg bw have been set for mice and ranging between 66 to 192 mg a.s./kg (bw) for rats (European Commission, 2005). For further information on toxicity see chapter 4 of this document.
53. Robles-Menoza (2011) found a BCF of 3632 in axolotl (*Ambystoma mexicanum*) in spite of a decrease in chlorpyrifos concentration in the water of 50%. Also, a reduction of >90 %, in relation to the control group, of normal activity (walking, swimming and prey attack) was seen.
54. Bioaccumulation in sediment dwelling organisms has been measured for the oligochaete *Lumbriculus variegatus* (Jantunen et al., 2008). Four different sediments were tested in a 10 d static exposure with concentrations ranging from 0.06 to 1.1 µmol/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 (BSAF). BSAFs ranged from 6 to 99 depending on the sediment and chlorpyrifos concentration.
55. In the earth worm species *Eisenia andrei*, Svobodová et al., (2018) measured bioaccumulation BAF values at steady state following OECD 317. Both soil types were sterilized with gamma radiation and the nominal concentration was set to 5 mg kg<sup>-1</sup> soil dry weight to represent worst case scenarios. BAF under steady state were calculated as  $6.34 \pm 1.30$  and  $4.51 \pm 0.76$  for the different soils.
56. 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 lipid weight 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 lipid weight. The uncertainty for plankton-based bioaccumulation stems from the high surface to volume ratio. Adsorption may occur and could skew bioaccumulation values upward.
57. A study in 2016, by Bonansea et al., investigated the accumulation of chlorpyrifos in the fish *Jenynsia multidentata* when exposed for 96 h to different mixtures. The exposure with only chlorpyrifos showed concentration <LOD in the muscles and brain,  $67 \pm 49$  µg/kg in intestines,  $58 \pm 25$  µg/kg in liver, and  $42 \pm 31$  µg/kg in gills. The technical mixture showed chlorpyrifos concentrations <LOD in all fish parts. The commercial product mixture showed chlorpyrifos concentrations <LOD in brain,  $8 \pm 5$  µg/kg in muscles,  $50 \pm 29$  µg/kg in intestine,  $323 \pm 187$  µg/kg in liver, and  $11 \pm 6$  µg/kg in gills. Fish exposed to the individual chlorpyrifos showed BCFs in a range from 133 L/kg to 212 L/kg in the intestine, liver, and gills, indicating that the 2 compounds have limited capacity to bioconcentrate in *J. multidentata*.

**Table 10. Bioaccumulation studies assessed for evaluation of chlorpyrifos**

Publication	Species	Endpoint type	Endpoint value	Unit	Comments
<b>Amphibia</b>					
Robles-Mendoza et al. (2011)	Axolotl ( <i>Ambystoma mexicanum</i> )	BCF	3632	mL/g	Decrease in chlorpyrifos concentration by 50% during exposure; behavioural effects
<b>Fish</b>					
Hansen et al. (1986)	Gulf toadfish ( <i>Opsanus beta</i> )	BCF	5100	mL/g	Toxic effects; increased mortality at 150 µg/L for which the BCF of >5000 was reported
Welling and Vries (1992)	Guppies ( <i>Poecilia reticula</i> )	BCF	1847	mL/g	Fish not fed during two-week experiment; static exposure, chlorpyrifos concentration decreased by 90%
Mulla et al. (1973)	Channel catfish ( <i>Ictalurus punctatus</i> )	BCF	4677	mL/g	Extreme fluctuations in temperature and O <sub>2</sub> concentration; fish analysed without gut
Mulla et al. (1973)	Black crappie ( <i>Pomoxis nigromaculatus</i> )	BCF	3333	mL/g	Extreme fluctuations in temperature and O <sub>2</sub> concentration; fish analysed without gut
Mulla et al. (1973)	Largemouth bass ( <i>Micropterus salmoides</i> )	BCF	1333	mL/g	Extreme fluctuations in temperature and O <sub>2</sub> concentration; fish analysed without gut
Mulla et al. (1973)	Bluegill ( <i>Lepomis microchirus</i> )	BCF	1200	mL/g	Extreme fluctuations in temperature and O <sub>2</sub> concentration; fish analysed without gut
Jarvinen et al. (1983)	Fathead minnow ( <i>Pimephales promelas</i> )	BCF	1673 ± 423	mL/g	Toxic effects
Deneer (1993)	Guppy ( <i>Poecilia reticulata</i> )	BCF	1580	mL/g	BCF calculated in Gisey et al. 2014
Thomas and Mansingh (2002)	Red hybrid tilapia ( <i>Oreochromis</i> sp.)	BCF	116 (semi static exposure); 3313 (pulse exposure)	mL/g	High fluctuation of chlorpyrifos; steady state not reached; Dursban 25 C used
J. Eaton et al. (1985)	Bluegills ( <i>Lepomis microchirus</i> )	BCF	600	mL/g	Toxic effects; high fluctuation in chlorpyrifos concentration; Lorsban 4C used

Publication	Species	Endpoint type	Endpoint value	Unit	Comments
J. Eaton et al. (1985)	Fathead minnow ( <i>Pimephales promelas</i> )	BCF	1150	mL/g	Toxic effects; high fluctuation in chlorpyrifos concentration; Lorsban 4C used
Goodman, Hansen, Cripe, et al. (1985)	California grunion ( <i>Leuresthes tenuis</i> )	BCF	1000	mL/g	Significant mortality and toxic effects; control fish contaminated with chlorpyrifos
Cripe et al. (1986)	Sheepshead minnows ( <i>Cyprinodon variegatus</i> )	BCF	1830	mL/g	Mortality in high concentrations; different feeding regiments tested; BCF increased with CPY concentration and higher feeding rates
Goodman, Hansen, Middaugh, et al. (1985)	<i>Menidia beryllina</i>	BCF	440	mL/g	Steady state not reached; mortality in higher concentrations
Goodman, Hansen, Middaugh, et al. (1985)	<i>Menidia peninsulae</i>	BCF	580	mL/g	Steady state not reached; mortality in higher concentrations; negative effect of solvent
Macek et al. (1972)	Bluegills ( <i>Lepomis microchirus</i> )	BCF	2304	mL/g	Extreme fluctuations in temperature and O <sub>2</sub> concentration; behavioural effects
Macek et al. (1972)	Largemouth bass ( <i>Micropterus salmoides</i> )	BCF	1440	mL/g	Extreme fluctuations in temperature and O <sub>2</sub> concentration; behavioural effects
Deneer (1994)	Three-spined stickleback ( <i>Gasterosteus aculeatus</i> )	BCF	21 140 (lipid-based) 1057 (5% lipid)	mL/g	Decrease of elimination rate upon increasing exposure concentrations=> BCF will increase with increasing exposure concentrations
Tsuda et al. (1992)	Carp ( <i>Cyprinus carpio</i> )	BCF	410 ± 100	mL/g	Steady state not reached, estimation of kinetic BCF not possible
Tsuda et al. (1997)	Guppies ( <i>Poecilia reticulata</i> )	BCF	1506 (female guppy), 2305 (male guppy)	mL/g	Steady state not reached
Tsuda et al. (1997)	Medaka ( <i>Oryzias latipes</i> )	BCF	1561	mL/g	Steady state not reached
Tsuda et al. (1997)	Goldfish ( <i>Carassius auratus</i> )	BCF	763	mL/g	Steady state not reached
Tsuda et al. (1997)	White cloud mountain minnow ( <i>Tanichthys albonubes</i> )	BCF	745	mL/g	Steady state not reached
report no ES-928 (J42) in Spain (2017)	Rainbow trout ( <i>Onchorhynchus mykiss</i> )	BCF	1374 ± 321	mL/g	Not normalized for lipid or growth

Publication	Species	Endpoint type	Endpoint value	Unit	Comments
El-Amrani et al. (2012)	Zebrafish ( <i>Danio rerio</i> )	BCF	5011	mL/g	Not normalized for lipid; eleuthero embryos with 11–20% lipid content
Alharbi et al. (2017)	Medaka ( <i>Oryzias latipes</i> )	BCF	2691	mL/g	Not normalized for lipid; eleuthero embryos with 11–20% lipid content
<b>Macroinvertebrates</b>					
Serrano et al. (1997)	<i>Mytilus galloprovincialis</i>	BCF	400 ± 119	mL/g	Concentration of test substance within 25% fluctuation
Thacker et al. (1992)	Eastern oyster ( <i>Crassostrea virginica</i> )	BCF	950 (whole oysters); 1600 (tissue fraction)	mL/g	Significant dip in CPY by day 21 (56%); chlorpyrifos concentration low in shell liquor
Woodburn et al. (2003)	eastern oyster ( <i>Crassostrea virginica</i> )	BCF	565 (whole oyster); 1400 (oyster tissue)	mL/g	Chlorpyrifos concentration low in shell liquor
Rubach et al. (2010)	15 Macroinvertebrate species	BCF	100–13930	mL/g	C <sup>14</sup> labelling of chlorpyrifos at the di-ethyl-phosphorothiol branch
Montañés et al. (1995)	<i>Asellus aquaticus</i>	BCF	1715	mL/g	Mesocosm experiment with time dependant significantly reduced survival
A. Jantunen et al. (2008)	<i>Lumbriculus variegatus</i>	BSAF	Range of 6 to 99		
<b>Plants</b>					
Prasertsup and Ariyakanon (2011)	Duckweed ( <i>Lemna minor</i> )	BCF	5700	mL/g	BCF calculated based on daily measurements
Prasertsup and Ariyakanon (2011)	Water lettuce ( <i>Pistia stratiotes</i> )	BCF	3000	mL/g	BCF calculated based on daily measurements
Lal et al. (1987)	Blue-Green Algae <i>Anabaena</i> sp.	BCF	678	mL/g	Concentration of test substance not maintained, no calculations reported
Lal et al. (1987)	<i>Aulosira fertilissima</i>	BCF	397	mL/g	Concentration of test substance not maintained, no calculations reported
<b>Monitoring data</b>					
Landers et al. (2008)	white fir ( <i>Abies concolor</i> )	chlorpyrifos concentration	first year not detected, second year 19.7	ng/g lipid weight	

Publication	Species	Endpoint type	Endpoint value	Unit	Comments
Landers et al. (2008)	Lodgepole pine ( <i>Pinus contorta</i> )	chlorpyrifos concentration	first year 11.6 , second year 20.5	ng/g lipid weight	
Aston and Seiber (1997)	<i>Pinus ponderosa</i>	BCF <sub>m</sub>	9800	mass: mass ratio	Combined from wax cuticle and cell
Kurt-Karakus et al. (2011)	Zooplankton	BAF	up to 117000		Possible adsorption
Jessup et al. (2010)	Sea otters ( <i>Enhydra lutris</i> ssp.)	concentration in blood serum	maximum 342.6	ng/g lipid weight	
Stansley et al. (2010)	River otters ( <i>Lontra canadensis</i> )	concentration in liver tissue	maximum 6.91	ng/g wet weight	
Adrogué et al. (2019)	Blackbrowed albatross ( <i>Thalassarche melanophris</i> )	concentration in feathers	58.64 ± 27.31 (male); 49.56 ± 18.45 (female)	ng/g	Feathers washed with deionized water before analysis
Adrogué et al. (2019)	Cape petrels ( <i>Daption capense</i> )	concentration in feathers	84.88 ± 50.57 (male); 75.98 ± 47.97 (female)	ng/g	Feathers washed with deionized water before analysis
Morris et al. (2014)	Mushrooms, lichen and green plants	BCF <sub>v</sub>	8.0–8.7	mass: mass ratio	Recovery rate of chlorpyrifos from biota samples 52 ±17%
Morris et al. (2014)	Caribou:vegetation	BMF	1.6 ± 0.31 (spring); 1.4 ± 0.43 (summer); 2.1 ± 0.64 (fall/winter)		Recovery rate of chlorpyrifos from biota samples 52 ±17%
Morris et al. (2014)	Wolf:caribou	BMF	0.078 ± 0.019		Recovery rate of chlorpyrifos from biota samples 52 ±17%
Morris et al. (2014)	Wolf <sub>liver</sub> :caribou <sub>liver</sub>	BMF	1.7 ± 0.52		Recovery rate of chlorpyrifos from biota samples 52 ±17%
Morris et al. (2014)	Green plants	TMF	0.61 (0.47–0.79)	pg/g lipid weight	Recovery rate of chlorpyrifos from biota samples 52 ±17%
Morris et al. (2016)	Plankton	BAF	7 943 282 ± 5 011 872	mL/g	Recovery rate of chlorpyrifos from biota samples 52 ±17%

Publication	Species	Endpoint type	Endpoint value	Unit	Comments
Morris et al. (2016)	Polar bear fat: seal blubber	BMF	$1.3 \pm 0.22$ and $0.90 \pm 0.27$		Recovery rate of chlorpyrifos from biota samples $52 \pm 17\%$ ; concentration in seal blubber not reported; detection in seal blubber below 20%
Morris et al. (2016)	Seal blubber	TMF	0.27, 0.57 and 0.18		Recovery rate of chlorpyrifos from biota samples $52 \pm 17\%$ ; concentration in seal blubber not reported; detection in seal blubber below 20%
Singh et al. (2008)	Chicken	mean concentration in blood	80	ppb	
Singh et al. (2008)	Goat	mean concentration in blood	70	ppb	
Singh et al. (2008)	Man	mean concentration in blood	40	ppb	
Shaker and Elsharkawy (2015)	Buffalo	concentration in raw milk	1.870–3.514	mg/kg	
Weldon et al. (2011)	<i>Homo sapiens</i>	concentration in breast milk	urban mean 40.5; agricultural mean 139	pg/g milk	
Bedi et al. (2013)	<i>Homo sapiens</i>	concentration in breast milk	median 1664.2	ng/g lipid weight	
Sanghi et al. (2003)	<i>Homo sapiens</i>	concentration in breast milk	mean value $0.230 \pm 0.024$	mg/kg	

BCF: bioconcentration factor, BMF: biomagnification factor, BAF: bioaccumulation factor, TMF: trophic magnification factor

**Table 11. Bioaccumulation studies not used for assessment but used in Spain 2017**

In summary as report number	Species	Endpoint type	Endpoint value	Unit	Publicly available	Comments
GHE-T-281 (J061)	Eel ( <i>Anguilla anguilla</i> )	BCF	400	mL/g	No	Non-guideline study, eel exposed to mud spiked with chlorpyrifos
GS 1318 (J41)	Mosquito fish ( <i>Gambusia</i> sp.)	BCF	65–472	mL/g	No	Non-guideline study, 6 days uptake phase no lipid correction, not considered to be valid in EU RAR (Spain 2017)
DECO-ES-2377 (J66)	Eastern oyster ( <i>Crassostrea virginica</i> )	BCF	430	mL/g	No	

## 6.2 Details of bioaccumulation studies not listed in the dossier

58. According to a review by (Giesy et al., 2014) relevant and reliable BCF values for aquatic plants range from 72 to 5700.
59. The highest BCF value of 5700 was measured for duckweed (*Lemna minor*) (Prasertsup & Ariyakanon, 2011). In a seven-day static experiment plants were exposed to a nominal concentration of 100 µg/L chlorpyrifos. Samples of plants and water were taken daily and analysed for chlorpyrifos content by gas chromatography at recovery rates of 98 ± 2%. With the same experimental set up, a BCF of 3000 was calculated for water lettuce (*Pistia stratiotes*). This study is considered unreliable as the chlorpyrifos concentration declined by more than 30% over the time of the experiment.
60. Rubach et al. (2010) conducted exposure experiments of 15 invertebrate species with C14 labelled chlorpyrifos. This resulted in highest BCF value for the diptera *Culex pipens* of 13 930. This value should be evaluated with caution as the C14 label was placed at the di-ethyl-phosphorothiol branch of the chlorpyrifos molecule. Accordingly radioactivity measured was not limited to chlorpyrifos but included phosphorylated proteins Mackay et al. (2014) and could result in an overestimated BCF.
61. The BCF for the axolotl (*Ambystoma mexicanum*) was determined in a 48 h static test (Robles-Mendoza et al., 2011). The nominal concentrations were 50 µg/L and 100 µg/L. Ten animals per concentration were tested. Chemical analysis of water and tissue samples were conducted with gas chromatography with a recovery rate of > 95%. Water samples were taken to determine chlorpyrifos concentration at 0 h, 24 h and 48 h. Chlorpyrifos concentration had declined up to 50% at the end of the experiment. The calculated BCF was 3632 at 100 µg/L. This value has some level of uncertainty as chlorpyrifos level were not stable. Additionally, toxicity test showed significant acetylcholinesterase inhibition, reduced motor activity and reduced hunting at 50 µg/L.
62. *Asselus aquaticus* was exposed to chlorpyrifos in the form of Dursban 4E. The nominal concentration of active substance were 0.7 and 5 µg/L (Montañés et al., 1995). Exposure took place in nature-like mesocosms, 40 m long ditches lined with water-tight, non-toxic PVC and a 0.25 m sediment layer and filled with water drawn from a underground well. Polythene spheres were used to hold 10 animal each. 120 animals per concentration were exposed this way. 50 animals were used as controls in a ditch without chlorpyrifos. Water samples were taken at 15 min and at 1, 2, 4, 7, 14 and 29 days after application. On days 1, 2, 3, 4, 6, 8, 13, 17 and 23 animals were sampled by harvesting one or two spheres. The recovery rate from biota was 54 + 4% and 82 + 5% from water. The limits of detection were 0.001 µg/L in water and 200 ng/g lipid weight (lw) for *Asselus aquaticus*. The concentration of chlorpyrifos was not stable and declined continuously over the course of the experiment with a decline above 25% in the first three days. Survival was significantly reduced in the course of the experiment, the authors noted that this may be due to predation or toxicity of chlorpyrifos. An average lipid content of 0.69 ± 0.26% was observed. Kinetic BCF were calculated for days two to seventeen. On average the BCF was 1715.
63. An extensive review on bioaccumulation was conducted by Giesy et al. (2014) with BCFs ranging from 0.6 to 6760 in fish. The highest valid study as assessed by the authors was Hansen et al 1986 with a BCF of 5100 for the gulf toad fish.
64. Hansen et al. (1986) conducted a 49-day early life stage toxicity test with the marine gulf toadfish (*Opsanus beta*). Embryos were exposed to chlorpyrifos concentrations ranging from 1.2 to 150 µg/L in a flow through system. The authors reported a range of BCFs from 100 to 5100. The results of this study must be interpreted with caution as toxic effects occurred at all concentrations higher than 3.7 µg/L. Effects included mortality, reduced size, retarded development and behavioural effects such as hyperactivity and hyperventilation. Mortality was significantly increased at the concentration 150 µg/L which produced the BCF of 5100.
65. In a 28-day field experiment, artificial ponds were dosed with a mosquito larvicide application of granular chlorpyrifos resulting in mean water concentrations between 0.6 µg/L and 0.1 µg/L, exposing four fish species (Mulla et al., 1973). Concentrations in the water declined as concentrations in the upper sediment layer increased to a maximum of 180 µg/kg. Sediment associated species such as channel catfish (*Ictalurus punctatus*) and black crappie (*Pomoxis nigromaculatus*) accumulated mean maximum residues of 0.8 mg/kg and 0.6 mg/kg, resulting in BCFs of 4667 and 3333 respectively. Free swimming species such as largemouth bass (*Micropterus salmoides*) and bluegill (*Lepomis microchirus*) accumulated 0.2 mg/kg and 0.1 mg/kg, resulting in BCF of 1333 and 1200. This study may underestimate chlorpyrifos bioaccumulation, as the viscera was removed from fish before analysis. Results should be interpreted with caution as chlorpyrifos concentrations varied above the 20% mark throughout the experiment.
66. A BCF of 1700 for juvenile guppies (*Poecilia reticulata*) was reported in a 14-day static exposure with chlorpyrifos (Welling & Vries, 1992). This study is considered unsuitable for BCF calculation as the nominal concentration of 10 µg/L decreased to below 1 µg/L by day 9. Furthermore, fish were not fed during the experiment.
67. Jarvinen et al. (1983) exposed fathead minnows (*Pimephales promelas*) to chlorpyrifos in a 200-day full life cycle experiment under flow through conditions. A BCF of 1673 ± 423 for first generation minnows at 60 days was calculated. Steady state was assumed. Effects occurred proportional to acetylcholinesterase inhibition. At the highest concentration of 2.68 µg/L reduction of growth, deformities and later significant mortality occurred. Growth reduction

was also observed for 1.21 µg/L, later in the test. Sexual maturation and reproduction were reduced in all exposure groups at concentrations as low as 0.12 µg/L. In the second generation, deformities occurred more frequently and at lower water concentrations. Based on the toxic effects, the BCF should be interpreted with caution.

68. Deneer (1993) calculated uptake and elimination constants for the guppy (*Poecilia reticulata*) under flow through conditions of 2 µg/L chlorpyrifos. The experiment lasted 24 days, 20 days of exposure and four days for depuration. The uptake constant was calculated as  $7000 \pm 2000$  L/kg/d, the depuration constant as  $0.40 \pm 0.11$  L/kg/d. The BCF was calculated in (Giesy et al. 2014) as 1580. Steady state was not reached and chlorpyrifos concentration showed a high fluctuation.

69. Thomas and Mansingh (2002) conducted two experiments exposing red hybrid tilapia (*Oreochromis* sp.) to the commercial product Dursban 25 C with 25% chlorpyrifos active ingredient. A three-day semi-static exposure, with the water concentration fluctuating between 48 µg/L and 35 µg/L chlorpyrifos, resulted in a BCF of 116. A four-day pulse exposure with water concentration between 4.9 µg/L and 3.6 µg/L resulted in a BCF of 3313. This study must be interpreted with caution, as steady state was not reached and the concentration of chlorpyrifos fluctuated highly. Moreover, Dursban 25 C contains other ingredients that can have effects on fish.

70. Artificial streams were exposed to Lorsban 4E with 40,7% active ingredient chlorpyrifos in a 100-day experiment (J. Eaton et al., 1985). One stream was continuously dosed, the other was subjected to pulse exposure every two weeks. Water concentration in the continuously dosed stream varied between 0.12 µg/L and 0.83 µg/L during the 100 days and also spatially between the sections of the stream up to 0.17 µg/L. The pulsed stream reached maximum concentrations of up to 7 µg/L directly after pulse events. Both streams received the equivalent amount of chlorpyrifos during the experiment. Bluegills (*Lepomis microchirus*) and fathead minnows (*Pimephales promelas*) were exposed. For fathead minnows deformities occurred in the pulse experiment only, reproductive losses and decreased body weight of second-generation fish occurred in both streams. For bluegills behavioural effects occurred. Both fathead minnows and bluegills showed acetylcholinesterase inhibition. For fatheaded minnow a tissue BCF of 760 was calculated and a lipid BCF of 23000. Normalised to 5% lipid content the BCF is 1150. For bluegill a tissue BCF of 100 was calculated and a lipid BCF of 12000, which gives a BCF of 600 when normalised to 5% lipid content. These values should be interpreted with caution as Lorsban was used instead of pure chlorpyrifos, in addition chlorpyrifos concentrations were not constant and toxic effects occurred. Additionally, the authors did not specify which tissue was analysed nor give the lipid content of the fish.

71. In a 30-day early life stage toxicity test, the california grunion (*Leuresthes tenuis*) was exposed to 0.14 µg/L chlorpyrifos under flow through conditions (Goodman, Hansen, Cripe, et al., 1985). A BCF of 1000 was determined. This result should be interpreted with caution, as chlorpyrifos residue was also found in fish sampled from the seawater and solvent control.

72. A BCF of 1830 was determined for sheepshead minnows (*Cyprinodon variegatus*) in a 28-day early life stage toxicity test under flow through conditions (Cripe et al., 1986). The effect of different feeding ratios and chlorpyrifos concentrations were examined. Fish were exposed to 10 different concentrations ranging from 0.6 µg/L to 52 µg/L and three different feeding regiments. BCF increased with increasing chlorpyrifos concentrations and increasing amount of feed. These results should be interpreted with caution as significant mortality occurred in higher concentrations.

73. Different silverside species were exposed to chlorpyrifos in a 28-day early life stage toxicity test under flow through conditions (Goodman, Hansen, Middaugh, et al., 1985). For *Menidia beryllina* a BCF of 440 was determined. For *Menidia peninsulae* a BCF of 580 was reported. BCFs increased with higher chlorpyrifos concentrations. Results should be interpreted with caution as mortality occurred in higher concentrations for both fish species and *M. peninsulae* survival was negatively affected by the solvent used.

74. Macek et al. (1972) described the uptake of chlorpyrifos in bluegills (*Lepomis microchirus*) and largemouth bass (*Micropterus salmoides*) during a 63-day field study with chlorpyrifos applied at mosquito larvicide rates to small ponds. Two applications were performed on day one and day 35. The maximum BCF for bluegill was 2304 on day seven and 1440 BCF for largemouth bass on day three. Water temperatures could rise up to 31 °C as the experiment was conducted during summer months. This influenced the dissolved oxygen, which could drop below 50%. Behavioural effects were noted shortly after each application. Results should be interpreted with caution as the variation of chlorpyrifos concentrations exceeded the 20% window.

75. For the three-spined stickleback (*Gasterosteus aculeatus*) a BCF of 1057 was derived from a 30-day laboratory experiment (Deneer, 1994). Fish were exposed to chlorpyrifos at  $0.19 \pm 0.03$  µg/L for 21 days under flow through conditions, depuration lasted 9 days. Insufficient information is reported on BCF calculation, therefore the BCF value should be interpreted with caution.

76. Tsuda et al. (1992) exposed carp (*Cyprinus carpio*) to  $0.49 \pm 0.11$  µg/L chlorpyrifos during a 14-day flow through experiment. A BCF of  $410 \pm 100$  was calculated on day 14. Although steady state was not reached, the BCF was calculated as it would be under steady state conditions. The same reason for caution applies to the study from Tsuda et al. (1997) with the same experimental set up, where a BCF of 2406 was calculated for male guppies (*Poecilia*

reticulata), a BCF of 1464 calculated for female guppies, 1561 for medaka (*Oryzias latipes*), 763 for goldfish (*Carassius auratus*) and 745 for white cloud mountain minnow (*Tanichthys albonubes*).

77. An experiment following the same setup was conducted for medaka (*Oryzias latipes*) at 10 µg/L chlorpyrifos (Alharbi et al., 2017). The LOD for chlorpyrifos was 0.19 ng/g. Steady state was not reached, therefore the kinetic BCF was calculated at 2187. In a separate experiment instead of exposure medium, processed water from surface level mining, containing chlorpyrifos, was used. This resulted in a kinetic BCF of 8912.

78. Chlorpyrifos and its transformation product chlorpyrifos oxon were detected in needles of potted ponderosa pines at three sites in California in 1994 (Aston & Seiber, 1997). Needle compartments were analysed separately and included a wash for polar and non-polar adsorbed substances, the waxy cuticle and the remainder needle. Values for chlorpyrifos residue in each compartment were combined to calculate total burden per sample. Two sites were sampled, one was located at the edge of the Central Valley (114 m altitude), while the others were situated at higher altitudes in the Sequoia National Park (533 and 1920 m, resp.). The detection frequency was significantly higher at the site in the Central Valley than those at the other two locations. The maximum level of chlorpyrifos in pine needles, which was found at the site in the Central Valley, amounted to ca. 129 ng/g dry weight, while the maximum level of chlorpyrifos oxon was about 110 ng/g dry weight at the same location<sup>7</sup>. Assuming that the needles of the potted pines, located at the site in the Central Valley, were in equilibrium with the compound in the surrounding air after 10 weeks of exposure, the vegetation: air BCF<sub>m</sub> was estimated as 9800.

## 7. Potential for long-range transport

### 7.1 Environmental fate properties and model results

79. The vapour pressure for chlorpyrifos has been estimated between  $1.0 \times 10^{-3}$  and  $3.35 \times 10^{-3}$  Pa at 25°C (see Table 1 above). Based on these values, chlorpyrifos in the atmosphere will exist mostly in the vapour phase and to a lesser extent the particulate phase.

80. For the vapour phase the dominant mechanism of degradation is based on a reaction with OH radicals (Zhou et al., 2010).

81. Using the Atmospheric Oxidation Program (AOPWIN; ver.1.89; (US EPA)), Simon (2001) calculated an OH radical reaction rate of  $9.16 \times 10^{-12}$  cm<sup>3</sup>/molecule-sec for chlorpyrifos. Atmospheric half-life depends on the atmospheric OH radical concentration used for calculation. The European REACH guidance applies an annual average OH radical concentration of  $0.5 \times 10^6$  molecules/cm<sup>3</sup> (ECHA 2016), which yields a half-life is 4.1 h. AOPWIN estimates half-life values using a default OH radical concentration of  $1.5 \times 10^6$  molecules/cm<sup>3</sup> and a 12-hour day, the corresponding half-life is 1.4 h (AOPWIN; ver.1.89; (US EPA)).

82. Muir et al., (2004) applied an OH concentration of  $1.5 \times 10^5$  molecules/cm<sup>3</sup> (12 h day) that resulted in a half-life of 14 h. The authors noted that the latter scenario was realistic for spring applications of chlorpyrifos in southern Canada (~45–50°N), when average OH concentrations could be an order of magnitude lower than the default AOPWIN concentration. Atmospheric half-life is impacted by seasonal variations of OH radical concentration. Calculations indicate that a reduced OH radical concentration would result in longer half-lives in the atmosphere. Hermanson et al., (2005) detected a continuous profile of chlorpyrifos in the upper 40cm of an ice core sampled in 1998 from Austfonna, Svalbard in the Norwegian Arctic, which corresponded approximately to the years 1943 to 1998. Chlorpyrifos first appeared at Austfonna in 1972; its concentration peaked in the 1980s, began to decline in the 1990s, and was not found in the surface layer of the core (1992-1998). Since chlorpyrifos was found at Austfonna despite its atmospheric half-life of 1.4 h from AOPWIN, Hermanson et al. (2005) concluded that its apparent atmospheric persistence likely resulted from little or no oxidation by OH radicals during the dark polar winter and in spring. The authors also speculated that peak ice core concentrations of chlorpyrifos (and other pesticides) after 1979 may have been associated with pesticide use in Russian farmlands north of 60°N.

83. Modelling results are corroborated by degradation experiments. In Muñoz et al., (2012) the atmospheric degradation of gas phase chlorpyrifos under sunlight conditions was observed in the outdoor European Photoreactor (EUPHORE). The rate constant for the reaction of chlorpyrifos with OH radicals was determined as  $(9.1 \pm 2.1) \times 10^{-11}$  cm<sup>3</sup>/molecule-sec at  $29 \pm 5^\circ\text{C}$ . The atmospheric half-life of chlorpyrifos was approximately 2 h. In the particulate phase, the reaction of chlorpyrifos with OH radicals is heterogeneous and significantly reduced (ATSDR, 1997; El Masri et al., 2014). El Masri et al., (2014) measured a heterogeneous OH radical reaction rate of  $5.8 \times 10^{-12}$

<sup>7</sup> The concentration values were estimated from a diagram of the cited publication.

<sup>8</sup> In this study the BCF<sub>m</sub> was defined as the mass : mass ratio of the concentration of a chemical in vegetation tissues to its concentration in air.

cm<sup>3</sup>/molecules-sec at 25°C. Half-lives of particulate chlorpyrifos were 66.4 h and 22.1 h, respectively, for OH radical concentrations of  $0.5 \times 10^6$  molecules/cm<sup>3</sup> and  $1.5 \times 10^6$  molecules/cm<sup>3</sup>

84. Socorro and co-workers showed that pesticides adsorbed to particulates may show an overall atmospheric half-life that exceeds values relevant for long range transport (Socorro et al., 2016). The heterogeneous OH oxidation of pesticides adsorbed on atmospheric particles is a very slow process suggesting that the pesticides can persist for a long time in the atmosphere prior to being either degraded or transferred to terrestrial and aquatic ecosystems. Although these experiments were not conducted with chlorpyrifos, but with 8 other pesticides, the results explain the general mechanisms.
85. Chlorpyrifos in the particulate phase was detected during monitoring in air from Spain (Borras et al., 2011; Coscollà et al., 2014). At a site in the Czech Republic (Degrendele et al., 2016), the average particulate fraction of chlorpyrifos was 0.037; Li and co-workers (Li et al., 2014) studied seasonal variation of atmospheric chlorpyrifos at Guangzhou, China. The percentage of chlorpyrifos was lowest in summer (1.4%) and highest in winter (27%). In the coincident samples of Arctic marine fog and air taken at an expedition at the Chukchi Sea near the Siberian coast the concentration of chlorpyrifos in the vapour phase was 0.76 pg/m<sup>3</sup> and bound to particles was 0.08 pg/m<sup>3</sup>, while the level in the water phase of a corresponding fog sample was 0.08 ng/L (Rice & Chernyak, 1997).
86. Zhong et al., (2012) sampled oceanic air at several sites from East Asia to the high Arctic. Chlorpyrifos was detected in all of the 17 analysed gaseous samples. The authors measured distributions between vapour and particulate phase. Particulate chlorpyrifos was observed in 5 out of 17 samples; these samples originated from the Sea of Japan, the North Pacific and the Bering Sea. The fraction of chlorpyrifos in the particulate phase of these samples ranged from 0.24% to 4% (Zhong et al., 2012).
87. A recent study analysed chlorpyrifos in soil and air from agricultural sites in South Africa (Degrendele et al., 2022). The observed fraction of particulate chlorpyrifos ranged from 0.806 to 0.973 which is considerably higher than expected (Degrendele et al., 2022). The authors consider that these high values might have been caused by the formulation or application technique as the study was conducted during the application season (Degrendele et al., 2022).
88. AEROWIN of US EPA Episuite<sup>9</sup> (v.4.11) was used to model the fraction of chlorpyrifos sorbed to atmospheric particulates. Inputs for physico-chemical properties were used.<sup>10</sup> AEROWIN has three models and the predicted fraction of chlorpyrifos sorbed to particulates in air was 6.9% (Junge-Pankow model), 14.1% (Mackay model) and 0.24% (Octanol/air (K<sub>OA</sub>) model).
89. As described in the section on persistence, chlorpyrifos binds strongly to soil and sediment. Coscollà et al., (2014) hypothesize that chlorpyrifos adsorbed to the coarse fraction (e.g., 2.5 – 10 µm) of soil particles could be transported by wind erosion as has been shown for other pesticides (Larney et al., 1999).
90. In summary, particulate chlorpyrifos appears to be more recalcitrant to atmospheric degradation and may thus be transported over longer distances. These attributes are relevant as per Annex D (d) (iii). However, the overall relevance of this mechanism in comparison with other routes of transport is still unknown. The observed percentage of particulate chlorpyrifos generally ranges from < 0.001% to 27% with a recent case even reaching more than 80%. Modelling results range from 0.24% to 14.1%. While the median percentage of particulate chlorpyrifos may be rather low, actual long-range transport might be dominated by the higher values that occur due to the high variance.
91. Once in the water compartment, chlorpyrifos bound to suspended solids and sediment is persistent. A recent study measured legacy POPs in the Fram Strait, the only deepwater passage to the Arctic Ocean from the Atlantic Ocean (Ma et al., 2018), and oceanic transport is probably relevant for chlorpyrifos as well. Chlorpyrifos bound to particles in the Arctic Ocean has been measured by Bigot et al., (2017) (chlorpyrifos was detected in two out of five samples) and Morris et al., (2016).
92. The OECD Pov and LRTP Screening tool<sup>11</sup> 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.<sup>12</sup> However, the results indicate that transport occurs both via air and water.

<sup>9</sup> <https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface>.

<sup>10</sup> Input physico-chemical properties: Log Kow: 5.00, Melting Point (deg C): 42.00, Vapor Pressure (mm Hg): 7.5006E-006, Water Solubility (mg/L): 1, Henry LC (atm·m<sup>3</sup>/mole): 1.98E-005.

<sup>11</sup> OECD POV and LRTP Screening Tool, Version 2.2, 2009.

<sup>12</sup> Input physico-chemical properties: log Kow 5.2, log K<sub>AW</sub> -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 =  $7.86 \cdot 10^{-2}\%$ .

Half-life data calculation 2: air 4.2 h, water 1080 h, soil 2640 h.

Results calculation 2: Pov = 158 × d, CTD (air) = 86 km, CTD (water) = 106 km, TE =  $7.69 \cdot 10^{-3}\%$ .

93. A recent study of Sühling et al., (2020) found that the long-range environmental transport of organophosphate esters and, potentially, other substances, is not adequately predicted by the OECD Pov and LRTP Screening Tool. Uncertainty in gas-particle partitioning of non-chlorinated organophosphate esters and river-based transport in the case of chlorinated organophosphate esters were discussed as potential reasons for the underestimation of long-range transport (Sühling et al., 2020). The authors suggest modifications to the OECD Pov and LRTP Screening Tool to account for transport mechanisms like episodic air and riverine transport. Chlorpyrifos is an organothiophosphate, and hence structurally related. The respective modelling results could be subject to similar problems. Particularly transport in water might be underestimated by the OECD Pov and LRTP Screening Tool.

## 7.2 Monitoring in abiotic compartments of remote regions

94. Chlorpyrifos has been detected in many different environmental matrices in remote regions; in Arctic air, snow, lake sediment, fresh water, sea water, marine fog and ice (Balmer et al., 2019; Bigot et al., 2017; Chernyak et al., 1996; Garbarino et al., 2002; Hermanson et al., 2005; Hermanson et al., 2020; Hermanson et al., 2021; Hung et al., 2013; Jantunen et al., 2007, as cited in Hoferkamp et al., 2010; Jantunen et al., 2015; Landers, 2008; Muir et al., 2004; Pučko et al., 2015; Pučko et al., 2017; Rice & Chernyak, 1997; Ruggirello et al., 2010; Zhong et al., 2012), in Antarctic air, ice and sea-ice meltwater (Bigot et al., 2017; Hermanson et al., 2021), in ice from the Lys Glacier and meltwater from six glaciers in the European Alps (Rizzi et al., 2019), as well as in air and precipitation in Sweden (Boström, 2020b). The results of these monitoring studies, which have been published in scientific literature, are summarized in Table 11 in document UNEP/POPS/POPRC.18/INF/8.

95. In several of the studies chlorpyrifos has been among the most abundant organochlorine pesticide detected. Chernyak et al., (1996) investigated current-use pesticides in the Bering and Chukchi marine ecosystems in the summer of 1993. Chlorpyrifos was measured in 4 of 6 fog condensates; the highest concentration was 5 ng/L. Chlorpyrifos was the third most abundant chemical identified at most sampling points. Among the five pesticides analysed, chlorpyrifos was the most frequently identified contaminant in sub-surface sea water with levels ranging from 18 to 67 pg/L in 6 of 9 samples. Chlorpyrifos was measured at 170 pg/L in the single melted ice sample, where only atrazine was found in higher concentrations. Winter snow from four glacial sites on Svalbard was analysed for atmospheric deposition of 36 organochlorine pesticides (OCPs) and 7 industrial compounds (OCICs). Chlorpyrifos dominated OCP flux at three of the sites and was the second highest at the fourth site (Hermanson et al., 2020). The study authors described that air mass frequency from likely source areas showed that Austfonna had the most frequent long-distance air flow, but showed lower amounts of chlorpyrifos, suggesting local sources to other sites. The same author investigated ice core samples from Svalbard and Antarctica in 2021 and chlorpyrifos had the greatest flux at both sampling sites (Hermanson et al., 2021). The study is further discussed below. 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 POPs 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.

96. Hermanson et al., (2005) analysed the upper 40 m of an ice core from Austfonna, the largest ice cap in Eurasia, for several current-use pesticides and other contaminants. There has never been outdoor agriculture on Svalbard. Chlorpyrifos first appears at Austfonna in 1972, and 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. A similar trend was observed by Ruggirello et al., (2010), who investigated the current use and legacy pesticide deposition to a 125 m deep ice core drilled at Holtedahlfonna in 2005 on Svalbard. Chlorpyrifos was first detected in 1971–1980 with a comparatively low input (64.8 pg/cm<sup>2</sup>/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/cm<sup>2</sup>/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 was the only organophosphorus current-use pesticide that was detected continuously in the Holtedahlfonna ice core, making up about 34% of the total pesticide burden in the core. 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. The authors also speculated that peak ice core concentrations of chlorpyrifos (and other pesticides) after 1979 may have been associated with pesticide use in Russian farmlands north of 60°N.

97. Ruggirello et al., (2010) compared the results from the Austfonna ice core with those from the Holtedahlfonna ice core, converting the concentration data determined at Austfonna 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 from populated and agricultural regions in northern Eurasia might be the cause for the greater burdens of some pesticides, including chlorpyrifos.

98. In 2015, a study by Bigot et al., (2017) investigated the chlorpyrifos levels as dissolved and in particle state in arctic snow, sea ice, and seawater samples at Arctic coastal sites in northeast Greenland and eastern Antarctica. The study found concentrations of dissolved chlorpyrifos to be 6.2–11.5 pg/L in five samples of the snow meltwater, 5.2–12.0 pg/L in five samples of Arctic sea-ice meltwater, and 0.74–1.0 pg/L in 5 samples of Arctic sea water. Chlorpyrifos was measured above the limit of detection in two of five samples of both seawater particles (< 0.099–0.29 pg/L) and sea-ice particles (< 0.86–15.5 pg/L) at the Arctic site, and concentrations on snow particles were less than the limit of detection of 0.66 pg/L. The dissolved fraction of chlorpyrifos was not measured above the limit of detection in seawater or snow meltwater at the Antarctic site, and was measured at 7.3 pg/L in one of four sea-ice meltwater samples. No chlorpyrifos was reported on particles from the Antarctic site. In another study by Pucko et al., (2017) examining currently-use pesticides, concentrations in Resolute Passage of the Canadian Arctic, average chlorpyrifos concentrations were reported as  $0.10 \pm 0.04$  pg/m<sup>3</sup>,  $4.8 \pm 1.3$  pg/L,  $14.4 \pm 2.5$  pg/L,  $14.1 \pm 6.1$  pg/L, and  $10.5 \pm 1.7$  pg/L in air, snow, meltponds, seawater (at 0m depth), seawater (at 5m depth), respectively.

99. Ice cores collected from polar ice sheets at Site M, Dronning Maud Land, East Antarctica (Lat 75.00 S, Long 15.00 E), and Holtedahlfonna, Svalbard (Lat 79.13 N, Long 13.27 E), were analysed for a net deposition of 25 organochlorine pesticides (OCPs) (including chlorpyrifos) and 16 organohalogen (chlorine/bromine) industrial compounds (OHICs). Long-range atmospheric transport delivers contaminants to both sites, but the processes are different: Site M is affected by subsidence of air from the stratosphere to the Antarctic Plateau, while Holtedahlfonna is affected by air moving through the free troposphere. The sample from Site M is a composite core covering 1958–2000, while the Holtedahlfonna sample includes a historic record from 1953 to 2005 in six discrete samples. Chlorpyrifos had the greatest flux of any of the analysed substances, including known POPs such as e.g., DDT, endosulfan, chlordane, hexachlorocyclohexane (HCH), at both sites (Hermanson et al., 2021).

100. The Western Airborne Contaminants Assessment Program (WACAP) (Landers, 2008) undertook an investigation on contaminations of lake sediment cores that provided information on the temporal changes of contaminant loadings in the eight national parks over about the last 150 years. Total chlorpyrifos (sum of chlorpyrifos and chlorpyrifos oxon) was detected in lakes situated in the three Alaskan national 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).

101. With regards to mechanisms of transfer Chernyak et al., (1996) who measured fog, sea water and marine ice in the Bering and Chukchi seas 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 their behaviour in a dissolved state. In this study, as well as in that conducted by Rice & Chernyak (1997) during the same expedition, concentrations of chlorpyrifos in fog were higher than in the air, in the seawater and melting ice (see Table 11 in document UNEP/POPS/POPRC.18/INF/8). The authors stated that chlorpyrifos was enriched in the fogwater, which was explained to be caused by increased solubility of the compound in the fogwater and surface sorption to the fog droplets. Hageman et al., (2006) estimated that deposition of total chlorpyrifos (sum of chlorpyrifos and chlorpyrifos oxon) that accumulated in snow in the Alaskan national parks collected March-April 2003 from WACAP sites amounted to 0.48 to 32 ng/m<sup>2</sup>.

102. Pućko et al., (2015) modelled the input of chlorpyrifos and other chemicals to the Beaufortt Sea via melt ponds based on Henry's Law Constants, exchange dynamics, and air measurements taken during a cruise in 2008 across the Beaufort Sea. Melt ponds occur during summer months as sea ice melts. Melt pond contaminant enrichment can be perceived as a hypothetical 'pump' delivering contaminants from the atmosphere to the ocean under ice-covered conditions. Current use pesticides are expected to present the highest risk of increased exposures through melt pond loading and drainage due to the high ratio of melt pond water to seawater concentration. The model suggested that, in 2008, 16 kg chlorpyrifos was discharged to the Beaufort Sea, in comparison to 6 kg of alpha-endosulfan. Hypothetically, 4% of chlorpyrifos (compared with 10% of alpha-endosulfan) may be expected to annually enter the Beaufort Sea via this route compared to the standing stock in the Polar Mixed Layer of the ocean.

103. 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 found in all samples of oceanic air (n=17; concentrations ranged from 1 to 146 pg/m<sup>3</sup> in the gas phase) and sea water (dissolved concentrations ranged from 0.1 to 111 pg/L). Along with alpha-endosulfan and dicofol it was the most abundant substance of the six current-use pesticides that were investigated in this study. 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.

104. Chlorpyrifos was monitored as part of the Swedish national monitoring program for pesticides from 2002 to 2018 on agricultural sites (Boström, 2020a). In Sweden, chlorpyrifos was never used as plant protection product, but as

indoor biocide in products until 2009. Chlorpyrifos was detected in air (from two sampling sites between 2009 and 2018, detection frequency of over 90% with median concentrations of 0.002 ng/m<sup>3</sup>) and precipitation (four sampling sites between 2002 and 2018, detection frequency 12% to 56% with maximum concentrations ranging between 0.0001 and 0.01015 µg/L, but not 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. Chlorpyrifos was also detected in an 102-m ice core taken from the Lys Glacier (Monte Rosa massif, Italy), and in meltwater samples from six glaciers distributed along the Alpine Arc during the summer of 2016 (Rizzi et al., 2019). The study authors described these measurements as being associated with medium-range atmospheric transport from agricultural areas beneath the Italian Alps, where chlorpyrifos is widely applied.

105. Chlorpyrifos was detected in particulate matter in air at a remote alpine site in the Southern Alps, New Zealand in 2009, with the Canterbury Plains as the likely source region. Chlorpyrifos was one of the most commonly detected pesticides, together with dieldrin, transchlordane and endosulfan (Lavin et al., 2012). This reported movement of chlorpyrifos indicates the potential for chlorpyrifos originating from Australia to be contributing to that from the agricultural areas in New Zealand.

106. Muir et al. (2004) compared their findings of current-use pesticides in remote areas with the predicted atmospheric half-lives and characteristic travel distances (CTDs). Predicted half-lives in air of most current-use pesticides do not exceed the Stockholm criterion for LRTP. The authors discussed that the discrepancy between modelling data and monitoring findings is due to an overestimation of the atmospheric OH radical concentration applied in the model calculations. Furthermore, precipitation scavenging may be overestimated by LRTP models assuming a high ability of current-use pesticides to dissolve in rain droplets. If the atmosphere is sufficiently cold, cloud water and falling hydrometeors will be frozen and have a much smaller capacity to take up water-soluble organic chemicals. Snow may have a considerably lower scavenging efficiency for the vapours of water-soluble pesticides compared to that of rain. Snow may limit the LRTP of these pesticides much less than rain. The accuracy of degradation rates estimated by AOPWIN was discussed as well. Referring to QSAR forming the basis of AOPWIN, “it is expected that the predictions will be more uncertain the more complex the chemical is (i.e., how many functional groups it contains) and especially if the chemical contains halogen atoms and/or N- or S-atoms.” (Atkinson et al. (1999) as cited in Muir et al. (2004)).

107. Additional studies on airborne chlorpyrifos in the particulate phase are available (Lopez et al (2017), Nascimento et al (2017), Wang et al (2018)). Lopez et al (2017) studied the concentration of chlorpyrifos in PM10 particles from a site in Spain and observed values ranging from non-detects up to 210 pg/m<sup>-3</sup> (Lopez et al (2017)). Another study found up to 47.1 pg/m<sup>-3</sup> particulate chlorpyrifos in air samples from Brazil, Nascimento et al (2017). Wang and co-workers observed both site-specific and seasonal variation of particulate chlorpyrifos concentrations in the Great Lakes Regions with median values in the range of 0.04 pg/m<sup>-3</sup> to 0,39 pg/m<sup>-3</sup> (Wang et al 2018).

**Table 12. Monitoring studies in abiotic environmental matrices in remote regions**

Publication	Medium	Time frame	Concentration	Handling of blanks	Comments
<b>Arctic</b>					
Chernyak et al. (1996)	Fog condensate	1993	< 0.9–5 ng/L (n=7)	Blanks analysed as field samples, no chlorpyrifos detected. Detection limits calculated using 3α x blank values. Detection limits are based on volumes which differed for each matrix.	CPY detected in four out of seven samples.
Bering and Chukchi sea	Sea water (0.5–1 m depth)	1993	< 0.84–65 pg/L (n=9)		CPY detected in six out of nine samples.
	Melted ice	1993	170 pg/L (n=1 (composite))		Ice was collected from six locations in the area of the sampling. Only atrazine found in higher concentrations
Rice & Chernyak (1997)	Air Fog	1993	0.76 pg/m <sup>3</sup> (vapour phase) 0.08 pg/m <sup>3</sup> (particle phase) 0.08 ng/l (water phase=fog)	Blanks analysed as field samples, no chlorpyrifos detected. Detection limits as above (same expedition).	The fog and air samples were collected over a three-day period as the expedition vessel was driven over the sampling area.
Garbarino et al. (2002)	Snow	1995/96	Estimated 70–80 ng/L	Laboratory and field blanks analysed, no target compounds detected.	CPY detected in snow at three out of five sampling sites at the Chukchi and Beaufort Seas. The concentration was semi-

Publication	Medium	Time frame	Concentration	Handling of blanks	Comments
					quantitatively estimated using the response for the injection standard (gas chromatography with electron-capture negative ion mass spectrometry (ECNI) was used).
Hermanson et al. (2005)	Svalbard, ice core Austfonna glacier	1972–1990	Max. 16.2 ng/L (representing early – mid-1980s)	Concentrations blank corrected.	One of 8 current-use pesticides with continuous profiles in the core. CPY not found in the surface layer of the core representing the period 1992–1998
Ruggirello et al. (2010)	Svalbardk, ice core Holtedahlfonna glacier	1971–2005	64.8 pg/cm <sup>2</sup> /year (representing input for 1971–1980) Max. 808 pg/cm <sup>2</sup> /year (representing 1995–2005)	Method detection limit (MDL, defined as mean blank value + 3 x SD of blank values)	CPY burden of entire ice core (1953 and 2005): 776 ng, highest of all analytes. CPY only OP current-use pesticide detected continuously, about 34% of total pesticide burden
Hermanson et al. (2020)	Svalbard, snow	2013–2014	16.37–81.66 pg/m <sup>3</sup> /yr, mean=44.03 pg/m <sup>3</sup> /yr (STD 32.46 pg/m <sup>3</sup> /yr)	MDL defined as 3 x SD of blank values. Detection limit (mean) for CPY 0.028 ng/l.	Four samples from four respective sampling sites (glaciers) Concentrations are snow surface flux values
Muir et al. (2004)	Lake water	1998–2001	Mean 0.27 ng/L (< 0.017 ng/L to 1.6 ng/L)		Results for six lakes in the Canadian Artic. CPY detected in one out of six samples. The levels in the seven sub-Arctic lakes were below detection limit
Hageman et al. (2006)	Snow	2003	0.010–0.030 ng/L (detected in > 70 % of samples) %RSD (percent relative standard deviation) =22.5% (as reported in Landers et al. (2008).	On average concentrations found in blanks were 3% of the concentration in snowpacks and the concentration in blanks was subtracted from concentrations found in snow samples. MDL (estimated) 6.9 pg/L (as reported in Landers et al. (2008).	CPY detected at the five sites in the three Alaskan national parks of the Western Airborne Contaminants Assessment Program (WACAP)
Landers et al. (2008)	Lake sediment	2003	Ca. 10 ng/m <sup>2</sup> /yr (detected in > 70 % of samples) Ca. 1 ng/m <sup>2</sup> /yr (detected in 50–70 % of samples) percent relative standard deviation =9.7%	MDL (estimated) 1.2 ng/g dw.	CPY detected in two lakes out of four in the three Alaskan national parks (Landers et al. 2008). The concentration of CPY has been estimated from graphs
Jantunen et al. (2007) (as cited in Hoferkamp et al. (2010)	Air	2007	0.36 to 30.4 pg/m <sup>3</sup>	No further information has been found.	Samples from a 2007 cruise of the Labrador Sea.
Pučko et al. (2015)	Air	2008	mean ± SD 3.1 ± 1.9 pg/m <sup>3</sup>		Samples from a cruise in 2008 across the Beaufort Sea.

Publication	Medium	Time frame	Concentration	Handling of blanks	Comments
Pučko et al. (2015)	Sea water	2008	mean $\pm$ SD 31 $\pm$ 19 pg/L		Same as above.
Pučko et al. (2015)	Melt pond water	2008	mean $\pm$ SD 131 $\pm$ 89 pg/L		Same as above.
Morris et al. 2016,	Seawater (dissolved & particulate phase,	2007, 2008,2010	Dissolved: up to 8.1 pg/L Particle-bound: up to 4.1 pg/L	Field, laboratory (resin) and procedural blanks were employed at each location	Samples from three sites in the Canadian Arctic, not detected in all samples, but detected at all three sites
Balmer et al. (2019)	Air	2006–2009	mean 0.27 ( $\pm$ 1 STD) pg/ m <sup>3</sup> (<MDL–6.8 pg/m <sup>3</sup> )	Results were field and laboratory blank-corrected.	Samples collected at the Canadian High Arctic station of Alert 2006 and 2009. Detection frequency 19 %, n=68.
Zhong et al. (2012)	Air	2010	Mean 13.5 ( $\pm$ 35 STD) pg/m <sup>3</sup> , 1–146 pg/m <sup>3</sup>	CPY was also measured in blanks. The MDL was therefore set at mean blank value added to three times its standard deviation. MDL 0.02 pg/m <sup>3</sup>	Samples taken during an expedition of a Chinese research vessel from East China Sea to the high Arctic. CPY was ubiquitously found in oceanic air and sea water with 100% detection frequencies, n=17
Zhong et al. (2012)	Sea water	2010	Mean 7.7 ( $\pm$ 26 STD) pg/L, 0.1–111 pg/L	MDL 0.06 pg/L	n=18
Pučko et al. (2017)	Snow	2012	mean $\pm$ SD, 4.8 $\pm$ 1.3 pg/L, range 3.5–6.6 pg/L	Was defined as mean laboratory blank + 3 times the standard deviation.	Resolute Passage of the Canadian Arctic. Detection frequency: > 50% of the samples in all media. n=4
Pučko et al. (2017)	Melt pond water	2012	mean $\pm$ SD, 14.4 $\pm$ 2.5 pg/L, range 11.3–17.9 pg/L	Same as above.	Resolute Passage of the Canadian Arctic. n=5
Pučko et al. (2017)	Sea water	2012	Depth 0m: mean $\pm$ SD, 14.1 $\pm$ 6.0 pg/L, range 8.3-23.2 pg/L Depth 5m: 10.5 $\pm$ 1.7 pg/L, range 9.1-12.6 pg/L	Same as above.	Resolute Passage of the Canadian Arctic. n=5 per depth (0 m and 5m)
Pučko et al. (2017)	Air	2012	mean $\pm$ SD, 0.10 $\pm$ 0.04 pg/m <sup>3</sup> , range n.d–0.14 pg/m <sup>3</sup>	Same as above.	n=9 Detected in seven out of nine samples.
Jantunen et al. (2015)	Air	2007, 2008, 2010, 2011 and 2013	mean $\pm$ SD, 1.1 $\pm$ 1.3 pg/m <sup>3</sup>	No chlorpyrifos measured in blanks, instrumental detection limits 0.02 pg/m <sup>3</sup> and 0.1 pg/L.	Detection frequency across all years was 85%. Sampling cruises in the Canadian Arctic Archipelago in the years 2007, 2008, 2010, 2011 and 2013 (same for below).
Jantunen et al. (2015)	Water	2007, 2008, 2010, 2011 and 2013	mean $\pm$ SD, 13 $\pm$ 12 pg/L	No chlorpyrifos measured in blanks, instrumental detection limits 0.02 pg/m <sup>3</sup> and 0.1 pg/L.	Detection frequency across all years was 95%, endosulfan detected more often (97 %), but lower concentrations (3.1 $\pm$ 1.9 pg/L)
Bigot et al. (2017)	Sea ice melt water Arctic	2015	5.2–12.0 pg/L	MDL=3.8 pg/L	Northeast Greenland
Bigot et al. (2017)	Sea water Arctic	2015	0.74–1.0 pg/L	MDL=0.44 pg/L	

Publication	Medium	Time frame	Concentration	Handling of blanks	Comments
Bigot et al. (2017)	Snow melt water Arctic	2015	6.2–11.5 pg/L	MDL=3.0 pg/L	
<b>Antartica</b>					
Bigot et al. (2017)	sea water	2015	< MDL	MDL=0.91 pg/L	n=4, CPY detected in one out of four samples
Bigot et al. (2017)	snow meltwater	2015	< 6.8 pg/L	MDL=6.8 pg/L	n=3, all below MDL, detected in all three samples.
Bigot et al. (2017)	sea-ice meltwater (Antarctica)	2015	< MDL–7.3 pg/L	MDL=5.2 pg/L	n=4 Detected in three out of four samples, 2 samples below MDL.
Bigot et al. (2017)	Air (Antarctica)	2015	4.1– 16.8 pg/m <sup>3</sup>	MDL=0.11	n=4. All samples below instrument limits of detection estimated for each individual sample.
<b>Tibetan plateau</b>					
Yong Sun et al. (2018)	Tibetan plateau, China, dated lake sediment cores	1950 - 2015	< MDL – 25.6 pg/g < MDL – 18.6 pg/g,	MDL = 0.4 pg/g	Levels of chlorpyrifos around one order of magnitude lower than legacy POPs (DDTs and HCHs), detection frequency 76.7 – 94.9 %
<b>Swedish region</b>					
Boström (2020)	Air	2009–2018	Median concentrations of 1 pg/m <sup>3</sup> .	No information.	Detection frequency of over 90%. Samples from two sampling sites of the Swedish national monitoring program for pesticides.
Boström (2020)	Precipitation	2002–2018	Max. concentrations between 100 and 10150 pg/L.	No information.	Detection frequency between 12–56 %. Samples from four sampling sites.
<b>Italian Alps</b>					
(Rizzi et al., 2019).	Dated ice chips, Lys Glacier	1990-2002	1110 - 5500 pg/L		Only terbuthylazine and chlorpyrifos detected in all samples, 5 other pesticides <MDL
(Rizzi et al., 2019).	Glacial meltwater, 6 glaciers	2016	1900 - 70.300 pg/L, 25 – 100 % of pesticides measured	Results have been corrected for blanks.	Detected in all samples as predominant substance of the 7 pesticides measured
<b>Southern Alps, New Zealand</b>					
Lavin et al., 2012	Air	2009	Max concentraton 12 pg/ m <sup>3</sup> (range as interpreted from a graph ( 0 - 12 pg/ m <sup>3</sup> ))	Results have been corrected for field blanks.	The Canterbury Plains was identified as the likely source region. Chlorpyrifos was one of the most commonly detected pesticides, together with dieldrin, <i>trans</i> -chlordane and endosulfan.

### 7.3 Monitoring in biotic compartments of remote regions

108. Within the WACAP the contamination of the vegetation was investigated 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. The mean level of total chlorpyrifos in two-year-old conifer needles from Sitka spruce 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 et al., 2008).

109. WACAP also undertook fish monitoring which 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 a second lake in the Denali National Park (Hoferkamp et al., 2010 and Landers et al. 2008). Fish of similar age and sex distributions were collected. Since levels of current-use pesticides in fish were not available in tabular form Hoferkamp et al., (2010) reported levels approximated from graphical illustrations. Total chlorpyrifos levels ranged from 0.041 to 0.1 ng/g wet weight among the four lakes. Pesticide deposition in the Alaska parks is attributed to long-range trans-Pacific transport, because there are no significant regional pesticide sources nearby.

110. A study from Norway included analyses of chlorpyrifos in several Arctic species like fish, seabirds, seabird eggs, 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 in a total of 59 samples of fish, seabirds, seabird eggs, and seals.

111. Feathers of blackbrowed albatross (*Thalassarche melanophris*) and Cape petrels (*Daption capense*) were sampled on the Patagonian Shelf of Argentina during the winter of 2011 (Adrogué et al., 2019). Chlorpyrifos showed the highest concentrations of all substances analysed with  $58.64 \pm 27.31$  ng/g feather in male and  $49.56 \pm 18.45$  ng/g in female Albatross and  $84.88 \pm 50.57$  ng/g for male petrels and  $75.98 \pm 47.97$  ng/g for female petrels. The study described that the presence of chlorpyrifos in bird feathers may reflect recent exposures, given that chlorpyrifos was the main insecticide used in the region, including Argentinean, Uruguayan, and Brazilian markets for soybean, wheat, and corn crops.

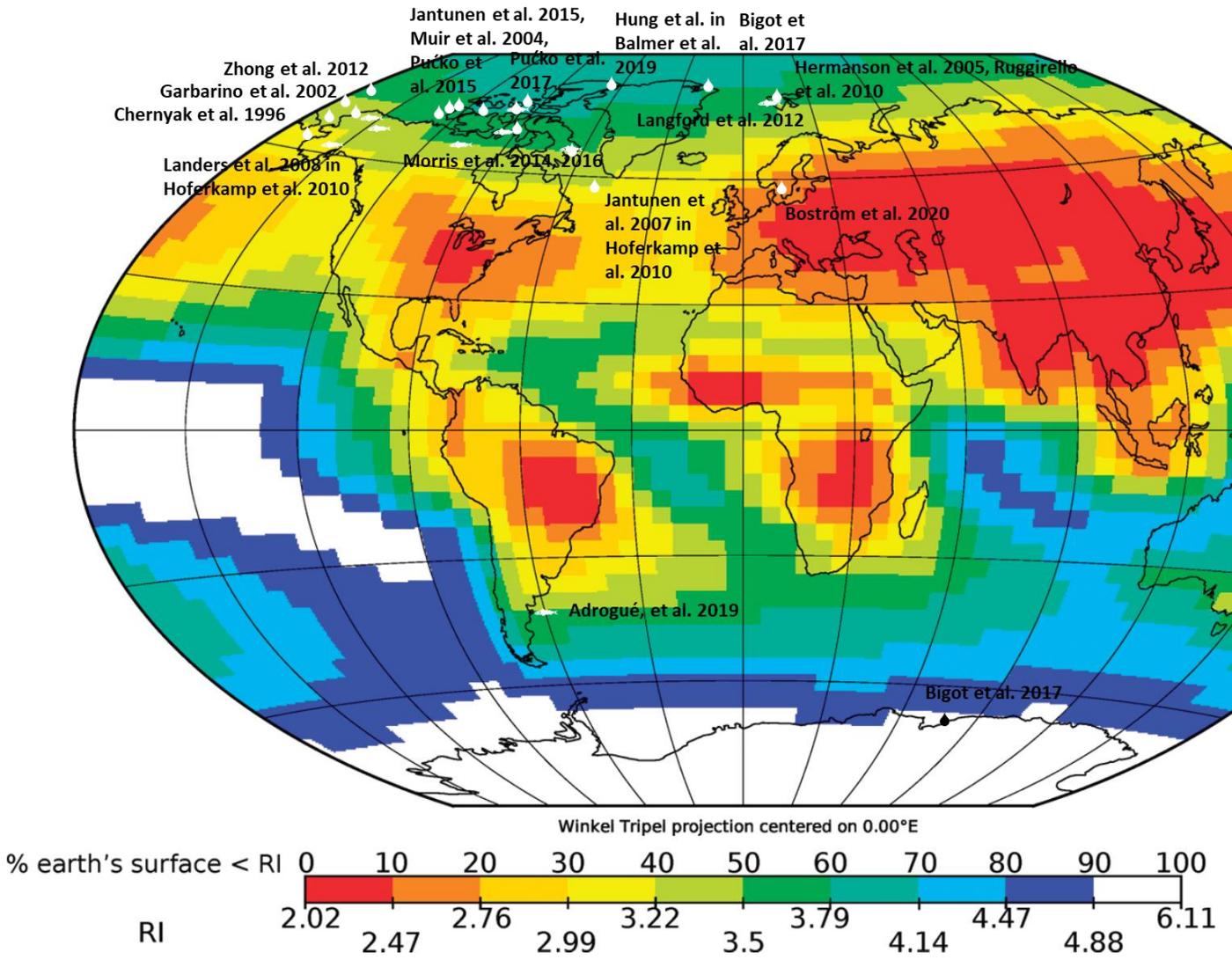
112. Morris et al., (2014) detected chlorpyrifos in the Canadian Arctic Archipelago in vegetation and mushrooms up to  $0.85 \pm 0.52$  ng/g lw. Additionally, chlorpyrifos was detected above the MDL in five of six samples of caribou muscle tissue at a mean lipid normalized concentration of  $0.40 \pm 0.16$  ng/g lw and in one of seven samples of wolf liver at  $0.06 \pm 0.033$  ng/g lw (Morris et al., (2014)). Because recoveries of chlorpyrifos were smaller than those of other current use pesticides (CUPs;  $52 \pm 17\%$ ), these data have a greater degree of uncertainty.

113. Chlorpyrifos was detected in seals and polar bears in the same region by Morris et al., (2016). 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  $52 \pm 17\%$ . 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 three 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 for eight samples. 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. (Morris et al., (2016)).

114. Chlorpyrifos was detected in all muscle and liver samples (n=41) of polar cod sampled in and outside Bessel Fjord (NE Greenland) (Spataro et al., 2021).

115. Figure 2 below has been taken from von Waldow et al. (2010) and modified by the drafters of this dossier to present chlorpyrifos findings in remote areas. The remoteness index expresses the effective distance of a given location on the earth's surface from the regions where environmental contaminants are typically released. The generic emission scenario for pesticides is used as a proxy emission scenario that does not refer to a particular chemical but describes the spatial distribution of potential pesticide emissions.

Figure 2. Map of chlorpyrifos findings in remote areas modified after von Waldow et al. 2010, using the generic emission scenario for pesticides (CROP); fish symbols indicate finding in biota, drop symbol indicate abiotic findings



## 8. Exposure

### 8.1 Environmental exposure

116. Chlorpyrifos has been detected globally, in all continents and in all compartments, including air, freshwater, saltwater, rain, snow, sea ice and biota, both in regions close to application areas and in remote locations.

Concentrations of chlorpyrifos were found in the air in North America as reported in several studies. In Ontario, Canada, between 2003 and 2005, passive air samplers were located at three sites in southwestern Ontario and also at two sites in non-agricultural areas just north of Lake Huron and Lake Superior. Chlorpyrifos was found in air samples at concentrations of  $< 0.0003$  to  $0.06 \text{ ng/m}^3$ , with a median value of  $0.007 \text{ ng/m}^3$  and 73% frequency of detection ( $n=11$ ) (Kurt-Karakus et al., 2011). Between 2004 and 2005 in 8 sites (including six agricultural sites, one receptor site, and one urban site) in Canada, chlorpyrifos was found at concentrations  $0.08$  to  $22 \text{ pg/m}^3$  in the air in areas of application and distant areas (Yao et al., 2008). At urban, rural, and suburban sites in the eastern part of the U.S. state of Iowa (one of the most intensively agricultural parts of the world, with  $\sim 90\%$  of the total land area dedicated to farming), chlorpyrifos was detected at an average concentration of  $1 \text{ ng/m}^3$  with 19% frequency of detection (Peck and Hornbuckle, 2005). In the Chesapeake Bay, USA, in 2000, chlorpyrifos concentrations of  $0.015$  to  $0.670 \text{ ng/m}^3$  were found with median value of  $0.11 \text{ ng/m}^3$  and an 87% frequency of detection in the air sampled at a single location in the watershed that is dominated by agricultural land use (Kuang et al., 2003).

117. California Department of Pesticide Regulation's Air Monitoring Network (AMN) detected chlorpyrifos in 244 of 923 samples taken between 2011-2016 (AMN 2018). The air samples, taken at three sites in major agricultural areas in California, USA ranged from  $3.95$ - $152 \text{ ng/m}^3$ , with a maximum 24-hour concentration at one site in 2013 of  $422.5 \text{ ng/m}^3$ . AMN sampling conducted in 2019 at eight sites found chlorpyrifos in five of 406 samples (AMN 2020). California announced the cancellation of almost all agricultural uses of chlorpyrifos in October 2019 (CDPR 2019).

118. In Canada, chlorpyrifos was measured in the atmosphere in Western Canada agricultural regions. At Bratt's Lake in Saskatchewan in the Canadian Prairies, chlorpyrifos was detected at concentrations of  $10$  to  $100 \text{ ng/m}^3$  with 3 concentrations exceeding  $100 \text{ ng/m}^3$  and a maximum of  $250 \text{ ng/m}^3$  for a 4-day sample in July and August 2003 before lowering to a maximum value of  $1.38 \text{ ng/m}^3$  in 2005. These chlorpyrifos measurements were related to its usage for grasshopper control in the province. During other seasons, chlorpyrifos was detected at concentrations of  $< 10 \text{ ng/m}^3$ . Tests of selected samples with high chlorpyrifos concentrations in the gas phase showed below MDL in the particle phase. In addition, only one of concentrations of values more than  $0.25 \text{ ng/m}^3$  but less than  $0.26 \text{ ng/m}^3$  were found and others were less than  $0.06 \text{ ng/m}^3$  in 2004 and 2005 in Abbotsford area, British Columbia (Raina et al., 2010). In 2003, Gouin et al., (2008) measured chlorpyrifos air concentrations along an urban-agricultural-forested gradient extending  $700 \text{ km}$  north from Toronto, Ontario. Air concentrations range between  $3.2$  and  $2700 \text{ pg/m}^3$  at the agricultural sites, and between  $0.3$  to  $7.6 \text{ pg/m}^3$  in forested areas located on the Precambrian Shield, a region with limited agricultural activity; all samples were collected during the growing season (i.e April-September) and were typically below the instrument quantification limit during the non-growing season. Air concentrations of currently used pesticides were measured at the Canadian High Arctic station of Alert (Nunavut) between 2006 and 2009 and the mean value of chlorpyrifos was  $0.39 \text{ pg/m}^3$  with values ranging from below detection limit to  $7.2 \text{ pg/m}^3$  (Hung et al., 2013). Chlorpyrifos was measured during five separate campaigns that sampled the Canadian Archipelago repeatedly. Mean concentrations of chlorpyrifos in air sampled between 2007 and 2013 ranged from  $0.17$  to  $2.4 \text{ pg/m}^3$  (Jantinen et al., 2015). The concentration range of chlorpyrifos in Arctic air and seawater measured during an oceanographic cruise from the North Pacific to the Arctic Ocean in 2010 was  $0.5$  to  $2 \text{ pg/m}^3$  in the air and  $0.08$  to  $0.85 \text{ pg/L}$  in seawater (Zhong et al., 2012).

119. Concentrations of chlorpyrifos have also been detected in precipitation and snow in North America. In Chesapeake Bay, USA, in 2000, chlorpyrifos concentrations were detected in the rain sampled at a single location in a watershed that is dominated by agricultural land use; values ranged between  $0.97$  and  $29 \text{ ng/L}$  and an average of  $4.8 \text{ ng/L}$ , with 14% frequency of detection (Kuang et al., 2003). Between 2000 and 2003, chlorpyrifos concentration in the rain collected during the main agricultural season at a rural location on the Delmarva Peninsula (in the Delaware and Maryland areas, USA) ranged between  $0.4$  and  $180 \text{ ng/L}$  with yearly average values ranging between  $1.0$  to  $4.5 \text{ ng/L}$  and 39% frequency of detection (Goel et al, 2005). With regard to seasonal snowpack concentrations, in 2003, total chlorpyrifos (the sum of chlorpyrifos and chlorpyrifos oxon) was found in two lakes in Sequoia National Park, USA, in March 2005, with average values in the first lake of  $2.8$  (before a snow event) and  $3.2 \text{ ng/L}$  (after a snow event), and  $1.3 \text{ ng/L}$  in the second lake; the average values in the other five parks were less than  $0.052 \text{ ng/L}$  (Hageman et al., 2006).

120. In Ontario, Canada, rain samples were collected at three sites in southwestern Ontario and also at two sites in non-agricultural areas just north of Lake Huron and Lake Superior. Between 2003 and 2005, chlorpyrifos was detected in rain with concentrations ranging between  $< 0.0042$  and  $43 \text{ ng/L}$  with a median value of  $0.76 \text{ ng/L}$  and 80% frequency of detection ( $n=51$ ) (Kurt-Karakus et al., 2011).

121. In the southern Sierra Nevada -mountains in California, USA, chlorpyrifos was found at concentrations less than  $0.07 \text{ ng/L}$  in four alpine lakes sampled in 2003 that were  $46$ - $83 \text{ km}$  from the nearest pesticide sources in the

intensively cultivated San Joaquin Valley (Bradford et al., 2010). In Ontario, Canada, it was found at concentrations ranging from less than 0.002 to 0.5 ng/L with a frequency of detection of 77% and a median value of 0.02 ng/L (n=164) (Kurt-Karakus et al., 2011). Chlorpyrifos was also detected in Chesapeake Bay, USA, in 2000, concentration of one site at ranging between 0.51 and 4.6 ng/L, the concentrations of other six sites were lower than the detection limit (Kuang et al., 2003). Moreover, in Australia, since 2006, Murrumbidgee Irrigation reported chlorpyrifos levels above the limit of detection but below the aquatic NOEC of 0.1 µg/L in surface water samples, with the exception of one sample (0.1 µg/L) and two samples in 2013 (0.138 and 0.250 µg/L). Likewise, Colleambally Irrigation reported water concentrations of chlorpyrifos below the limit of detection, with the exception of two samples in 2015 (< 0.20 µg/L) and one sample in 2006 (30 µg/L) (The Australian Pesticides and Veterinary Medicines Authority, 2019). A monitoring programme in the Niagara fruit belt, Canada, detected chlorpyrifos in 12 of 76 surface water samples with concentrations up to 0.417 µg/L, during the period of chlorpyrifos application (Struger, 2000). The results from a Norwegian screening programme from 2017 have shown that chlorpyrifos was detected with an average concentration of 0.30 ng/L and detection frequency of 83% in the effluent samples from one of the wastewater treatment plants in Tromsø, which is an urban area in Northern Norway. Chlorpyrifos was otherwise not detected in air, bird, polar bear, or mink sampled in the Arctic in Norway in 2017, or in common gulls sampled in the urban area (Schlabach et al., 2018). Chlorpyrifos was found during grab water sampling of agricultural streams in New Zealand at a maximum concentration of 180 ng/L (which measured in a site that was surrounded by dairy/beef/sheep pasture), higher than any other pesticide. Two out of 36 sites levels were above the NOEC values for fish, and in several other cases close to the New Zealand Environmental Exposure Limits (Hageman et al., 2019).

122. In Canada, between 2001 and 2017, around 7786 water samples were analysed; chlorpyrifos was detected in 841 samples (11% detection) with a maximum concentration of 44 µg a.i./L. This could be broken down to several regions (Health Canada Pest Management Regulatory Agency, 2019):

- Atlantic Region (2003, 2009, 2014–2015): 103 samples, detected in 3 with a maximum concentration of 0.09 µg a.i./L.
- Quebec (2002–2017): 2819 samples, detected in 387, with a maximum concentration of 44 µg a.i./L;
- Ontario (2002–2015): 1435 samples, detected in 289, with a maximum concentration of 0.52 µg a.i./L;
- Manitoba (2001–2015): 928 samples, detected in 1, with a maximum concentration of 0.02 µg a.i./L;
- Saskatchewan (2000–2011): 449 samples, detected in 1, with a maximum concentration of 0.96 µg a.i./L;
- Alberta (2000–2005): 1701 samples, detected in 2, with a maximum concentration of 0.005 µg a.i./L;
- British Columbia (2004–2014): 454 samples, detected in 161, with a maximum concentration of 1.1 µg a.i./L.

In Sweden, data from the Swedish national monitoring programme from 2002–2018 include 4,114 measurements where chlorpyrifos has been analysed. Including air, precipitation, surface water, ground water and sediments, the substance was detected 359 times. The monitoring programme for pesticides is focused on agricultural areas and includes surface water, groundwater and sediment sampling. Chlorpyrifos has almost exclusively been detected in precipitation and air samples but also in flow proportional surface water samples on four occasions, three of them at 0.0002 µg/L and one at 0.0001 µg/L. Chlorpyrifos' concentrations in precipitation are higher in the very south of Sweden, closer to continental Europe, than at the sampling point further north (Boström, 2020b).

123. Chlorpyrifos was reported in the list of pesticides designated as priority substances in 2001 and listed with an environmental quality standard (EQS) in 2008 (Environmental Quality Standards Directive 2008/105/EC) for surface water bodies in Europe. The annual average EQS (AA-EQS) for surface water is 0.03 µg/L and the maximum allowable concentration (MAC-EQS) is 0.1 µg/L according to Directive 2013/39/EU. These values are currently under revision and will be lowered. In 2018, 8 EU Member States had incidences of exceedance, covering a total of 70 water bodies. Also, 7 EU Member States (Belgium, Spain, Italy, France, Czechia, Cyprus and Germany) failed to achieve good status for chlorpyrifos levels, covering a total of 66 surface water bodies. In regard to groundwater, only one country, Spain, (for two water bodies) exceeded EQS levels in the 2nd RBMPs. In Austria, in 2018, chlorpyrifos was found at concentrations of 0.018 µg/L in surface water ([EEA Report No 7/2018](#)).

124. Chlorpyrifos was detected in 204 276 river and lake samples (8.6% quantified samples) from 6 002 sites in 23 Member States (UK included) for the period 2006–2019 (LOQ is 0.00003–10 µg/L), and in 5 439 coastal and transitional surface water samples (4.2% quantified samples) from 364 sites in 9 Member States (UK included) for the period 2008–2019 (LOQs is 0.0001–0.5 µg/L) (WISE database 2021, European Environment Agency) (In groundwater, chlorpyrifos was detected in 97 896 samples (5.1% quantified samples) from 10 509 sites in 14 Member States (UK included) for the period 2006–2019 (LOQs is 0.0004–2 µg/L).

125. In the Pilot Project for monitoring pesticide residues in environmental matrices conducted by the Brazilian Institute of Environment and Natural Resources (IBAMA) from 2017 to 2020, chlorpyrifos was detected in 11 surface water samples and was quantified in 10 samples at concentrations ranging from 0.008 to 0.071 µg/L.

## 8.2 Human exposure

126. The results from the Norwegian pesticide residues monitoring programme have shown maximum residue level (MRL) exceedances for chlorpyrifos in various food commodities. For 2021 residues of chlorpyrifos were found above the MRL (0.01 mg/kg) in oranges from Egypt at 0.034 mg/kg, in parsley from Laos at 0.064 and 0.95 mg/kg, in dried beans from Madagascar at 0.028 mg/kg, in organic sesame seeds from India at 0.043 mg/kg, and in wheat flour at 0.024 and 0.19 mg/kg, from United Arab Emirates and India, respectively. For 2020 residues of chlorpyrifos were found above the MRL (0.01 mg/kg) in dried beans at 0.1 mg/kg and 0.14 mg/kg, from Madagascar and Turkey, respectively. For 2019 residues of chlorpyrifos were found above the MRL (0.02 mg/kg) in coriander leaves from Laos at 0.29 mg/kg, while for 2018 they were found above the MRL (0.01 mg/kg) in pears from China at 0.033 mg/kg and in table grapes from Chile at 0.029 mg/kg. Furthermore, it has been reported in 2018 that one sample of organic lime from Colombia contained chlorpyrifos (Mattilsynet, 2019, 2020, 2021, 2022).

127. In the Norwegian screening programme from 2019, chlorpyrifos was found in 16 of 58 of house dust samples from private homes at the levels ranging from < 3.0 to 1300 µg/kg dw; all samples but one were < 72 µg/kg dw (Henninge 2020).

128. In Colombia, chlorpyrifos, among many other pesticides, was tested in 24 samples of potatoes, tamarillos, goldenberries, tomatoes and sugarcane each, only to be found once in potato at 5.27×10<sup>-3</sup>mg/kg. Chlorpyrifos was also tested in about 160 samples of raw cow's milk, and found in 31.6% of them, in concentrations between 0.001 and 0.179 mg/kg (Mesa et al., 2013; Restrepo et al., 2014). The study notes that "The presence of this pollutant does not represent a risk in the milk consumer's health, as its concentration is considerably lower than the EPA reference dose; nevertheless, its presence needs to be controlled."

129. Shaker and Elsharkawy (2015) detected chlorpyrifos in raw buffalo milk samples offered for sale in the Egyptian city of Assiut in 2013. The compound was found in 5 of 15 samples collected from vendors in three areas of Assiut city. The average concentration was 3.01 ± 1.0 mg/kg in milk from the north area; chlorpyrifos was not measured in samples collected from the middle and south areas of the city. All measured values significantly exceeded the maximum residue level of 0.01 mg/kg set by the European Commission (EC, 2008) for chlorpyrifos. Contaminated feed, grass or corn silage, and direct application on dairy cattle were assumed as the main sources of the chlorpyrifos residues in milk.

130. 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.

131. Urine is the most common matrix used for biological monitoring of OP insecticide exposure in humans (Barr and Angerer, 2006). In the case of chlorpyrifos, levels of the metabolite 3,5,6-trichloro-2-pyridinol (TCP) have frequently been used as a biomarker of exposure to chlorpyrifos (see Andersen, 2019; Bevan et al., 20179). The vast majority of reported monitoring data in humans has been from studies analysing urine samples (Albers et al., 2004; Atabila et al., 2018; Dalsager et al., 2018; Ismail et al., 2021; Koch and Angerer, 2001; Paglia et al., 2021; Phung et al., 2012; Wang et al., 2016; Ye et al., 2008; Ye et al., 2009). Other studies investigate chlorpyrifos concentrations in blood samples or breast milk.

132. 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. Chen et al., (2014) found chlorpyrifos in 100% of 10 samples each of breast milk, cow's milk and infant formula in the USA. Different brands of cow milk and powdered baby formula were selected based on availability in local grocery stores in Atlanta, Georgia; human milk samples were manually expressed and collected in 2010-2011 from local volunteers.

133. 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 the samples with mean and median values of 84.1 ± 355.4 and 1664.2 ng/g lw, respectively, when only positive samples are considered. 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 out of 53 samples exceeded the ADI/PTDI of 0–0.001 mg/kg bw set by FAO/WHO, which equals the acceptable daily intake for infants set by EFSA (2014) at 0.001 mg/kg bw. There are considerable uncertainties for dose-response relationship concerning neurodevelopmental effects (US EPA, 2020b, EFSA, 2019) and the ADI by EFSA is considered outdated because no reference values could be set also based on the unclear genotoxicity potential (EFSA, 2019).

134. 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/L. Here, all samples tested positive for chlorpyrifos with a mean value  $\pm$  SE of  $0.230 \pm 0.024$  mg/L and a range between 0.085 and 0.355 mg/L. Assuming the consumption of 500 mL of milk daily, exposure was calculated to exceed the WHO acceptable daily intake of 0.01 mg/kg bw for an infant by a factor of 4.1.
135. In a 2017 study conducted by Brahmnd et al., (2019) in Iran, breast milk and urine were examined in mothers and their infants under six months to determine chlorpyrifos and metabolite concentration levels. The samples (n=61) were taken from the households between August and November 2017. The mean concentration of chlorpyrifos in mother's breast milk samples was  $1.3 \pm 0.6$   $\mu$ g/L. The mean concentration of chlorpyrifos metabolite in mothers' and infants' urine was found to be  $2.1 \pm 1.4$  and  $1.4 \pm 0.7$   $\mu$ g/L, respectively.
136. Another study was conducted in Thailand in 2016 by Naksen et al., (2016) to examine pesticide residues in human plasma and breast milk. Samples were collected from 63 individuals, breastfeeding farmworkers (n=33) and their spouses (n=30). The LOD was set at 0.18 ng mL for chlorpyrifos. The concentration levels in the plasma samples had a range of < LOD to 0.66 ng/mL with a median value of < LOD, while the concentration levels in milk samples had a range of < LOD to 0.46 ng/mL, with a median value of 0.1 ng/mL.
137. In a study by Casey (2005), a total of 26 breast milk samples, 52 plasma samples and 52 saliva samples were collected to examine the chlorpyrifos concentrations. The plasma and saliva samples each were put into two groups, namely, 26 non-lactating, and 26 lactating. The mean concentration of chlorpyrifos in 25 of 26 breast milk sample was  $1.10 \pm 0.503$  ppb, and when above LOD set at 0.1 ppb, the range was 0.32 to 2.29 ppb. For the lactating group, the mean concentration of chlorpyrifos in 19 of 26 plasma was  $0.186 \pm 0.299$  ppb, and when above LOD, the range was 0.066 to 0.972 ppb. In the non-lactating group, the mean concentration of chlorpyrifos all in plasma but three sample was  $0.149 \pm 0.111$  ppb, and when above LOD, the range was 0.20 to 0.395 ppb. Meanwhile, sixteen of the saliva samples were positive for chlorpyrifos with a mean of  $0.044 \pm 0.061$ , and when above LOD, the range was 0.008 to 0.230 ppb.
138. In another study by Hartle et al., (2018), breast milk from 21 women who voluntarily donated their milk in 2015 to the Mothers' Milk Bank in San José, California, USA was analysed for chemical contaminants. The concentration of chlorpyrifos found in breast milk had a range of 4.2 to 54.6 pg/g with a median of 20.5 pg/g.
139. A study was conducted, between 1998 and 2001, with a sample of 263 African American and Dominican women living in an urban environment in New York, USA (Perera et al., 2003; Whyatt et al., 2002). Maternal blood (30–35 mL) was collected within 1 day postpartum and umbilical cord blood (30–60 mL) was collected at delivery. Chlorpyrifos was detected in 98% of the maternal blood samples with concentrations of 7.1 pg/g at a mean of  $4.8 \pm 5.5$  pg/g, with an LOD set at 0.5–1 pg/g. Chlorpyrifos was detected in 94% of the cord plasma samples with concentrations of 7.6 pg/g at a mean of  $4.7 \pm 6.5$  pg/g, with LOD set at 0.5–1 pg/g (Perera et al., 2003; Whyatt et al., 2002, 2004). APVMA (Australia, 2017) however, reviewed the study and concluded that the findings are considered inconclusive due to the small sample size, lack of statistical significance and failure to consider the potential impacts of other pesticides on the observed effect on fetal development.
140. In a study by Cui et al., (2005), the capacity of blood proteins to store chlorpyrifos was investigated. It was found that binding to blood proteins decreases the chlorpyrifos concentration in blood plasma which in turn reduces its toxicity. Binding to bovine serum albumin (BSA) was significantly stronger than binding to bovine hemoglobin (BHb). The authors noted that this process of protein binding with toxic insecticides could affect distribution, metabolism, and excretion of insecticides.
141. Diethyl alkyl phosphates (DEAP), which are common metabolites associated with several different organophosphate pesticides, including chlorpyrifos, have been measured in first trimester urine from pregnant Canadian women (n=1884) in the Maternal Infant Research on Environmental Chemicals (MIREC) study. Geometric mean concentration of the specific gravity corrected urinary  $\Sigma$ DEAP was 21 nmol/L (95% CI 20–22 nmol/L), with a 95% percentile value of 86 nmol/L and a maximum concentration of 13666 nmol/L (Sokoloff et al., 2016). These data need to be interpreted with caution, as they cannot be used as a specific indicator of chlorpyrifos exposure. Only two of the six DEAP metabolites are associated with chlorpyrifos. These metabolites, namely diethylphosphate (DEP) and diethylthiophosphate (DETP), are also produced by other OP pesticides (that is, coumaphos, diazinon, phorate and terbufos). In addition, these metabolites, which are generally less toxic than the parent insecticides, may be formed in the environment, including in foods, through breakdown of the parent pesticide. Therefore, it also cannot be distinguished whether the presence of the metabolite in the biomonitoring sample is from exposure to the parent OP pesticide or from direct exposure to the metabolite in the environment.
142. The Canadian Health Measures Survey (CHMS) is an ongoing direct health measures survey launched in 2007 to collect health and wellness data and biological specimens on a nationally representative sample of Canadians. Chlorpyrifos metabolite, 3,5,6-trichloro-2-pyridinol (TCP), also a metabolite of chlorpyrifos-methyl, was measured in the urine of a nationally representative sample of Canadians as part of the CHMS in survey cycles 3 (2012–2013) and 4 (2014–2015). The metabolite was detected in >95% of the general population of Canada aged 3–79 years with a

geometric mean concentration of 1.0 µg/L (95% confidence interval: 0.87–1.2 µg/L; n=2439) in Cycle 3, and 1.4 µg/L (95% confidence interval: 1.2–1.5 µg/L; n=2422) in Cycle 4 (Health Canada, 2017). TCP is also measured as part of a biobank analysis in approximately 2400 samples from CHMS cycle 5 (2016–2017) with results being expected in 2023. Similar to the DEAP metabolites, these data need to be interpreted with caution, as TCP has limitations as a biomarker for chlorpyrifos exposure. TCP is also an environmental degradate of chlorpyrifos and is absorbed and excreted unchanged in human urine. Urinary TCP was originally interpreted as a specific marker of exposure to chlorpyrifos. However, analyses of foods and environmental media demonstrate that the majority of human urinary TCP in the general population likely arises from direct exposure to TCP, which is less toxic than chlorpyrifos, rather than human exposure to chlorpyrifos. Thus, urinary TCP levels are not necessarily meaningful as markers of chlorpyrifos exposure (Health Canada, 2016.)

143. Exposure patterns of chlorpyrifos and other pesticides were investigated in the cohort of Czech adults and children (in urine samples) – CELSPAC-SPECIMEn. Increased levels of chlorpyrifos were found especially in children's samples. Chlorpyrifos metabolite levels were significantly higher in the winter season in comparison to the summer season (Sulc et al., 2022). Effects of chlorpyrifos and other pesticides on DNA methylation (epigenetic markers) and oxidative stress were also investigated in the same population in the Czech Republic. Among others, chlorpyrifos metabolite was found to be associated with higher urinary levels of cytosine methylation biomarkers. These results suggest adverse effects of chlorpyrifos on methylation in human biomonitoring samples (Janos et al., 2023).

## 9. Hazard assessment for endpoint of concern

### 9.1 Hazard assessment for the environment

#### 9.1.1 Hazard assessment for aquatic organisms

144. Chlorpyrifos exposures in aquatic organisms occur primarily through direct uptake from water, although some exposure may result from residues adsorbed on food such as algae, macrophytes and invertebrates, or from ingested sediment particles (Moore et al., 2014). The 50 lethal concentration 50 (LC50) values of 188 species that include bacteria, algae, fish, crustaceans, rotifers and mollusks almost half (45 %) of the ecotoxicological species did not exceed 10 µg/L, showing that CPF is extremely toxic to these aquatic organisms (Huang et al., 2020). CPF is slightly toxic to extremely toxic to freshwater fish, and highly toxic to extremely toxic to marine fish. The main action mechanism of CPF is related to the ability of the metabolite chlorpyrifos oxon to inhibit the enzyme acetylcholinesterase (AChE). Exposure to CPF has generated different effects: neurotoxic in fish (Bernal-Rey et al., 2017; Bonifacio et al., 2017; Banaee et al., 2019), crustaceans (Narra, 2014; Bertrand et al., 2016) and mollusks (Cooper and Bidwell, 2006; Amanullah et al., 2010) by inhibiting the enzyme AChE present in the nervous system of vertebrates and invertebrates (Thompson, 1999). The physiological role of this enzyme is to hydrolyze the neurotransmitter acetylcholine. Inhibition of this enzyme generates accumulation of acetylcholine neurotransmitter in neuromuscular and neuronal synaptic junctions and can alter locomotor behaviour in these organisms. Alterations of antioxidant defenses have been reported in fish, mollusks and amphibians the alteration of antioxidant enzymes superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), which neutralize the increase of reactive oxygen species (ROS) (Stara et al., 2012; Bonifacio et al., 2017). Oxidative stress exposure to CPF can generate a cellular oxide-reduction imbalance between the production of ROS and antioxidant defenses, which all living beings rely on. Different authors have proposed oxidative stress as a nonspecific pathway present in different toxicity scenarios in aquatic organisms exposed to this insecticide. Exposure to this pesticide has generated genotoxicity in algae, mollusks and fish, causing DNA damage. Other authors have reported oxidative damage to lipids in fish and amphibians after exposure to commercial CPF formulations (Huang et al., 2020). Histopathological changes: some studies have reported tissue damage in liver and gills in fish after exposure to low concentrations of CPF (Xing et al., 2012). Alterations in fish of gill structure may affect respiration, osmotic and ionic regulation, and in the liver could affect absorption, storage and secretion (Stalin et al., 2019).

#### 9.1.1 Hazard assessment for terrestrial organisms

145. Chlorpyrifos exposure has been shown to reduce cholinesterase activity in plasma, erythrocytes and brains of laboratory rats (Marty et al., 2012). Risks to young birds are greatest when the main food source is from fields treated with liquid CPF formulations (Solomon et al., 2001). Exposure to CPF can generate different effects on terrestrial species: **neurotoxicants** inhibition of brain cholinesterase enzymes and locomotor damage in rats (Dam et al., 2000; Silva et al., 2020) and nematode (Silva et al., 2020) were reported. In birds, inhibition of the enzyme AChE was reported (Miladinović et al., 2018). **Alterations of antioxidant defenses** in rats the alteration of antioxidant defenses SOD and CAT was observed after one month of exposure to CPF (Nikbin et al., 2020), in birds the increase of ROS, SOD, total glutathione (GSH) was reported (Miladinović et al., 2018). **Oxidative stress:** in birds was observed the

increase of malondialdehyde (MDA) (Miladinović et al., 2018). Some authors reported that 20% of the study population of pregnant women were at risk of chronic health effects after CPF exposure (Taheri et al., 2022). Exposure of CPF at high doses can induce systemic toxicity, such as loss of body weight, decreased food intake, pathology-hepatic, renal and adrenal (US EPA, 2000). Although the acute toxicokinetic and toxicological properties related to CPY-mediated oxon formation and AChE enzyme inhibition have long been known, hundreds of thousands of deaths from exposure to this insecticide per year are still reported in developing countries (Testai et al., 2011).

146. As additional information, toxicity of chlorpyrifos is compared to that of the two POPs endosulfan and lindane in Table 12 below. It can be seen that chlorpyrifos has a higher toxicity to aquatic and terrestrial organisms than endosulfan and lindane and it is also more toxic to mammals.

Table 12: Comparative analysis of the toxicity for chlorpyrifos, endosulfan and lindane.

Comparison of toxicity of chlorpyrifos with endosulfan and lindane				
		Endosulfan	Lindane	Chlorpyrifos
Toxicity to aquatic organisms	Lowest aquatic NOEC (fish)	0.05 µg/L (Knacker et al., 1991)	2.9 µg/L (lindane risk profile)	0.14 µg/L (embryo weight) 0.3 µg/L (lethality) (Goodman et al., 1985b)
	<i>Hyalella azteca</i> 10-days LD <sub>50</sub> <i>Mysidopsis bahia</i> , NOEC (mortality and growth impairment)	.		0.037 µg/L (Brown et al., 1997b) 0.0046 µg/L (Sved, 1993)
Toxicity to mammals	Lowest NOAEL for mammals	0.6 mg/kg bw day rats (Ruckman et al., 1989) dogs (Brunk 1989-1990)	0.8 mg/kg bw day rabbit (lindane risk profile)	0.1 mg/kg bw d (RBC AChE inhibition, two-year chronic toxicity study in dogs and rats, EFSA, 2017)

## 9.2 Hazard assessment for human health

147. Developmental neurotoxicity has been reported in rat and mouse studies, at doses that elicit minimal or no foetal brain AChE inhibition. The developmental neurotoxicity database for chlorpyrifos is evolving and contains several in vivo animal studies that explore effects on the developing nervous system in rodents further detailed later in this section.; however, uncertainty remains with respect to several aspects, including the dose level, timing, and duration of exposure required to produce adverse effects in the developing nervous system, as well as the mode of action underlying these effects

### 9.2.1 Cholinesterase inhibition

148. Coulston et al. in 1972 conducted an intentional chlorpyrifos dosing study in human. Chlorpyrifos was administered in the form of an oral tablet at the doses of 0 (placebo), 0.014, 0.03, 0.1 mg/kg bw/day with food. As result of the study the NOAEL of 0.03 mg/kg bw/day was derive based on the statistically significant difference in plasma ChE activity between the control group and the 0.1 mg/kg bw/day dose group ( $p < 0.05$ ).

149. Sheppard et al. (2020) reanalysed the human study by Coulston (1972) using the original statistical method and modern computational tools and considering limitation of the study. It was suggested by Sheppard et al. that the statistical method used by Coulston 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 suggested a lower NOAEL of 0.014 mg/kg-day, and that use of statistical methods first available in 1982 (available but not used by Coulston) would have shown that even the lowest dose in the study had a significant treatment effect.

150. The study of Coulston et al. (1972) was evaluated also by the APVMA (APVMA, 2019a). The APVMA concluded that the study has numerous deficiencies and therefore is regarded as Klimisch score 3 (i.e not reliable). As a result, the NOEL for this study was considered not sufficiently reliable as a point of departure for the determination of health-based guidance values for chlorpyrifos (as cited in APVMA, 2019a).

151. US EPA used as points of departure for HHRA the PBPK-PD model 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) (US EPA, 2020b). 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 (US EPA, 2020b). 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, 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 US EPA is applying the standard 10X intra-species extrapolation factor for women of childbearing age (US EPA, 2014).

## 9.2.2 Developmental neurotoxicity

### Animal experiments

152. Silva et al. (2017) investigated the effects on complex behaviours (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 (GD) 14–20. Behavioural 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. As a result, the authors set the lowest observed effect level (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 behaviours such as these. The data were presented without reporting individual data, means, or standard deviations. 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 or NOAEL below the reported threshold established for RBC AChE inhibition.

153. The US EPA (2020) and APVMA (2019a) evaluated the study of Silva et al. (2017) and regarded it as of unacceptable quality due to a number of deficiencies related to the study design. The following deficiencies were identified in the study design: lacking information regarding measures taken to control for confounding factors (lighting, noise, transport/room acclimation and handling stress), missing information on thigmotaxis, only male offspring were evaluated, inadequacies of the statistical methods used, insufficiently detailed published study report (US EPA, 2020a). Further, lack of blinding of the observer and/or other techniques to reduce observer bias, lack of assay validation by incorporation of appropriate control groups and lack of historical control data were highlighted (APVMA 2019a). The study of Silva et al. (2017) is due to this fact considered as supportive information only.

154. Gómez-Giménez et al., (2017, and 2018) conducted studies to determine if spatial learning was affected in either sex after prenatal exposure and if hippocampal inflammation was associated with effects on spatial learning. Pregnant Wistar rats (6/dose) were fed chlorpyrifos mixed in sweet jelly from GD 7-GD20 (0, 0.1, 0.3 and 1.0 mg/kg/d). Pups were weaned on PND21 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 the 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 behavioural tests, rats were terminated, and the hippocampus was analysed 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/day led to a LOEL for neuroinflammation of 0.1 mg/kg/d for both males and females.

155. 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 on GD 7 through PND21. The pups, weaned on PND21, 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 assessment. 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.

156. The publications by Gómez-Giménez et al., (2017 and 2018) were considered to be of unacceptable quality by the US EPA (2020a) due to numerous deficiencies in the studies design, and thus have been included only as supportive evidence.

157. Lee et al., (2015) conducted a study to determine if learning and cognitive behaviour was affected by exposure to chlorpyrifos in neonatal test subjects. 60 mouse pups (neonataly exposed to a single oral dose 0.1, 1.0 or 5mg/kg body weight) at doses of 5.0 mg/kg bw. Male NMRI mice were treated by gavage with chlorpyrifos during rapid brain growth and maturation to investigate whether an acute perinatal exposure of 5 mg/kg bw could be associated with behavioural 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 behaviour 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 (brain growth spurt) of CaMKII (calcium calmodulin-dependent protein kinase 11II) may lead to irreversible behavioural effects lasting into adulthood (Lee et al., 2015). The results from the study show that chlorpyrifos induced decreased levels of CaMKII which has a pivotal role in memory and learning, as it is required for hippocampus-dependent memory formation by autophosphorylation mediated by long term potentiation (LTP), regulation of calcium homeostasis and signalling. Consequently, disturbed CaMKII expression may lead to further downstream alterations, such as altered levels of synaptophysin.

158. The study by Lee et al., (2015) was considered acceptable by US EPA but only for qualitatively use due to the several major deficiencies which were identified in the conduct and interpretation of this study. The number of litters and sample size was not identified in the study; information about assessment of the sacrificed female pups for BChE inhibition was unclear; inadequate sample size was used for motor activity assessments, and finally appropriate statistical analysis was not used in the study.

159. Both anxiogenic and anti-anxiogenic responses were observed in some developmental neurotoxicity studies (Carr et al., 2017; Silva et al., 2017), highlighting the possibility that the effects were mutable and possibly toxicologically insignificant. However, the California EPA noted that the anxiogenic behaviour observed by Silva et al., (2017) resulted from gestational exposure, while the anti-anxiogenic behaviour observed by Carr et al., (2017) resulted from postnatal exposure (CalEPA, 2018). For limitations of the Silva [study please see document UNEP/POPS/POPRC.18/INF/8](#). 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.

## Human Studies

160. An additional 28 epidemiological studies have been identified subsequently to the CalEPA review in 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.

161. Epidemiological evidence suggesting associations between chlorpyrifos exposure during neurodevelopment and adverse health effects is derived from three cohort studies conducted by the Columbia Center for Children's Environmental Health (CCCEH), the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) and Mt Sinai Children's Environmental Health centre.

162. In a follow up study, children (n=271) from the same cohort 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 studies include the small sample size, the extent of the cognitive assessment, chlorpyrifos exposure was measured at a single timepoint rather than through longitudinal testing, the lack of information regarding qualifications of researchers administering certain questionnaires, and methodological issues with brain MRI data analysis and methods used for comparing brain images (APVMA 2017).

163. The CHAMACOS project within the UC Berkeley 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 enrolment (Oct 1999–Oct 2000). Bouchard et al., (2011) reported that children 7 years old in the highest quintile of prenatal dialkyl phosphate (DAP) concentrations had 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. Limitations of the study were noted by regulatory authorities (USEPA, 2014; APVMA, 2017). These include the lack of exposure data specific to chlorpyrifos (and reliance on DAP measurements, which is a non-specific metabolite of OP pesticides), which limits the regulatory utility of the CHAMACOS studies, the fact that authors did not discuss the passage of OP across the placental barrier, or how measurement of OP metabolites in the mother's urine relate to in utero exposure, and the

lack of detail provided regarding the techniques used for statistical analyses (USEPA, 2014; APVMA, 2017). Stein et al., (2016) 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 had experienced certain adversities related to their home environments (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.

164. 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).

165. In 2015 US EPA updated a literature review (summarized in US EPA, 2016a). 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). The literature review was subsequently further updated (in the same year) to address public comments and incorporate additional epidemiological papers from the open literature (US EPA, 2016b). Despite differences in study design, with the exception of the Guodong et al., 2012; Oulhote & Bouchard Maryse, 2013 and Engel et al., 2016 studies, all other studies identified adverse neurodevelopmental outcomes associated with OP exposure; these conclusions were across four cohorts and twelve study citations. The US EPA concluded that the 3 US cohort studies (CCCEH, CHAMACOS, and Mt. Sinai) provide the most robust available epidemiological evidence (US EPA, 2016a). However, several limitations and uncertainties associated with the epidemiological studies have been identified as part of Scientific Advisory Panel reviews (FIFRA SAP, 2012; FIFRA SAP, 2016), particularly with respect to the exposure measures.

166. In a cohort of male adolescents from Spain, chlorpyrifos exposure measured by urinary TCPy (3,5,6-trichloro-2-pyridinol) was associated with significant decreases in E2 (estradiol), follicle-stimulating hormone, anti-Mullerian hormone, and an increase in dehydroepiandrosterone sulfate (DHEAS). Carriers of the PON1 (paraoxonase 1) genotype 55MM, had significantly higher increases of free T4 (thyroxine) for detected TCPy Suarez et al., 2021).

167. 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 studies.

168. Ntantu Nkinsa et al., (2020) investigated the impact of organophosphate pesticide (OP) exposure during fetal development on IQ in young Canadian children in the MIREC study described above in section 3.4. Non-specific OP urinary metabolites were measured in urine samples from pregnant Canadian women between 2008-2011. Children were given IQ tests between the ages of 3 and 4 years old. An association between higher DEAP concentrations (common OP metabolites) in maternal urine with lower verbal IQ in males was found (for a 10-fold increase in concentration, -6.28; 95% CIs, -12.13, -0.43). As noted above, these data need to be interpreted with caution, as the urinary metabolites measured in this study cannot be used as a specific indicator of chlorpyrifos exposure.

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