Prioritization of Pesticides for Assessment of Risk to Aquatic Ecosystems in Canada and Identification of Knowledge Gaps

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Abstract Pesticides can enter aquatic environments via direct application, via overspray or drift during application, or by runoff or leaching from fields during rain events, where they can have unintended effects on non-target aquatic biota. As such, Fisheries and Oceans Canada identified a need to prioritize current-use pesticides based on potential risks towards fish, their prey species, and habitats in Canada. A literature review was conducted to: (1) Identify current-use pesticides of concern for Canadian marine and freshwater environments based on use and environmental presence in Canada, (2) Outline current knowledge on the biological effects of the pesticides of concern, and (3) Identify general data gaps specific to biological effects of pesticides on aquatic species. Prioritization was based upon recent sales data, measured concentrations in Canadian aquatic environments between 2000 and 2020, and inherent toxicity as represented by aquatic guideline values. Prioritization identified 55 pesticides for further research nationally. Based on rank, a sub-group of seven were chosen as the top-priority pesticides, including three herbicides (atrazine, diquat, and S-metolachlor), three insecticides (chlorpyrifos, clothianidin, and permethrin), and one fungicide (chlorothalonil). A number of knowledge gaps became apparent through this process, including gaps in our understanding of sub-lethal toxicity, environmental fate, species sensitivity distributions, and/or surface water concentrations for each of the active ingredients reviewed. More generally, we identified a need for more baseline fish and fish habitat data, ongoing environmental monitoring, development of marine and sediment-toxicity benchmarks, improved study design including sufficiently low method detection limits, and collaboration around accessible data reporting and management.

Keywords ECOTOX · Fish · Fungicide · Herbicide · Insecticide · Primary producers

1 Introduction

The very properties of pesticides that make them effective for their registered uses (i.e., those imparting biological activity towards targets) can also pose issues for the wider environment (Johnson et al. 2020). Pesticides can enter aquatic environments via direct application (e.g., for controlling aquatic plants), via overspray or drift during application, or by runoff or leaching from fields during rain events (Breckels and Kilgour 2018; Bartlett et al. 2016; Struger et al. 2016). Registrations for direct use in water tend to be fairly limited, aside from pesticides used specifically for aquaculture, and labels typically instruct the use of buffer zones or other approaches to prevent the entry of pesticides via spray drift, so runoff and leaching poses arguably the biggest challenge for controlling the unintended entry of current-use pesticides into aquatic environments. This is consistent with reported detection rates and concentrations of pesticides that are strongly correlated to season (i.e., application timing), precipitation (i.e., driven by runoff events), pesticide use patterns, and

land use (Fairbairn et al. 2016; Metcalfe et al. 2016; Harris et al. 2008; Baldwin et al. 2016; Rosic et al. 2020; Sanford and Prosser 2020).

Long-term bivalve (Alvarez et al. 2014) and land-locked Arctic char (*Salvelinus alpinus;* Cabrerizo et al. 2018) monitoring studies suggest that concentrations of banned or restricted organic contaminants (e.g., PCBs [polychlorinated biphenyls], organochlorine pesticides) in aquatic environments have decreased over time, resulting in a shift in research focus towards contaminants of emerging concern (CECs), including current-use pesticides. Newer pesticide chemistries tend to be less persistent and bioaccumulative than previous generations of contaminants, as well as less likely to partition into food web-associated lipids (Harris et al. 2008; Alvarez et al. 2014; Daughton and Ternes 1999). For example, in coho salmon (*Oncorhynchus kisutch*) habitat in British Columbia, current-use pesticides were the most prominent active ingredients detected in water and air samples, while sediment and biota samples contained both current-use and legacy pesticides (Harris et al. 2008).

Health Canada's Pest Management Regulatory Agency (PMRA) is responsible for the registration of pesticides in Canada, including the evaluation of potential for human or environmental risks. In order to make (re-)evaluations of the economic benefits and potential environmental and human health risks of particular pesticide ingredients, PMRA requires data pertaining to chemical fate and movement in the environment, toxicity towards non-target receptors, and where available, measured concentrations from environmental media. Although pesticide use data are not collected in Canada, under the *Pest Control Products Act* (S.C. 2002, c. 28; Government of Canada 2002), registrants are required to report annual sales to PMRA (Health Canada 2017, 2020). As such, extrapolations to pesticide use can be made based on the assumptions that all purchased products will be applied in the region in which they were purchased and will be applied within the year of purchase (Government of British Columbia 2015; ECCC 2011).

Over 132 million kilograms of active ingredient (kg a.i.) was sold in Canada in 2017 and over 121 million kilograms in 2018 (the most recent year for which complete data were available at the time of review), comprising >7,400 registered products (Health Canada 2017, 2020) and 658 active ingredients (PMRA 2019a). While sales declined in 2018 relative to the previous year, there was an increasing trend in sales over the preceding 5-year period (Health Canada 2017, 2020). Pesticide use has generally increased over the past 35 years, and this has been attributed to shifts from livestock to food cropping, as well as adoption of no-till or reduced tillage practices, which can increase the need for pesticide use and consequently increase the potential for runoff (Agriculture and Agri-Food Canada 2020; Malaj et al. 2020). The agricultural sector is the greatest user of pesticides (Sheedy et al. 2019; Health Canada 2017) and a relatively small number of active ingredients constitute the majority of pesticides purchased and applied in Canada (Health Canada 2017, 2020; Table S1), though dominant active ingredients can vary by geographical region (Table 1), posing a challenge for determining priorities on a national scale.

As noted by Fairbrother et al. (2019), the identification of research priorities is crucial for government organizations in allocating finite resources in the face of

Table 1 National and provincial pesticide sales for the top ten pesticide active ingredients in each jurisdiction based on the most recently published reports. Note: Manitoba data reflect average use between 1996 and 2006, and Ontario data are use data as opposed to sales

Canada (2017)[a]		Canada (2018)[b]		British Columbia (2015)[c]		Alberta (2013)[d]		Manitoba (1996–2006)[e]		Ontario (2013–2014)[f]		PEI (2014)[g]	
Active ingredient	Kg ai	Active ingredient	Kg ai	Active ingredient	Kg ai	Active ingredient	Kg ai	Active ingredient	Kg ai	Active ingredient	Kg ai	Active ingredient	Kg ai
Glyphosate	>50,000,000	Glyphosate	>25,000,000	Mineral oil	262,513	Glyphosate	8,667,959	Glyphosate	832,651	Glyphosate	2,909,184	Mancozeb	303,957
Available chlorine (as sodium hypochlorite)	>10,000,000	Available chlorine (as sodium hypochlorite)	>10,000,000	Hydrogen peroxide	257,332	MCPA	920,011	MCPA	478,520	Metolachlor	768,804	Chlorothalonil	140,491
Creosote	>5,000,000	Creosote	>5,000,000	Glyphosate	250,505	Glufosinate	694,347	Bromoxynil	191,016	Atrazine	297,603	Mineral oil	140,961
Surfactant blend	>1,000,000	Prothioconazole	>1,000,000	Sulphur	57,875	2,4-D	565,726	Ethalfluralin	169,077	Mancozeb	256,042	Mono and di-potassium phosphite	124,733
Glufosinate ammonium	>500,000	Glufosinate ammonium	>1,000,000	*Bacillus thuringiensis*	48,657	Triallate	367,417	2,4-D	164,929	Chlorothalonil	99,286	Glyphosate	57,696
Borates	>500,000	Bromoxynil	>1,000,000	Diazinon	42,651	Bromoxynil	315,621	Glufosinate ammonium	141,507	Metribuzin	90,922	Metiram	39,535
2,4-D	>500,000	MCPA	>1,000,000	Mineral spirits	40,180	Surfactant blend	299,028	Trifluralin	116,457	Captan	88,851	Phorate	27,557
Mineral oil	>500,000	Surfactant blend	>1,000,000	Chlorothalonil	40,051	Petroleum hydrocarbon blend	215,139	Sethoxydim	96,530	MCPA/MCPB	87,431	Linuron	27,528
Available chlorine (as trichloro-s-triazinetrione)	>500,000	Borates	>1,000,000	Carbon dioxide gas	35,139	Fluroxypyr	156,866	Dichlorprop	91,632	Dimethenamid-P	62,618	Diquat	22,409
Mancozeb	>500,000	2,4-D	>1,000,000	Clodinafop-propargyl	27,687	Methylated canola oil	134,649	Imazamethabenz	68,784	Bromoxynil	60,330	MCPA	18,361
Total herbicides	77,765,728	Total herbicides	66,232,905	Total herbicides	1,175,251	Total herbicides	13,200,340	Total Herbicides	n/a	Total herbicides	4,564,800	Total herbicides	161,568

Total insecticides	4,932,766	Total insecticides	3,836,995	Total insecticides	1,177,716	Total insecticides	200,572	Total insecticides	n/a	Total insecticides	57,500	Total insecticides	190,713
Total fungicides	9,928,052	Total fungicides	13,724, 886	Total fungicides	507,373	Total fungicides	807,883	Total fungicides	n/a	Total fungicides	774,600	Total fungicides	647,644
Total antimicrobials	34,864,449	Total antimicrobials	34,822,207			Total surfactants and adjuvants	1,010,265						
Total vertebrate control	163,405	Total vertebrate control	156,629										
Total other	5,958,314	Total other	3,980,511										

References: [a]Health Canada (2017), [b]Health Canada (2020), [c]Government of British Columbia (2015), [d]Government of Alberta (2015), [e]Wilson (2012), [f]Farm and Food Care Ontario (2015), [g]PEI Environment, Water, and Climate Change (2015)

infinite research questions. With the increasing number of active ingredients registered for use in Canada (PMRA 2017), there is a considerable challenge to balance deepening our understanding of compounds deemed to be of greatest concern with expanding the research to cover a greater proportion of compounds (Johnson et al. 2020).

The specific objectives of this literature review were as follows:

1. To identify those current-use pesticides of potential concern for Canadian marine and freshwater environments;
2. To outline current knowledge on the biological effects with a focus on apical endpoints (i.e., those related to survival, growth, and reproduction), but also with consideration of other sub-lethal effects of the identified pesticides of top concern on aquatic organisms;
3. To identify and review any important data gaps specific to biological effects on aquatic species that became evident during the detailed review of the literature.

Where possible, focus was placed on species that are part of, or contribute to, fisheries, including Indigenous fisheries. Fish are defined broadly under Canada's Fisheries Act (R.S.C., 1985, c, F-14; Government of Canada 1985) including not only fish, but also marine mammals, shellfish, and crustaceans. These species include those accessed as part of fisheries, but also many organisms that act as prey and contribute to habitat structure. Outcomes of this exercise were intended to inform policymakers on current concerns regarding pesticides and Canadian fisheries, and to guide considerations for future research priorities.

2 Methods

2.1 Scope of the Review

The aim of this literature review was to focus on current-use pesticides with the greatest potential to enter aquatic environments via terrestrial runoff and leaching, intentional or incidental overspray, and long-range transport to remote regions (e.g., the Arctic). An emphasis was made on published literature because, although part of the pesticide registration process in most jurisdictions includes submission of data on the fate and effect of pesticides in the environment by the registrant to government regulators, these data are often not publicly available. For all literature searches, emphasis was placed on recent research, particularly peer-reviewed works published since 2016. Active pesticide ingredients detected in the environment but not currently registered for use in Canada by the PMRA (e.g., carbofuran, bendiocarb) were excluded because these are no longer "current-use" and concentrations are expected to continue to decrease over time. Products used as pesticides for which environmental concentrations of their components could not be solely attributed to a pesticide-related application were excluded from this review, including antimicrobials (e.g., available chlorine, hydrogen peroxide), those lacking an explicitly-defined or consistent chemical structure (e.g., surfactant blend, mineral

spirits, mineral oil, creosote, petroleum hydrocarbon blend), and sulphur, carbon dioxide gas, and borates. Drugs used in aquaculture, which are sometimes categorized as pesticides, were additionally deemed out of scope and excluded from the review.

2.2 *Identification of Pesticides of Top Concern for Aquatic Biota*

The first step in determining current-use pesticide active ingredients of top concern for Canadian waters was to construct a long list of candidates based on (1) quantities used and (2) environmental presence of analytes (pesticide active ingredients, their degradates, and/or metabolites). To determine the quantity of use by volume, recent sales numbers were obtained as a proxy, based on the assumption that all products purchased were applied in the same year. Specifically, the top ten active ingredients sold nationally and for each province were determined where sales data were made voluntarily available (see Table 1). To determine environmental concentrations of analytes, a detailed literature search was conducted in February 2020 using various sources including peer-reviewed journal articles, government reports, university theses, and publicly-available databases. Data on concentrations of pesticides in the environment reported in studies were compiled (mean, median, maxima, as available) since availability of raw data tended to be limited and reporting varied among sources (e.g., detection limits, raw data versus summary statistics). Analytes occurring at "high concentrations" in the environment were defined as those within the top ~10% of measured means and/or maximum concentrations of all analytes in the collected dataset. Data were considered from 2000 to the present to account for the cyclical nature of monitoring programs and large number of Canadian water bodies.

The next step in the process was to reduce the long list of candidates and identify those of top priority using a series of criteria: (1) volume of sales in Canada in 2017 or 2018 (as reported by Health Canada 2017, 2020; score based on the greater of the 2 years); (2) mean environmental detection rate, based on available data; (3) mean, 95th percentile, and maximum reported concentration in Canadian surface water between 2000 and present (each as a separate criterion); (4) most conservative Canadian Water Quality Guideline for the Protection of Aquatic Life (CWQG-PAL) (or USEPA guideline, if no CWQG-PAL available); (5) whether the 95th percentile of measured concentrations exceeds the guideline value; (6) ratio of the 95th percentile concentration to the guideline threshold (representative of a hazard ratio), and (7) the registration status in the European Union (according to European Commission 2016). The EU was used as a representative international jurisdiction as their review process tends to be one of the most stringent globally, and represents a large number of member nations (Handford et al. 2015; Bozzini 2017). The USA was not used as there is typically synergy with Canadian regulations. Each active ingredient was then assigned a graded score between 0 and 3 for each of 9 criteria (Table 2). The scores for the guideline value and whether the guideline was exceeded

Table 2 Criteria and scoring matrix for ranking relative priority of pesticide active ingredients, including sales, detection frequency, measured concentrations, inherent toxicity (as indicated by guideline values), and regulatory status in other jurisdictions (i.e., European Union)

Scoring rubric	2017/2018 sales (kg a.i.)	Mean study detection rate (where reported)	Most conservative guideline (µg/L) (weighted x2)	Mean concentration (µg/L)	95th percentile reported concentrations (µg/L)	Max reported concentration (µg/L)	95th percentile exceeded guideline (weighted x2)	Ratio of 95th: guideline	EU Status
3 points	>500,000	≥50%	<1 µg/L	≥1.0 µg/L	≥100 µg/L	>100 µg/L	Yes	>10/ Not monitored	Not approved
2 points	>100,000	<50%/Not monitored	<10 µg/L or none	<1.0 µg/L	<100 µg/L/Not monitored	<100 µg/L/Not monitored	Not monitored	>5	N/A
1 point	>50,000	<10%	<100 µg/L	<0.5 µg/L	<10 µg/L	<10 µg/L	No, but few data	>1	Not approved in EU, but in many European countries
0 points	<50,000	<5%	>100 µg/L	<0.1 µg/L	<1 µg/L	<1 µg/L	No	<1	Approved

were doubled to avoid decisions made with an over-reliance on measured concentrations. As such, a total score of 33 points was possible. A balanced degree of conservatism was imparted by assigning scores of 2 points for situations where data were limited (e.g., compounds not typically monitored or where samples have only been collected in a small number of locations or sampling events). As a final screening step to select the most important top-priority pesticides for detailed review, those active ingredients receiving 23 points or more (averaging over 2/3 on each criterion) were retained as the final list. A state of the science review on biological effects in aquatic biota was conducted for these top-scoring active ingredients, including an assessment of the availability of aquatic toxicity data.

To gather supporting data for this scoring process and state of the science review, peer-reviewed literature key word and Boolean searches were made using the Web of Science and the following keywords: "pesticide*", "herbicide*", "insecticide*", "fungicide*", "aquatic", "freshwater", "marine", "ecosystem", "Arctic", "remote", "Canada", "fish", "invertebrate", "algae", "toxic*", "effect*", and "emerg*". From the search results, abstracts were reviewed as a screening step to deem the article of potential relevance or not based on the objectives of determining environmental presence and effects in aquatic biota. Articles were then read in full, and reference lists reviewed for further useful publications. Additional searches were also made on Government of Canada websites (PMRA, Department of Fisheries and Oceans – DFO, Northern Contaminants Program – NCP, Environment and Climate Change Canada – ECCC) and provincial/territorial government websites. Data were queried from the ECCC National Long-term Water Quality Monitoring database (Government of Canada 2016) to identify pesticides that have been measured/detected by federal programs and those that are not currently monitored in Canadian waters.

To evaluate the current availability of aquatic toxicity data for the final list of top-priority pesticide active ingredients for detailed review, the United States Environmental Protection Agency ECOTOX database (USEPA 2020a) was queried for all effects, all endpoints, for algae, crustaceans, molluscs, insects, other invertebrates, and fish, for all aquatic-only exposures. For quality assurance, data were retained only for studies where concentrations of active ingredient had been measured, as recommended by Hanson et al. (2019a) and Van Der Kraak et al. (2014) in their evaluations of strength and relevance of atrazine studies. Further searches of USEPA and PMRA regulatory documents plus within Web of Science and Google Scholar were performed for each active ingredient in an effort to find any studies that had not been entered into ECOTOX as of March 31, 2020.

The intention of this evaluation approach was to cast a wide net of active ingredients and identify those that are relatively likely to be found in Canadian surface waters (and above guideline values), those that are inherently toxic to aquatic organisms, and those that have been identified in other jurisdictions as posing a potential risk. This approach was consistent with previous work conducted to identify priority pesticides in other countries (Australia: Rosic et al. 2020; UK: Johnson et al. 2020).

It is important to recognize that the prioritization process employed in this study was simple and conservative, as the objective was to prioritize, from a relatively long

list, the pesticides of potential concern for Canadian marine and freshwater environments. This simplistic and conservative approach was necessitated by having limited access to all of the raw data on exposure and effect that have been generated for each pesticide. It is also important to recognize the limitations in each of the criterion used in this prioritization exercise. The quantity of an active ingredient sold in a particular year does not directly relate to the quantity entering aquatic ecosystems and the toxicity of the active ingredient. The criterion related to the measurement of the active ingredient in aquatic ecosystems does bias the prioritization towards active ingredients that are included in monitoring efforts and are appreciably soluble in water. The use of the maximum reported concentration in the environment can give weight to measurements that could be considered outliers. For this reason, the mean and 95th percentile of measured concentrations were also included as criteria. The use of detection of frequency is also problematic because the significance of this criterion is dependent on the temporal and spatial extent of sampling. It is also important to recognize that relatively high concentrations measured in aquatic ecosystems do not justify an active ingredient being considered a priority. Those measured concentrations need to be related to a threshold of toxicity. For this reason, the criterion of the ratio of 95th centile of measured concentrations to the most conservative water quality guideline was included. This criterion relates the level of exposure to the potential level of effect. Consequently, this criterion was also given twice as much weight as the other criteria (Table 2). While each criterion has limitations when used in isolation, the combination of the criteria in priority setting should limit the influence of the bias present in any one criterion (Egeghy et al. 2011; Salvito et al. 2002).

3 Pesticides in the Canadian Aquatic Environment

3.1 National Results and Regional Contexts

In the course of the literature review, increased use of pesticides generally indicated that pressures on water quality would also be expected to increase. The ECCC Water Quality in Canadian Rivers sustainability indicator concluded that water quality was generally lower in areas with high populations and agriculture or forestry pressures (ECCC 2020). A related indicator, the Indicator of the Risk of Water Contamination by Pesticides, declined from 2006 to 2011 as a result of increased pesticide use, indicating increased risk of contamination (Agriculture and Agri-Food Canada 2020). Based on a recent risk assessment for pesticide use in Ontario, adoption of newer chemical formulations has generally resulted in growers applying greater amounts of less hazardous active ingredients because they are also less potent towards targets (Van Eerd 2016). Likewise, pesticide use intensity (kg applied per area of cropland) increased in Alberta from 0.76 kg/ha in 1988 to 1.33 kg/ha in 2013 (Government of Alberta 2015).

The most recent Government of Quebec pesticide sales report suggested that of all pesticide types, herbicides pose the greatest current risk to the environment in that province, consistent with herbicides comprising 69% of active ingredients purchased for agricultural use (Government of Québec 2011, 2017). The five active ingredients deemed to pose the greatest environmental risks in Quebec were atrazine, chlorpyrifos, S-metolachlor, imazethapyr, and chlorimuron-ethyl based on the Quebec pesticide risk indicator, which integrates data related to fate, behaviour, toxicity, and usage patterns (Government of Québec 2017). It was noted in the Quebec Pesticide Strategy 2015–2018 that atrazine and chlorpyrifos accounted for <5% of sales but 20% of environmental risk indicators for the province (Government of Québec 2015).

In Ontario and Quebec, S-metolachlor has been identified as one of the pesticides of greatest risk to environmental receptors in those regions (Van Eerd 2016; Government of Québec 2017; Corsi et al. 2019). The risk assessment by Van Eerd (2016) also identified dimethenamid-P, chlorothalonil, and metribuzin as top active ingredients of potential concern for the environment in Ontario based on Environmental Impact Quotients (EIQs) calculated using the method developed by Kovach et al. (1992). This approach integrates toxicity data for human health, fish, birds, bees, and arthropods, as well as environmental fate data to determine the EIQs, which are then multiplied by application rate (kg a.i.) to determine risk (Van Eerd 2016). Chlorothalonil is applied in large volumes across Canada (>500,000 kg a.i. in 2017 and 2020; Health Canada 2017, 2020) and in Ontario (fifth largest volume pesticide applied in 2013–2014; Farm and Food Care Ontario 2015), and has relatively low toxicity benchmarks for sensitive non-target organisms (Van Eerd 2016). In national surface water monitoring, chlorothalonil was among the top five active ingredients most likely to exceed CCME guideline values, particularly in British Columbia and the Atlantic region (ECCC 2011).

The intensity of pesticide use in farming on Prince Edward Island (PEI) and in the Lower Fraser Valley, British Columbia, is high due to the climates and type of crops grown and as a result, most local water bodies are susceptible to contamination by pesticides (ECCC 2011). Specifically, ECCC (2011) noted that approximately 20% of the land area in PEI is involved in potato production (relatively high pesticide-intensity required compared to other crops under local conditions), and over 40% of pesticides purchased in British Columbia are applied in the Lower Fraser Valley. Likewise, greater than two million kg a.i, were sold in 2013 in the North Saskatchewan River, Battle River, and Red Deer River basins in Alberta, with between 1.5 and two million kg a.i. sold in both the Oldman River and Peace River basins (Government of Alberta 2015). In a survey of southern Alberta watersheds, the most frequently detected pesticides were those that had the highest sales, the greatest solubility in water, and relative stability in the environment; these were namely auxin mimics (2,4-D, dicamba, MCPA, mecoprop, fluroxypyr, and clopyralid; Sheedy et al. 2019). As such, monitoring of fish-bearing habitats for the most commonly purchased pesticides (by sales volume) would be prudent in those regions, especially if species at risk are present.

3.2 Top-Priority Active Ingredients

As noted by Malaj et al. (2019) and Anderson et al. (2015), the lack of centralized tracking of pesticide use and presence in the aquatic environment in Canada presents a challenge in assessing their potential environmental risks. Concentration data were obtained from government databases, provincial and national reports, and peer-reviewed papers for pesticides measured in Canadian waters from 2000 to the present. The details for each of the references used including which pesticides were measured, the sampling location, and in what type of water body were tabulated (Table S2). Contemporary sales information was not available for several provinces, but recent annual reports (within the past 5 years) were obtained for Ontario, Quebec, Prince Edward Island, Alberta, and British Columbia, and average use data were located for Manitoba between 1996 and 2006. The active ingredients constituting the greatest sales by volume for each province are shown in Table 1, along with the national sales data (Health Canada 2017, 2020). Of the top ten active ingredients sold in Canada annually between 2013 and 2018 (i.e., previous three sales reports), six have remained consistent – glyphosate, available chlorine (as sodium hypochlorite), creosote, 2,4-D, surfactant blend, and glufosinate ammonium (Health Canada 2017, 2020; Table 1, Table S1). Several of these were not considered further in the prioritization process as they contained multiple components whose presence in the aquatic environment may not be confidently attributed to pesticide application (i.e., mineral oil, surfactant blend, creosote, and available chlorine).

The environmental concentrations representing the top ~10% of pesticides in Canadian waters were identified from water quality monitoring data as $\geq$0.5 μg/L or 1.0 μg/L for mean and maximum concentrations, respectively. Using the inclusion data described in Sects. 2.1 and 2.2 (i.e., sales data and measured concentrations), a total of 55 pesticide active ingredients were screened into the initial long list for further consideration as potential priorities for Canadian fisheries. Of these, 8 achieved a score of 23 or greater, based on some combination of large sales volumes, frequent detection, low toxicity thresholds, measured concentrations exceeding the most sensitive guideline, and registration status in the EU. These formed a final short list of top-priority pesticides for aquatic environments in Canada. Diazinon was removed from the final list by professional judgement because sales declined sharply from 2017 to 2018 (<50,000 kg a.i. and <5,000 kg a.i., respectively) in response to recent registration reassessment (Health Canada 2017, 2020). Several previous label uses of diazinon were phased out between 2013 and 2016 (PMRA 2013), and reduced concentrations in water would be expected as a result, as was observed in the U.S. following additional label restrictions (USDA 2018 and references therein).

As such, the final list of top-priority active ingredients included a total of seven pesticides: three herbicides (atrazine, diquat, and S-metolachlor), three insecticides (chlorpyrifos, clothianidin, and permethrin), and one fungicide (chlorothalonil). These active ingredients will be reviewed in more detail in the sections below.

Ranked lower than the final list of top-priority active ingredients, were two tiers of active ingredients with scores slightly below the cut-off of 23. Carbaryl, imidacloprid, malathion, mancozeb, metiram, prothioconazole, thiamethoxam, trifluralin, and 2,4-D received scores between 20 and 22 (Table 3). Clodinafop-propargyl, deltamethrin, metribuzin, pyraclostrobin, and sethoxydim received scores between 18 and 19 (Table 3). These active ingredients are worth mentioning as a number of them (e.g., 2,4-D, mancozeb, prothioconazole) are widely used in Canada (Table 1) or are closely related to active ingredients in the top-priority list. For example, thiamethoxam was not in the top-priority list with a score of 22 but it is metabolized into clothianidin (Nauen et al. 2003), which did make the top-priority list. Consequently, consideration should also be given to the risk that these active ingredients with relatively high priority scores could pose to aquatic ecosystems.

3.3 Review of Top-Priority Active Ingredients

Overall, the seven top-priority active ingredients from the current review ranged from practically non-toxic (LC50 >100,000 μg/L) to very highly toxic (LC50 <100 μg/L) towards fish, aquatic invertebrates, and aquatic primary producers under acute exposure scenarios (categories determined according to USEPA 2017a). In terms of data availability on ECOTOX or in the published literature, datasets were typically more complete for freshwater than marine species, though there was considerable variation between active ingredients (Table S3). Generally, those compounds ranking highest in priority had broader data coverage. For example, atrazine had at least one toxicity endpoint from a study with measured exposure concentrations for nearly all acute, chronic, growth/development, and reproduction/population abundance study classes outlined in Table S3. Acute and chronic survival data were available for most active ingredients, but data were sparser for other apical endpoints (i.e., growth, development, and reproduction). Molluscs generally represented the least-studied class of organism, while fish, primary producer, and crustacean datasets were complete for all seven active ingredients for acute exposures. Whiteside et al. (2008) similarly noted the greater availability of fish and crustacean data for agricultural active ingredients registered in Canada compared to other taxa. For some active ingredients, PMRA and/or USEPA explicitly noted that additional data were required to support regulatory risk assessment (Table S3).

3.3.1 Herbicides

Atrazine

Atrazine is a broad-spectrum herbicide commonly used to control weeds, particularly in corn crops, as well as sorghum, sugarcane, and fallow, and for non-agricultural applications such as sod and Christmas tree farms (USEPA 2016).

Table 3 Outcome of the ranking exercise to determine relative priority of pesticide active ingredients, including sales, detection frequency, measured concentrations, inherent toxicity (as indicated by guideline values), and regulatory status in other jurisdictions (i.e., European Union). The list of 55 candidate compounds was derived based on relative use volume and/or measured concentrations in Canadian surface waters between 2000 and 2020. Active ingredients are listed in order from highest score to least based on an assigned score between 0 (white) and 3 (darkest shade) for each criterion (details provided in the notes and scoring rubric below). Active ingredients scoring of 23 or greater are indicated in green shading and were selected for detailed review ($n = 7$)

Active ingredient	Type	2017 sales (kg a.i.)	2018 sales (kg a.i.)	Mean study detection rate (where reported)	Most conservative guideline (µg/L) (x2)[c]	Mean concentration (µg/L)	95th concentration (µg/L)	Max reported concentration (µg/L)	95th exceeds guideline (x2)[c]	Ratio of 95th: guideline	EU status	Score (/33)	Reviewed
Atrazine	Herbicide	>500,000	>500,000	65%	1.8	2.0	9.7	62.0	Yes	5.4	Not approved	27	✓
Chlorothalonil	Fungicide	>1,000,000	>500,000	19%	0.18	0.56	3.7	7.83	Yes	20.4	Not approved	27	✓
Diazinon[b]	Insecticide	<50,000	>1,000	10%	0.08	1.3	8.3	12.5	Yes	104	Not approved	26	
Clothianidin	Insecticide	>100,000	>25,000	80%	0.05	0.16	0.51	3.1	Yes	10.3	Not approved	25	✓
Chlorpyrifos	Insecticide	>100,000	>100,000	28%	0.002	0.21	0.60	4.00	Yes	301	Not approved	24	✓
Diquat	Herbicide	>500,000	>500,000	Not monitored	0.75	Not monitored	Not monitored	Not monitored	Not monitored	Not monitored	Not approved in EU, but approved in many European countries	24	✓
Permethrin	Insecticide	>50,000	>25,000	LOD>guideline[d]	0.004	0.14	0.83	1.1	Yes	208	Not approved	24	✓
S-metolachlor	Herbicide	>500,000	>1,000,000	61%	7.8	2.1	9.9	41	Yes	1.3	Approved in S-metolachlor form; metolachlor not approved	24	✓
Carbaryl	Insecticide	<50,000	>25,000	12%	0.2	0.45	1.8	2.90	Yes	8.95	Not approved	22	
Imidacloprid	Insecticide	<50,000	>100,000	37%	0.23	0.38	2.2	10.4	Yes	9.7	Approved	22	
Thiamethoxam	Insecticide	>100,000	>100,000	72%	0.74	0.32	1.4	4.5	Yes	1.9	Not approved in EU, but approved in many European countries	22	
2,4-D	Herbicide	>500,000	>1,000,000	53%	4	0.81	4.2	8.2	Yes	1.1	Approved	21	
Mancozeb	Fungicide	>1,000,000	>1,000,000	Not monitored	1.35	Not monitored	Not monitored	Not monitored	Not monitored	Not monitored	Approved	21	
Prothioconazole	Fungicide	>500,000	>1,000,000	Not monitored	None	Not monitored	Not monitored	Not monitored	Not monitored	Not monitored	Approved	21	
Trifluralin	Herbicide	>500,000	>100,000	8%	0.2	0.07	0.24	1.2	Yes	1.2	Not approved	21	
Malathion	Insecticide	>100,000	>25,000	2%	0.049	0.44	1.4	5.5	Yes	28	Approved	20	
Metiram	Fungicide	>100,000	>100,000	Not monitored	1	Not monitored	Not monitored	Not monitored	Not monitored	Not monitored	Approved	20	
Deltamethrin[a]	Insecticide	<50,000	>25,000	LOD>guideline[d]	0.0004	0.10	0.10	0.10	Yes	250	Approved	19	
Metribuzin	Herbicide	>100,000	>100,000	15%	1	0.50	2.9	7.1	Yes	2.9	Approved	19	
Pyraclostrobin	Fungicide	>100,000	>100,000	52%	1.5	0.38	1.79	2.31	Yes	1.2	Approved	19	
Clodinafop-propargyl	Herbicide	>100,000	>100,000	Not monitored	14	Not monitored	Not monitored	Not monitored	Not monitored	Not monitored	Approved	18	
Sethoxydim	Herbicide	>50,000	>100,000	Not monitored	210	Not monitored	Not monitored	Not monitored	Not monitored	Not monitored	Not approved	18	
Dimethenamid-P	Herbicide	>100,000	>100,000	32%	5.6	7.0	4.8	130	No	0.86	Approved in dimethenamid-P form; dimethenamid not approved	16	
Phorate	Insecticide	<50,000	>10,000	3%	0.03	0.02	0.06	0.06	Yes	2.0	Not approved	16	
Bentazon	Herbicide	>500,000	>500,000	60%	510	5.3	16.9	34.0	No, but few sampling locations	0.03	Approved	15	
Dicamba	Herbicide	>100,000	>100,000	58%	10	3.3	5.0	105	No	0.50	Approved	14	
Diuron	Herbicide	<50,000	>5,000	1%	1.6	0.45	2.9	2.86	Yes	1.8	Approved	14	
Glyphosate	Herbicide	>50,000,000	>25,000,000	75%	800	7.30	22.5	140	No	0.03	Approved	14	

Imazethapyr	Herbicide	>100,000	>100,000	59%	8.1	0.26	0.96	1.9	No	0.12	Not approved	**14**	
EPTC	Herbicide	<50,000	>25,000	6%	39	2.31	15.9	69	No	0.41	Not approved	**13**	
Linuron	Herbicide	>100,000	>100,000	7%	7	0.32	1.3	1.7	No	0.18	Not approved	**13**	
MCPA	Herbicide	>1,000,000	>1,000,000	34%	2.6	0.51	2.5	4.9	No	0.94	Approved	**13**	
Mecoprop	Herbicide	>100,000	>100,000	42%	13	3.0	3.0	103	No	0.23	Approved	**13**	
Dimethoate	Insecticide	>100,000	>25,000	6%	6.2	0.78	4.1	8.50	No	0.66	Not approved in EU, but approved in many European countries	**12**	
Ethalfluralin	Herbicide	>500,000	>500,000	0%	0.4	0.01	0.02	0.02	No	<1	Not approved	**12**	
N-N-diethyl-meta-toluamide (DEET)	Insecticide	>100,000	>100,000	60%[d]	37500	1.5	4.5	5.1	No, but few data	0.0001	Approved	**12**	
Boscalid	Fungicide	>100,000	>100,000	33%[d]	116	1.4	9.7	14.2	No	0.08	Approved	**11**	
Flumetsulam	Herbicide	<50,000	>1,000	30%	3.1	0.18	0.64	1.14	No	0.21	Not approved	**11**	
Bromoxynil	Herbicide	>1,000,000	>1,000,000	16%	5	0.15	0.69	0.95	No	0.14	Approved	**10**	
Simazine	Herbicide	<50,000	>10,000	17%	10	0.35	2.8	3.7	No	0.28	Not approved	**10**	
Captan	Fungicide	>100,000	>100,000	5%[d]	1.3	0.03	0.06	0.06	No, but few data	0.05	Approved	**9**	
Glufosinate ammonium	Herbicide	>1,000,000	>1,000,000	2%	72	0.30	1.5	5.60	No	0.02	Not approved in EU, but approved in many European countries	**9**	
Metalaxyl	Fungicide	>50000	>100,000	27%	374.0	0.51	1.3	10.3	No	0.003	Approved	**9**	
Fluroxypyr	Herbicide	>500,000	>500,000	11%[d]	7150	0.05	0.06	0.06	No, but few data	0.00001	Approved	**8**	
Triallate	Herbicide	>100,000	>100,000	1%	0.24	0.01	0.02	0.05	No	0.10	Approved	**8**	
Clopyralid	Herbicide	<50,000	>100,000	25%	6900	0.22	1.1	2.3	No	0.0002	Approved	**7**	
Tebuconazole	Fungicide	>100,000	>1,000,000	29%	11	0.04	0.27	0.31	No	0.02	Approved	**7**	
Flonicamid	Insecticide	<50,000	>500	23%	3000	0.56	3.2	5.9	No	0.001	Approved	**6**	
MCPB	Herbicide	<50,000	>5,000	2%	7.3	0.20	0.77	3.1	No	0.10	Approved	**6**	
Clomazone	Herbicide	>50,000	>25,000	4%[d]	167	0.15	0.51	0.51	No, but few data	0.003	Approved	**5**	
Myclobutanil	Fungicide	<50,000	<500	7%	11	0.39	0.29	7.5	No	0.03	Approved	**5**	
Dichloroprop (2,4-DP)	Herbicide	<50,000	>10,000	13%	40	0.05	0.11	0.81	No	0.00	Approved	**4**	
Imazamethabenz	Herbicide	<50,000	>25,000	6%	5000	0.01	0.02	0.13	No	0.00	Not approved	**4**	
Picloram	Herbicide	<50,000	>10,000	2%	29	0.14	0.34	1.55	No	0.01	Approved	**4**	
Nicosulfuron	Herbicide	<50,000	<500	36%	43000	0.15	0.54	0.56	No	0.00001	Approved	**3**	

Notes: Sales scores were based on the greater sales volume of 2017 or 2018 (Health Canada 2017; Health Canada 2020)

[a]Deltamethrin was included in the long list by professional judgement based on the very low CCME value, which was exceeded in monitoring data, despite not meeting the criteria for top compound and/or mean concentration $\geq$0.5 µg/L and/or maximum concentration $\geq$1.0 µg/L

[b]Diazinon was removed from the top-priority list by professional judgement based on phasing out of uses by PMRA in 2013 and 2016 (PMRA 2013), and sales <5,000 kg a.i. in 2018 reflecting those usage changes

[c]A double weighting was applied to two criteria to avoid excessive reliance on measured environmental concentrations, particularly in cases where data were not available, but rather to consider inherent toxicity and the context of the guideline as more than merely presence is required to indicate a potential issue

[d]Denotes a compound for which few data were available for comparison to a specific criterion or for which sampling had a very limited geographic coverage. As such, these scores were bumped up to the next level to impart conservatism. e.g., mean detection rate for boscalid was based on data from only two provinces, so the score of 2 for 33% was upgraded to a 3 to account for uncertainty

Atrazine acts by binding to the plant-specific plastoquinone-binding protein in photosystem II, resulting in oxidative damage and cell plant death via starvation (Zhu et al. 2009). It is among the most well-studied current-use pesticides, with nearly 2000 records in the ECOTOX database for studies with analytical confirmation (USEPA 2020a), and has recently been reviewed by de Albuquerque et al. (2020).

Presence in the Aquatic Environment

Atrazine is frequently detected in Canadian freshwater samples (Table 3), particularly in Ontario and Quebec where it is one of the most commonly purchased pesticides (Table 1). In a 2010–2013 study in Great Lakes tributaries, atrazine was the pesticide most commonly measured above water quality guidelines, with overall detection rates of 30% and maximum concentration of 40 μg/L (Baldwin et al. 2016). In another study, atrazine was detected in all monitored sites in watersheds and receiving waters of Lake Ontario (Metcalfe et al. 2016), as well as frequently in studies in the Niagara Region (Bartlett et al. 2016), and in Quebec rivers (Giroux 2010, 2015; Giroux and Pelletier 2012) and rural drinking water (Husk et al. 2019). Concentrations of atrazine up to 0.52 μg/L were reported in the lower Red River, Manitoba, in 2014–2015, with a general increase in measured mean, median, and maximum concentrations compared to concentrations measured in a 1993–1995 study (Challis et al. 2018). Desethylatrazine, a metabolite of atrazine, was one of the most frequently detected pesticide analytes in a surface water study along the St. Lawrence River and its tributaries (Montier-León et al. 2019).

Toxicity Towards Aquatic Organisms

Atrazine is classified as moderately toxic towards fish, highly toxic towards freshwater aquatic invertebrates, and very highly toxic towards marine aquatic invertebrates based on acute toxicity data deemed appropriate for risk assessment (USEPA 2016, 2017a). Recent weight-of-evidence reviews have been conducted with regard to effects in fish, amphibians, and reptiles (Van Der Kraak et al. 2014; Hanson et al. 2019a), aquatic plant communities (Moore et al. 2017), and periphyton, phytoplankton, and macrophytes (Hanson et al. 2019b). It was noted by Hanson et al. (2019b) that there were insufficient marine studies on primary producers of sufficient quality for risk assessment, so there might yet be gaps in our understanding of atrazine in the environment, albeit fewer than some other less-studied pesticides. An extensive discussion of toxicity data available from the open literature is provided by USEPA (2016) as part of its recent ecological risk assessment of atrazine, with evaluation of study quality.

The exercise by Moore et al. (2017) compared four methods for establishing a protective level of concern (LOC) for aquatic plant communities against which USEPA could compare monitoring data as part of the risk assessment process. Based on mesocosm, microcosm, and individual species data for 26 primary producers, 60-day LOCs ranged from 19.6 to 26 μg/L. Using a weight-of-evidence

approach, the authors concluded that the most statistically reliable method resulted in a weighted LOC of 23.6 µg/L. Below this concentration, atrazine would not be expected to cause significant adverse effects in aquatic plant assemblages (Moore et al. 2017). Two high quality studies on freshwater primary producers were evaluated by Hanson et al. (2019b) that were not captured in the Moore et al. (2017) weight-of-evidence. Knežević et al. (2016) reported 7–12-days EC50 concentrations ranging from 100.9 to >1,280 µg/L for frond weight and number in the duckweed (*Lemna minor*) and Baxter et al. (2016) reported 96-h EC50s of 87.6 µg/L and 41.9 µg/L for phytoplankton growth and photosystem II yield, respectively. The reported EC50 values were >23.6 µg/L, consistent with the conclusions from Moore et al. (2017).

The risk assessment endpoints used for freshwater invertebrates by USEPA (2016) were an acute LC50 of 720 µg a.i./L for the midge *Chironomus dilutus* (formerly *Chironomus tentans*) and a chronic lowest observed adverse effect concentration (LOAEC) of 140 µg a.i./L for second generation growth in the shrimp, *Gammarus fasciatus*. For estuarine and marine invertebrates, the most sensitive endpoints were an acute LC50 of 48 µg a.i./L and a chronic no observable effect concentration (NOAEC) of 3.8 µg a.i./L for opossum shrimp (*Neonmysis integer*; USEPA 2016). More recent studies in aquatic invertebrates (crustaceans, insects, and molluscs) reported by de Albuquerque et al. (2020) and Brain et al. (2021) generally indicate biochemical effects (e.g., antioxidant biomarker activity, DNA damage) could occur at environmentally relevant concentrations (<100 µg/L), with changes to growth, reproduction, or community endpoints at concentrations greater than would be expected under typical atrazine use.

With respect to fish, acute toxicity is low and studies selected for the USEPA Ecological Risk Assessment reported LC50 (concentration resulting in 50% mortality) values of 5,300 µg a.i./L for rainbow trout (*Oncorhynchus mykiss)* and 2,000 µg a.i./L for sheepshead minnow (*Cyprinodon variegatus*) (USEPA 2016). Based on over 1,290 data points, Van Der Kraak et al. (2014) concluded that at environmentally relevant concentrations (defined as 100 µg/L or less), atrazine and its metabolites can cause significant changes in gene expression, biochemical endpoints (e.g., induction of detoxification enzymes), or concentrations of hormones in fish, amphibians, and reptiles, but that these did not translate into adverse outcomes at higher levels of biological organization including those that might impact population stability (i.e., mortality, fecundity) and community-level effects. Additional weight-of-evidence evaluation from Hanson et al. (2019a) supported these conclusions for fish, amphibians, and reptiles. Likewise, studies with fathead minnow (*Pimephales promelas*) and Japanese medaka (*Oryzias latipes*) reported no adverse effects on reproduction at concentrations up to 105 µg/L and 244 µg/L, respectively (Brain et al. 2018), and a life-cycle assessment with fathead minnow found no significant effects on growth, survival, or reproduction at concentrations up to 150 µg/L (Dionne et al. 2021).

The high solubility and low octanol-water partitioning coefficient (log K_{ow} of 2.70, Table 4) of atrazine suggest a low potential for bioaccumulation. Studies in

Table 4 Physical and chemical properties of current-use pesticides deemed to be of top tier concern ($n = 7$) for Canadian aquatic environments and fisheries based on the scoring criteria outlined in Table 2

Pesticide	Group[a]	Mechanism/ mode of action	Crops/uses	Log K_{ow}	Log K_{oc}	Degradates, metabolites	Solubility	Half-life in water (days)	References
Herbicides									
Atrazine	Triazines, Tetrazines	PSII inhibitor	Corn, sorghum, fallow, turf/control broadleaf and grassy weeds	2.70	1.88	DIA, DEA, DACT/DDA, OIET, OIAT, OEAT	33 mg/L	38–155	USEPA (2016)
Diquat	Quaternary ammoniums	Formation of peroxide and free radicals	General weed control, aquatic plant control, dessication of seed, fruit, vegetable, and ornamental crops	−4.6	2.84–6.90	None	700,000 mg/L	74	USEPA (2015a); Roede and Miller (2014)
S-Metolachlor	Anilides/ anilines	Inhibition of cell division	Corn, soybeans, ornamental crops/pre-plant, pre-emergence, or early post-plant control of grasses and broadleaf weeds	3.05	1.33–2.57	CGA-354743, CGA-51202, CGA-40172, CGA-41507, CGA-351916	530 mg/L	33–150	USEPA (2019b)
Insecticides									
Chlorpyrifos	Thiophosphates	AChE inhibitor	Grains, corn, fruit and vegetable crops, ornamentals/control insects and mites	5.0	1.61–4.72	Chlorpyrifos-oxon, TCP	0.73 mg/L	30–50	CCME (2008); Giesy and Solomon (2014)
Clothianidin	Guanidines	Nicotinic ACh receptor binding	Corn, cereal crops/control of piercing sucking pests, coleopteran pests, others	0.7–1.12	1.78–2.54	MNG, TMG, TZNG, TZMU	327 mg/L	10–158	PMRA (2018a); USEPA (2017a, 2020b)

Permethrin	Pyrethroids	Nerve axon Na+ channel modulation	Control insects on agricultural crops, public health mosquito control	6.1	4.45–5.69	trans-DCVA, 3-phenoxybenzoic acid, phenoxybenzyl alcohol, phenoxybenzoic aldehyde, cis-DCVA	0.006–0.2 mg/L	38–175	USEPA (2007); PMRA (2017)
Fungicides									
Chlorothalonil	Benzonitriles	Unknown; inhibits spore formation by binding with glutathione	Food crops, feed crops, greenhouse crops, industrial preservative/ fungicide, antimicrobial	2.88–3.8	3.05–4.08	SDS-3701, SDS-46851, SDS-47523, R417888, R471811, R419492, SDS-67042, SDS-66382, others	0.8–0.96 mg/L	<1–21.5	USEPA (2012); PMRA (2011)

[a]Group information derived from Health Canada (2017)

bluegill sunfish (*Lepomis macrochirus*) have reported maximum bioconcentration factors of 7.7–15, and >70% depuration after 21 days (USEPA 2016).

The current CWQG-PAL for atrazine in freshwater is 1.8 μg/L; no marine guideline has been recommended (CCME 1999a). It was derived based on the most sensitive plant-based maximum allowable toxicant concentration (MATC) value of 17.6 μg/L divided by a safety factor of 10 (CCME 1999a). An aquatic plant community Concentration Equivalent Level of Concern was established by USEPA to be 3.4 μg a.i./L. Above this level, changes in productivity, structure, and/or function of aquatic plant communities could be expected (USEPA 2016).

Exposure Risks for Aquatic Organisms

Over 500,000 kg a.i. of atrazine was purchased in each of 2017 and 2018 in Canada (Health Canada 2017, 2020). Corsi et al. (2019) concluded that atrazine was among the priority chemicals of ecological concern for the Great Lakes region. Atrazine is both persistent and mobile in the aquatic environment, so runoff and leaching into surface waters is predicted (USEPA 2016), and does occur, as evidenced by ubiquitous detection of atrazine in the environment. As noted, concentrations have been reported above this guideline, suggesting potential risks to aquatic organisms, if concentrations reach toxicological thresholds for sensitive species of primary producers, invertebrates or fish.

Few data were available in the ECOTOX database for aquatic insects or invertebrates (USEPA 2020a), but data available for molluscs and crustaceans indicate these taxa might be less sensitive to atrazine than fish, macrophytes, or algae (Fig. 1). Using the 23.6 μg/L aquatic plant LOC from Moore et al. (2017) as a protective threshold for effects, concentrations have very rarely been reported to exceed this concentration; the only exceedances in the collected data set were in Baldwin et al. (2016) in tributaries of the Great Lakes (40.2 μg/L – sampling location actually in the USA) and in a Quebec river studied by Giroux (2010; mean concentration of 62.0 μg/L). As such, atrazine has reached concentrations in Canadian waters that could have effects on algae and aquatic plants, but monitoring data indicate this would be expected very infrequently. Continued monitoring of atrazine in aquatic environments is recommended, particularly in regions of common use, but ideally should also be performed within the context of monitoring for changes in primary producer communities.

Diquat

Diquat is most commonly applied as diquat dibromide or in formulation with paraquat. It can be used for general weed control on non-cropped land, as well as for pre- or post-harvest desiccation of alfalfa, cotton, flax, and other fruit, vegetable, or ornamental crops (Roede and Miller 2014; USEPA 2015a). Diquat exerts its toxicity on plants by inhibiting photosynthesis via repeated sequestration of electrons from photosystem I and generation of peroxide and free radical by-products

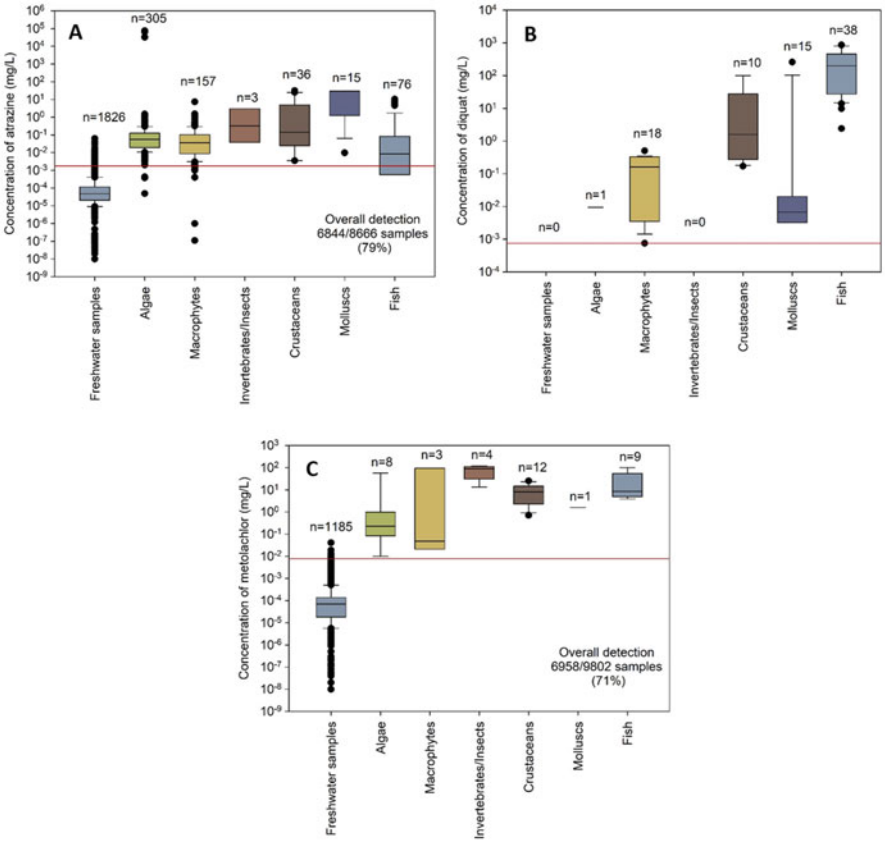

Fig. 1 Comparison of detectable concentrations of herbicides ((**a**)-atrazine, (**b**)-diquat, and (**c**)-metolachlor) measured in Canadian freshwater samples with effective concentrations (LCXX, ECXX, LOEL, LOEC values, where XX can be any number, e.g., LC10, EC50) reported in the ECOTOX database for aquatic toxicity tests using algae, invertebrates/insects, fish, molluscs, and crustaceans. Horizontal lines within each box indicate the 25th, 50th, and 75th percentiles of measurements reported, while the tenth and 90th percentiles are indicated by the whiskers (note: concentrations <LOD are not included, and values reflect data available in raw and summary form. The *n*-value reflects the number of measured concentrations >LOD or the number of toxicity data records). The red line represents the Canadian Water Quality Guideline for the Protection of Aquatic Life (CWQG-PAL; atrazine, S-metolachlor) or USEPA OPP Aquatic Life Benchmark for those active ingredients without a CWQG-PAL (diquat). The overall detection is the per cent of samples in which the herbicide was detected. The difference between *n* and the total number of samples used in the calculation of the overall detection is due to studies reporting a summary statistic of concentration, e.g., mean, the frequency of detection, and the total number of samples collected without providing the raw data

(Homer et al. 1960). Diquat is also registered in Canada for direct application to water for the control of aquatic plants, particularly free-floating weeds (Breckels and Kilgour 2018).

Presence in the Aquatic Environment

With spray application, diquat is anticipated to enter the aquatic environment directly (in the case of aquatic applications), via spray drift, or by runoff. Diquat degrades rapidly in water, with a half-life of <48 h (Roede and Miller 2014). However, it binds very tightly to soil and sediment particles, making it biologically unavailable, but potentially extending the persistence in aquatic and terrestrial systems (Roede and Miller 2014). In the preliminary ecological risk assessment for diquat dibromide performed by USEPA (2015a), it was noted that surface water monitoring data for diquat in the USA was very limited and likely did not capture higher-level exposure scenarios. Data also did not represent aquatic applications (USEPA 2015a). This situation was also observed in Canada in this review, whereby monitoring data were not found in the government databases accessed nor peer-reviewed literature, which has also been noted by others (e.g., Sesin et al. 2018).

Toxicity Towards Aquatic Organisms

As diquat is used to control aquatic plants, it is unsurprising that diquat was highly toxic towards model species of aquatic plants and algae. In a 14-day test with the duckweed *L. gibba*, the EC50 for frond number was 0.0047 mg/L, while in a 120-h exposure with the freshwater diatom *Navicula pelliculosa*, the EC50 value for reduced yield was 0.00070 mg/L. A 96-h LC50 value of 0.01 mg/L was reported for the *L. minor* duckweed species, by Garlich et al. (2016). A 42-day outdoor mesocosm study was conducted with native and non-native macrophytes collected in Ontario at concentrations corresponding to 0.4 to 100% of recommended label rate for managing nuisance macrophytes. In both the mesocosms and in 14-days single species greenhouse tests, almost 100% mortality was observed in all test species of aquatic macrophytes (*Elodea canadensis* Michx., *Myriophyllum spicatum* L., *Ceratophyllum demersum* L.,) and flowering plants (*Hydrocharis morsus-ranae* L.) at 0.074 mg/L (6% of label rate; Sesin et al. 2018).

Both freshwater and estuarine/marine invertebrates are highly sensitive to diquat. For example, the reported 96-h EC50 value for the model invertebrate amphipod, *Hyalella azteca* was 0.09 mg/L. In a chronic test (168-days) with the freshwater snail species *Lymnaea stagnalis,* development was delayed and food consumption reduced at a concentration of 0.0032 mg/L in formulation (USEPA 2015a). The reported 21-day LOAEC for survival of *D. magna* was 0.057 mg/L. Similar toxicity of diquat was also observed in the marine mysid shrimp (*Americamysis bahia*), with reported 96-h LC50 and 31-day LOAEC (female dry weight) values of 0.42 mg/L and 0.104 mg/L, respectively (USEPA 2015a). Given that diquat binds tightly to sediment, potential toxicity of diquat towards benthic invertebrates was investigated using the amphipods *H. azteca* and *Leptocheirus plumulosus.* The 42-day LOAEC

for reproduction of *H. azteca* was 23 mg/kg of sediment, while no effects were observed in *L. plumulosus* after a 10-day exposure to concentrations of diquat up to 110 mg/kg (USEPA 2015a).

Acute exposure to diquat can result in slight to high toxicity in freshwater and marine fish species (Fig. 1, USEPA 2017a). For freshwater fish, a 96-h LC50 value of 0.75 mg/L was reported for walleye (*Stizostedion vitreum*) and growth of fathead minnow was reduced in early-life stages at concentrations ≥0.316 mg/L (34-days LOEAC; USEPA 2015a). In the marine sheepshead minnow, these same endpoint effects thresholds were considerably higher, with values of 51.1 and 7.7 mg/L, respectively (USEPA 2015a). A study with juvenile rainbow trout reported a continuous exposure 96-h LC50 of 9.8 mg/L (McCuaig et al. 2020). Under pulsed conditions, embryos/alevin had decreased survival and changes in body morphometrics (decreased length and weight) following two 24-h pulses exposures at 9.3 mg/L, while juveniles were not significantly affected at this concentration (McCuaig et al. 2020). The toxicity of diquat towards fish is likely attributable to the habitat-level depletion of oxygen levels in aquatic systems following decomposition of targeted aquatic plants (Roede and Miller 2014; USEPA 2015a).

Diquat is not expected to bioaccumulate, as evidenced by reported BCF values ranging from 0.7 to 2.5, strong binding to sediment and soil particles, and a log K_{ow} value of −4.6 (Breckels and Kilgour 2018 and references therein, USEPA 2015a). No freshwater or marine CWQG-PAL has been recommended (CCME n.d.), but the lowest USEPA Aquatic Life Benchmark is 0.75 µg/L, based on vascular plant toxicity (USEPA 2019a).

Exposure Risks for Aquatic Organisms

Diquat was among the top ten herbicides sold in Canada in 2017, and had a sales volume of >500,000 kg a.i. in both 2017 and 2020 (Health Canada 2017, 2020). Toxicity incidents in aquatic organisms have been reported in the USA as a result of exposure to diquat, and the USEPA reported potential risks for fish, aquatic invertebrates, and/or aquatic plants for both terrestrial and aquatic use patterns (USEPA 2015a). Notably, non-target aquatic vascular and non-vascular plants were deemed at risk of experiencing toxic effects as a result of nearly all uses (USEPA 2015a).

It was highlighted by Breckels and Kilgour (2018) that despite the use of diquat in aquatic applications for 20 years in Canada, few studies had been conducted under field conditions to assess the risks to Canadian aquatic organisms. However, available field studies summarized by Breckels and Kilgour (2018) suggested that direct applications of diquat showed little if any effect on aquatic invertebrates, fish, and amphibians, even at concentrations initially exceeding LC50 or EC50 values reported from laboratory studies.

The conservative nature of the scoring system used for this review was such that by having few measured data available for diquat in Canadian systems, it was deemed one of the active ingredients of greatest interest or concern. Increased monitoring data would help to fill this knowledge gap and provide a clearer picture of the true risks posed by diquat under current-use patterns.

S-Metolachlor

S-metolachlor is applied pre-plant, pre-emergence, or early post-plant control of grasses and broadleaf weeds in crops such as corn, soybean, and ornamental crops. S-metolachlor is the enantiomerically-enriched form of metolachlor (88% S-metolachlor, 12% R-metolachlor) and has a separate registration, as well as greater potency. Metolachlor disrupts plant cell elongation and division by inhibiting enzymes involved in the production of long-chain fatty acid and the growth hormone gibberellin (Rose et al. 2016). Toxicological and environmental measurements are fluid between the two forms and data are generally bridged for risk assessment purposes (USEPA 2019b).

Presence in the Aquatic Environment

Metolachlor is highly water soluble and moderately mobile in the environment. It is primarily degraded by aerobic metabolism with half-lives of 14.6 to 231 days in soil and 33 to 54.5 days in water (USEPA 2019b). The physical and chemical properties of S-metolachlor (e.g., log K_{ow} of 3.05) suggest potential movement into benthic sediments; however, concentrations are expected to remain considerably lower than those measured in the water column (USEPA 2019b; Elias 2016).

Metolachlor has been detected frequently in water samples collected in Canadian waters (up to 100% of samples in some cases), particularly those from Ontario and Quebec (ECCC 2011; Bartlett et al. 2016; Larue 2019). The maximum reported concentration of 41 µg/L (Giroux 2010) was exceptional, but concentrations between 5 and 10 µg/L were reported by several studies (Fig. 1). Fewer data are available for sediments; for example, from Great Lakes tributaries (maximum of 12.8 µg/kg, 3% detection rate – Elliot et al. 2017) and Nathan Creek, British Columbia (mean of 35 µg/kg – Harris et al. 2008).

Toxicity Towards Aquatic Organisms

S-metolachlor was classified as moderately toxic towards fish and aquatic invertebrates under acute exposure conditions (USEPA 2017a, 2019b). The most sensitive NOAEC values used for the ecological risk assessment by USEPA were as follows: freshwater fish – 30 µg/L, marine fish – 1,000 µg/L, freshwater invertebrates – 3,200 µg/L, marine invertebrates – 130 µg/L, aquatic vascular plants – 14 µg/L (duckweed, *L. gibba*), and aquatic non-vascular plants – 8 µg/L (green algae) (USPEA 2019b).

As indicated by the risk assessment values from USEPA (2019b), aquatic plants and primary producers can be susceptible to S-metolachlor, but toxicity thresholds vary. For green algae, chlorophyll concentration, growth, and cell morphology endpoints of *Chlorella pyrenoidosa* had a 96-h LC50 value of 68 µg/L (Liu and Xiong 2009). The microalga *Parachlorella kessleri* had a reported 72-h EC50 value of 1,090 µg/L, but sub-lethal effects, including decreased growth, changes in cellular antioxidant activity, and decreased pigment concentrations, were observed following

exposure to S-metolachlor at concentrations ≤200 μg/L (Maronić et al. 2018). In the green algae, *Scenedesmus obliquus,* 100 μg/L induced generation of reactive oxygen species and increased cell membrane permeability after 96 h, while significant changes in chlorophyll-*a* and -*b* were reported at 50 μg/L (Liu et al. 2016). A comparison of sensitivities among three marine microalgae (chlorophyte *Tetraselmis suecica*, diatom *Ditylum brightwellii*, and dinoflagellate *Prorocentrum minimum*) reported 72-h EC50 values of 21,300, 423, and 70 μg/L, respectively, with significant reductions in cell counts and chlorophyll-*a* production (Ebenezer and Ki 2013). Similar responses were observed for the freshwater alga *Raphidocelis subcapitata* and marine alga *Dunaliella tertiolecta*, with reported EC50 values for growth of 118 μg/L and 11,300 μg/L, respectively, after 72–96 h (Machado and Soares 2019). Literature EC50 values cited by Machado and Soares (2019) for *R. subcapitata* ranged from 44.3 μg/L for chlorophyll concentration to 5,510 μg/L for growth rate. A 10% inhibition of growth (EC10) was observed at 45 μg/L for *R. subcapitata* and at 5,620 μg/L for *D. tertiolecta (*Machado and Soares 2019), demonstrating the wide range of sensitivities across primary producers.

A wide range of effect concentrations for invertebrates have been reported in the literature, some examples of which are described below. Exposure to 100 μg/L of metolachlor induced an eight-fold reduction in egestion rates of the aquatic gastropod *Physa acuta*, but had no significant effects on another species, *Helisoma anceps* (Elias and Bernot 2017). The amphipods *Gammarus* cf. *orinos* and *G. pulex* exhibited similar sensitivity to S-metolachlor as the isopod *Asellus aquaticus,* with reported 96-h EC50 values of 8,470–11,780 μg/L (Maazouzi et al. 2016). Metolachlor concentrations up to 100 μg/L caused immobilization of up to 10% of chironomids (*Chironomus tentans*) in a 72-h assay; at 1000 μg/L, 58% of test organisms were immobilized and AChE activities were significantly reduced (Jin-Clark et al. 2008). Chronic bioassays with the water flea *Daphnia longispina* revealed greater toxicity of S-metolachlor in formulation (Primextra® GOLD) compared to the technical product, with 21-day reproduction EC50 values of 4,100 μg/L and 8,240 μg/L, respectively (Neves et al. 2015).

Juvenile marbled crayfish (*Procambarus virginalis*) exhibited slower growth, increased mortality, behavioural excitation, and delayed ontogenetic development with chronic exposure (45 days) to concentrations of 1.1 μg/L. Long-term exposure to 11 and 110 μg/L of S-metolachlor caused significant changes in levels of oxidative stress biomarkers and antioxidant enzymes, with histopathological changes in the hepatopancreatic tissue observed only at the highest exposure concentration (110 μg/L) (Velisek et al. 2019). Chronic toxicity of metolachlor OA (a major metabolite of S-metolachlor and metolachlor) was also evaluated in juvenile marbled crayfish. Exposure to 4.2 μg/L for 45 days resulted in significantly reduced growth and antioxidant enzymatic activity. At 42 and 420 μg/L, changes in hepatopancreas and gill histomorphology were observed, but there were no changes in behavioural endpoints (Velisek et al. 2018). In the benthic clam *Scrobicularia plana,* acute (96 h) exposure to relatively high concentrations of S-metolachlor (2,048–46,410 μg/L) resulted in changes to fatty acid composition, and increased glucose and decreased glycogen in tissues, indicating stress response (Gutiérrez et al. 2019a). The LC10

concentrations of S-metolachlor for mortality in this clam species were previously determined to be 16,285 µg/L for smaller individuals and 30,065 µg/L for larger individuals (Gutiérrez et al. 2019b).

Among acute toxicity studies for fish species, reported 96-h LC50 values have included 10,000 µg/L in bluegill, 45,210 µg/L in zebrafish (*Danio rerio*), 8,850 in sheepshead minnow, 4,900 in channel catfish (*Ictalurus punctatus*), and 8,600 µg/L in guppy, and 3,900 µg/L in rainbow trout (Quintaneiro et al. 2017; CCME 1999b; Munn et al. 2006). Short-term exposure to 29,000 µg/L of metolachlor induced significant malformations in early-life stage zebrafish, with biochemical changes at 500 µg/L and higher (Quintaneiro et al. 2017). The CCME guideline of 7.8 µg/L was derived based on the lowest reproduction endpoint for fathead minnow (780 µg/L) with a safety factor of 0.01 to account for limited chemical fate and chronic toxicity data (CCME 1999b). However, more conservative aquatic quality indices of 1.62 µg/L for acute exposure and 0.162 µg/L for chronic exposure were recommended by Tsaboula et al. (2019).

The log K_{ow} value (3.05) suggests potential for bioaccumulation, but a bioconcentration study submitted for the USEPA risk assessment concluded that this potential is small (USEPA 2019b).

Exposure Risks for Aquatic Organisms

Sales of S-metolachlor exceeded 500,000 kg a.i. in 2017 and 100,000 kg a.i. in 2020 (Health Canada 2017, 2020), thus large quantities of this compound are being applied, and concentrations in the environment have been measured (though infrequently reported in the literature) above the CCME guideline and above toxicity endpoints for sensitive aquatic species (Fig. 1). In both Ontario and Quebec, S-metolachlor has been identified as one of the pesticides of greatest risk to environmental receptors in those regions based on measured concentrations, ecotoxicity data, and risk indicators such as hazard quotients (Van Eerd 2016; Government of Québec 2017; Corsi et al. 2019). S-metolachlor is currently under evaluation by PMRA with anticipated public consultation activities to begin late 2020 (PMRA 2019b).

In the recent risk assessment by USEPA (2019b), potential risks were identified for freshwater fish under chronic exposure and for water column invertebrates, though these were considered relatively low (risk quotients of 0.22–3.70 and 0.13–1.05, respectively). Likewise, benthic invertebrate risk quotients exceeded the level of concern. True risks were presumed to be low; however, lack of measured sediment concentrations resulted in uncertainty in the assessment (USEPA 2019b). Risks to aquatic plants as a result of runoff were identified under all use scenarios (USEPA 2019b).

Given the sensitivity reported in non-vascular plant studies (EC50 of 8.0 µg/L and NOAEC of 1.5 µg/L), the Canadian guideline value of 7.8 µg/L might not be protective of these species. Generally, fish would be expected to be more tolerant of the typical S-metolachlor concentrations anticipated in Canadian waters, and

effects on fisheries would be more likely via indirect habitat or food web-mediated effects resulting from damage to sensitive aquatic plants.

3.3.2 Insecticides

Chlorpyrifos

Chlorpyrifos is used agriculturally for insect control in a variety of field and greenhouse crops, as well as for control of mosquito larvae in standing water and management of destructive forestry pests (PMRA 2019c). Chlorpyrifos inhibits acetylcholine (AChE) breakdown by binding to cholinesterase in axon synapses (Giesy and Solomon 2014). Like atrazine, chlorpyrifos is one of the most studied pesticide active ingredients, with over 2000 records in the ECOTOX database (USEPA 2020a) and several reviews or risk assessments available in the published literature (e.g., Giesy and Solomon 2014; Giddings et al. 2014; Alvarez et al. 2019; Giesy et al. 2014; Juberg et al. 2013). As such, only a brief review of the state of the science with respect to aquatic biota will be provided below.

Presence in the Aquatic Environment

Chlorpyrifos has moderate environmental persistence and may dissipate via photolysis, hydrolysis, microbial degradation, and/or volatilization (CCME 2008; Giesy and Solomon 2014). Its major metabolite, chlorpyrifos-oxon, is toxicologically active but does not persist in the environment and is not found in surface waters (Giesy and Solomon 2014). Immediately following application, volatilization is the dominant process, but within days of application, chlorpyrifos will be strongly bound to soil (Giesy and Solomon 2014). Half-lives in soil can vary considerably, depending on soil properties and microbial activity, with reported values ranging from <1 week to >24 weeks (CCME 2008). Under field conditions, chlorpyrifos does not persist in the water column, but tends to be bound to sediment. Reported half-lives in water range from <1 to 50 days, and in sediment from 1 to 34 days (CCME 2008, Giesy and Solomon 2014).

As is true for many pesticides, chlorpyrifos presence in flowing waters tends to occur in pulses, with peak concentrations persisting only for a limited period (estimated as 2 days for chlorpyrifos) and concentrations declining thereafter (Giesy and Solomon 2014), so exposure duration and recovery are important considerations for assessment of risk.

Chlorpyrifos has been detected in water bodies across Canada since 2000, including remote lakes in Ontario and Arctic seawater (Hoferkamp et al. 2010; Kurt-Karakus et al. 2011). Reported concentrations have surpassed both acute and chronic CCME guideline values – 0.02 and 0.002 μg/L, respectively – reaching up to 4 μg/L in Quebec rivers (as reported by Giroux 2010; Fig. 2).

Toxicity Towards Aquatic Organisms

As noted in the risk assessment by Giddings et al. (2014), and observed in the ECOTOX database results (USEPA 2020a, Table S3), data on toxicity of chlorpyrifos towards aquatic plants are limited, but this is consistent with the lack of AChE receptors in plants and tolerance reflected in reported marine algae tests (EC50s of 138–769 μg/L). The 72-h EC50 values for growth of two freshwater microalgae, *Chlorella pyrenoidosa* and *Merismopedia* sp., were even greater, at 11,460 μg/L and 25,800 μg/L, respectively (Chen et al. 2016). Changes in chlorophyll-*a* concentrations were observed with 8-day exposure to concentrations ≥2,400 μg/L, as well as concentration-dependent growth inhibition at concentrations up to 38,400 μg/L (Chen et al. 2016).

In the risk assessment conducted by Giddings et al. (2014), acute toxicity data were included from 23 crustacean species, with LC50 values ranging from 0.035 to 457 μg/L, and an HC5 value (the concentration at which 5% of species are expected to exhibit effects) of 0.034 μg/L. Aquatic insects were similarly sensitive, with LC50 values for 17 species ranging from 0.05 to >300 μg/L and an HC5 of 0.087 μg/L (Giddings et al. 2014). Some insects also exhibit sub-lethal sensitivity at very low concentrations of chlorpyrifos. For example, the swimming behaviour of the Alpine chironomid *(Diamesa zernyi*) was significantly affected after 72-h exposure to chlorpyrifos at 0.11 μg/L (Di Nica et al. 2019). Fish were less sensitive as a group (Fig. 2), with LC50 values of 0.53 to >806 μg/L for 25 assessed species and an HC5 of 0.812 μg/L. Aquatic molluscs were deemed to be relatively insensitive, with LC/EC50 values of 154 to >806 μg/L (Giddings et al. 2014).

A more recent risk assessment by Alvarez et al. (2019) included chronic toxicity data for aquatic species ranging from 0.21 μg/L (AChE inhibition) to 171,000 μg/L (immobility) and noted that shrimp, cladoceran, and amphipod species were generally most sensitive to chlorpyrifos. Acute and chronic HC5 values for all taxa were calculated as 0.064 and 0.007 μg/L (Alvarez et al. 2019), indicating that the CCME chronic benchmark (0.002 μg/L) may not be protective of the most sensitive members of arthropod taxa. More conservative aquatic quality objectives were also recommended by Tsaboula et al. (2019) – 0.01 μg/L for acute exposure and 0.001 μg/L for chronic exposure.

Zooplankton assemblages in mesocosm studies were significantly shifted as a result of exposure 0.17–2.3 μg/L of chlorpyrifos (Pereira et al. 2017; Xiao et al. 2017). Recovery to control conditions was not observed over 56 days, despite rapid disappearance of chlorpyrifos from the system (Xiao et al. 2017). The growth, longevity, and reproduction of the rotifer *Brachionus koreanus* were not significantly affected by 10-day exposure to 10 μg/L, but at a concentration of ≥100 μg/L, growth was reduced, lifespan was shortened, and fewer offspring were produced (Kim et al. 2016).

Inhibition and recovery of AChE activity (whole body) was observed in post-larval American lobster (*Homarus americanus*) following exposure to 0.5 μg/L for 48-h and recovery for 9–15 days. A concentration of 0.82 μg/L caused sub-lethal effects on lobster growth, including decreased growth rate, decreased moult

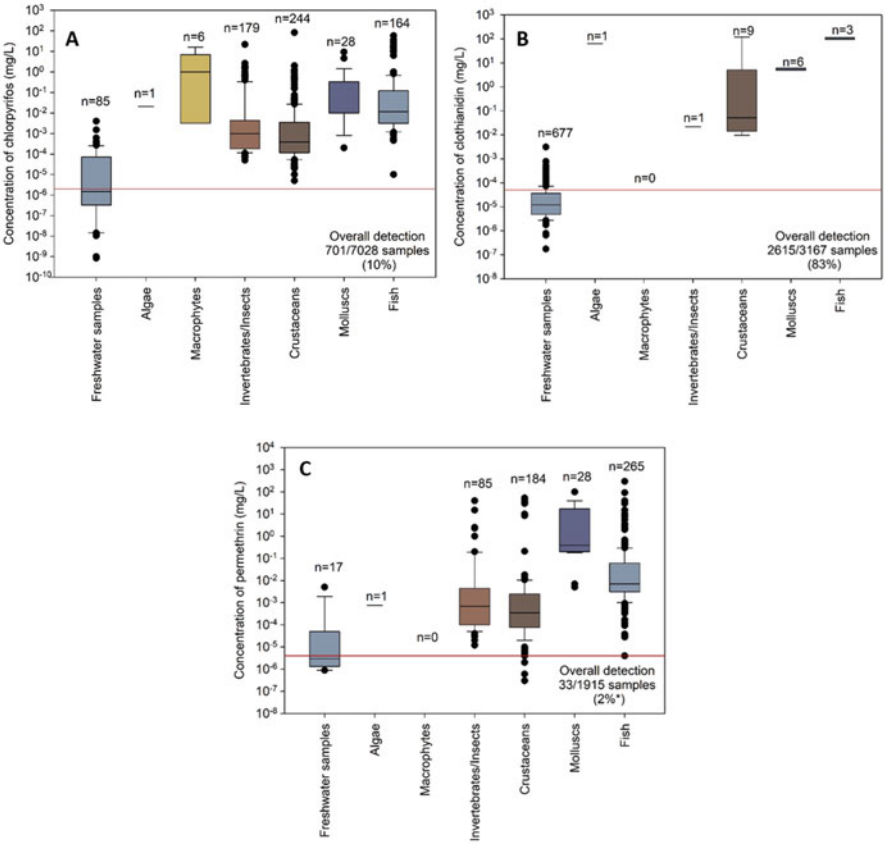

Fig. 2 Comparison of detectable concentrations of insecticides ((**a**)-chlorpyrifos, (**b**)-clothianidin, and (**c**)-permethrin) measured in Canadian freshwater samples with effective concentrations (LCXX, ECXX, LOEL, LOEC values, where XX can be any number, e.g., LC10, EC50) reported in the ECOTOX database for aquatic toxicity tests using algae, invertebrates/insects, fish, molluscs, and crustaceans. Horizontal lines within each box indicate the 25th, 50th, and 75th percentiles of measurements reported, while the tenth and 90th percentiles are indicated by the whiskers (note: concentrations <LOD are not included, and values reflect data available in raw and summary form. The *n*-value reflects the number of measured concentrations >LOD or the number of toxicity data records). The red line represents the Canadian Water Quality Guideline for the Protection of Aquatic Life (CWQG-PAL; chlorpyrifos and permethrin) or USEPA OPP Aquatic Life Benchmark for those active ingredients without a CWQG-PAL (clothianidin). The overall detection is the per cent of samples in which the insecticides were detected. The difference between *n* and the total number of samples used in the calculation of the overall detection is due to studies reporting a summary statistic of concentration, e.g., mean, the frequency of detection, and the total number of samples collected without providing the raw data

increment, and increased intermoult period, while the 48-h IC50 for normal movement was 0.66 µg/L (Taylor et al. 2019). At sub-lethal concentrations ranging from 0.03 to 100 µg/L, acute chlorpyrifos exposure induced changes in protein content of tissues and enzymatic activity in digestive glands and gills of the mussel *Mytilus galloprovincialis* (Kovačić and Medić 2016). In another mussel species (*Villosa iris*), mean viability of glochidia was not significantly different from the control at a concentration of 360 µg/L following a 48-h exposure period. This species is listed as of "special concern" in Canada, but it was suggested that chlorpyrifos would pose a minimal risk for survival and viability of its glochidia (Salerno et al. 2018).

Short-term (36- to 96-h) LC50 values for fish species used in the development of Canadian guidelines ranged from 1.3 to 280 µg/L ($n = 12$), and those for invertebrates ranged from 0.04 to 10 µg/L ($n = 9$; CCME 2008). Using a species sensitivity distribution approach, a guideline of 0.02 µg/L was established, reflecting the toxic nature of chlorpyrifos towards aquatic organisms. Long-term guidelines for freshwater and marine exposure are both set at 0.002 µg/L, based on a 96-h LC50 of 0.04 µg/L for *Hyalella azteca* and a safety factor of 20 (CCME 2008).

Sub-lethal studies in fish have often examined AChE activity (as this is the pathway targeted by chlorpyrifos), as well as growth, histological, developmental, and behavioural endpoints. Swimming behaviour in Japanese medaka (0, 20, and 40-days post-hatch) was significantly impacted by chlorpyrifos at concentrations $\geq$12.5 µg/L (Sastre et al. 2018). The liver somatic index of fingerling African sharptooth catfish (*Clarias gariepinus*) was significantly increased by exposure to 12.8 µg/L, and exposure to 400 µg/L caused erratic swimming, hyperactivity, and lack of startle response (Kanu et al. 2019). A study in adult zebrafish reported structural damage (vacuolization) in gonads after 96-h exposure to chlorpyrifos at 200 µg/L (Manjunatha and Philip 2016). Concentrations $\geq$150 µg/L caused histopathological changes in both testes and ovaries of banded gourami (*Trichogaster fasciata*) over a 60-day exposure period (Sumon et al. 2019). In another reproductive study, significant decreases in Coruh trout (*Salmo coruhensis)* spermatozoa motility rate and duration as a result of in vitro exposure to 5 µg/L or more of chlorpyrifos (Kutluyer et al. 2019). Long-term (30-day) exposure to 5 µg/L caused severe behavioural changes in spotted snakehead (*Channa punctatus*), as well as pathological lesions in gill tissue, and structural changes in hepatic and intestinal tissues (Stalin et al. 2019).

Changes to histological endpoints have been identified in fish gill, eye, and brain tissues in a number of species. Histopathological changes and loss of structural integrity were observed in gill tissues of common carp following a 45-day study with 14.5 µg/L chlorpyrifos, likely caused via oxidative stress and cell apoptosis (Jiao et al. 2019). Similar histopathological changes were observed in fingerling barramundi (*Lates calcifer*) following chronic (30-day) exposure to concentrations of chlorpyrifos as low as 0.04 µg/L. Specifically, the intercellular space in the photoreceptor of the fish retina increased at 0.04 µg/L, and exposure to 0.09 µg/L also induced changes to the primary and secondary lamellae of the gill (Marigoudar et al. 2018a). A concentration of 0.09 µg/L was also reported by Marigoudar et al. (2018b) as causing hyperplasia of secondary lamellae in fingerling flathead grey mullet

(*Mugil cephalus)*, while in milkfish (*Chanos chanos)*, gill histopathology was observed at 0.32 μg/L. Qiu et al. (2017) similarly observed changes in fish eyes as a result of chlorpyrifos exposure, reporting increased AChE activity in eyes and consequent persistent startle response in Japanese medaka following a 4-day exposure to 24 μg chlorpyrifos/L. In addition, transient hyperactivity and increased brain AChE activity were observed, but did not persist past the 21-day recovery period (Qiu et al. 2017). Long-term (90-days) exposure to 12 μg/L caused anaemia and reduced growth in freshwater Nile tilapia (*Oreochromis niloticus*; Majumder and Kaviraj 2019).

Although the high log K_{ow} that is generally cited for chlorpyrifos suggests the potential for bioaccumulation (Table 4), a weight-of-evidence review by Giesy et al. (2014) concluded that chlorpyrifos did not meet the criteria to be classified as "bioaccumulative" as per European EC Regulation No. 1107/2009 classifications, only "toxic". Likewise, another weight-of-evidence review concluded that chlorpyrifos does not demonstrate potential for interaction with oestrogen, androgen, or thyroid pathways at concentrations less than those causing effects via cholinesterase inhibition, so additional endocrine testing is not warranted (Juberg et al. 2013). Generally, the only toxicity data gaps identified by Giesy and Solomon (2014) in terms of risk assessment were related to terrestrial pollinators and not aquatic organisms.

Exposure Risks for Aquatic Organisms

Chlorpyrifos was among the top 20 chemicals (not just pesticides) of concern in a UK review, based on the overlap of measured river concentrations and aquatic toxicological effects thresholds (Johnson et al. 2017). Mesocosm studies reviewed in Giddings et al. (2014) generally support the conclusion that concentrations of chlorpyrifos <0.1 μg/L would not be expected to cause significant effects to aquatic communities; however, concentrations above this threshold have been measured in Canadian surface waters (Fig. 2).

Chlorpyrifos recently underwent a re-evaluation review by the PMRA and risks to aquatic biota were found to be unacceptable for most uses. As such, continued registration will only be for a limited number of uses, including treatment of temporary standing water for mosquito larvae and use in greenhouse ornamentals (PMRA 2019c). It is expected that these changes will result in decreased entry of chlorpyrifos into aquatic environments, and thus, reduced risk to fish and fish habitat. Continued monitoring of water concentrations would be advisable for tracking outcomes of the proposed registration changes.

Clothianidin

Clothianidin is both an active ingredient in its own right and a degradate of thiamethoxam (Anderson et al. 2015); as such, some information for thiamethoxam has also been included in this review. Clothianidin and thiamethoxam are

neonicotinoid insecticides used for the control of piercing sucking pests, coleopteran pests, and other pests in corn and cereal crops (PMRA 2018a; USEPA 2017b, c, 2020b). Clothianidin, like other neonicotinoid insecticides, inhibits the insect nicotinic acetylcholine receptor (Anderson et al. 2015 and references therein). In August 2018, the PMRA proposed a phase out of all outdoor agricultural applications of clothianidin and thiamethoxam (PMRA 2018a). A recent Special Review of these two active ingredients was undertaken by PMRA with particular focus on potential effects on aquatic invertebrates (PMRA 2019b). The decision outcome released in March 2021 resulted in cancellation of certain uses found to pose an unacceptable risk, as well as reduced application rates for acceptable uses and new or revised spray buffers (PMRA 2021a, b).

Presence in the Aquatic Environment

Both clothianidin and thiamethoxam are water soluble, allowing them to be readily transported systemically in plants, but also causing potential for leaching and runoff into surface water systems (Anderson et al. 2015 and references therein). Neonicotinoids have also been shown to persist through water treatment systems without being removed (Klarich et al. 2017); however, half-lives in aquatic environments are typically on the order of hours to weeks (Anderson et al. 2015; USEPA 2017b, c; PMRA 2018a). Reported soil half-lives for clothianidin range from 34 to >5,000 days, and from 46 to 464 days for thiamethoxam, suggesting potential for persistence and availability for movement into aquatic environments (USEPA 2017b, c).

Surface water sampling of neonicotinoids in Canada and elsewhere has expanded since 2010 to include clothianidin, thiamethoxam, and others, as neonicotinoids became of greater environmental and public interest. Maximal concentrations of clothianidin and thiamethoxam up to approximately 3–5 μg/L have been reported in Canadian surface waters, typically in agricultural areas (Giroux 2019, Main et al. 2016, PMRA 2018a, Fig. 2). In the PMRA proposed special review decision, a lack of Canadian estuarine or marine monitoring data was noted (PMRA 2018a), representing a gap for risk assessment.

Toxicity Towards Aquatic Organisms

Generally, clothianidin is more toxic towards aquatic organisms than its parent compound thiamethoxam (USEPA 2017c). Algae and macrophytes did not demonstrate sensitivity towards either clothianidin or thiamethoxam (Anderson et al. 2015 and references therein), with reported chronic NOAEC values of 6,350 and 12,000 μg/L, respectively, for the saltwater diatom *S. costatum,* and 520 and 22,000 μg/L, respectively, for duckweed (*L. gibba*) (USEPA 2017b, c). Further studies with primary producers reported acute toxicity thresholds (NOEC, ECx) ranging from 47,000 to >100,000 μg/L (Finnegan et al. 2017).

Broadly, aquatic invertebrate species are very sensitive to clothianidin, based on available data for amphipods, molluscs, dipteran insects, and cladocerans (USEPA

2017b; PMRA 2018a). However, data from the ECOTOX database (USEPA 2020a, Fig. 2) and literature suggest molluscs are slightly more tolerant than other invertebrate taxa. For example, Prosser et al. (2016) reported 48-h LC10 (mean viability) values of >478 and >691 μg/L for clothianidin and thiamethoxam, respectively, for wavy-rayed lampmussel (*Lampsilis fasciola)* glochidia. For juvenile rams-horn snails (*Planorbella pilsbryi*), clothianidin induced a 50% reduction in growth and biomass at 122.0 and 33.2 μg/L, respectively. Thiamethoxam reduced snail growth and biomass by 50% at concentrations of 52.1 and 51.3 μg/L, respectively (Prosser et al. 2016). Glochidia of another mussel species, *V. iris*, did not experience reductions in viability after 24 or 48-h exposure to 13,800 μg/L of clothianidin or 17,400 μg/L of thiamethoxam (Salerno et al. 2018).

As expected, based on the mode of action and insecticidal properties of neonicotinoids, aquatic insects are most susceptible to acute toxicity from exposure to neonicotinoids (Anderson et al. 2015; Sànchez-Bayo et al. 2016). The most sensitive effects values for chronic clothianidin exposures deemed acceptable for risk assessment by USEPA ranged from 0.020 μg/L (*Chironomus dilutus*, 40-days emergence) to 120 μg/L (*D. magna*, 21-days reproductive NOEC; USEPA 2017b). In a mesocosm study with eight species of aquatic invertebrates, the reported 48-h LC50 values ranged from 2 μg/L for diving beetle (*Graphoderus fascicollis)* to 1,245 μg/L for damselfly (*Lestes unguiculatus*) (Miles et al. 2017). Interestingly, Shahid et al. (2018) demonstrated adaptation of the amphipod, *G. pulex,* such that individuals from pesticide-exposed populations had a mean clothianidin EC50 of 218 μg/L compared to 81 μg/L for non-exposed populations. Data from exposure of cladocerans to formulated clothianidin suggest that components of the formulations can contribute additive toxicity with respect to the technical ingredient (PMRA 2018a; Takács et al. 2017). Two sediment studies of quality suitable for risk assessment were identified, with a most sensitive endpoint of 1.1 μg/L in pore water (10-days NOEC, dry weight of *C. dilutus*; PMRA 2018a). Notably, sub-lethal effects have been reported for aquatic invertebrates at concentrations of clothianidin well below immobilization/mortality endpoints, with effects including reduced reproduction, growth, and emergence, as well as changes to population sex ratios (USEPA 2017b).

While toxicity endpoint values were slightly higher for thiamethoxam than for clothianidin, some aquatic invertebrates were still very sensitive to exposure. For example, the acute 48-h EC50 (mobility) and chronic NOAEC (larval survival) values reported for *Chironomus riparius* midges were 35 μg/L and 0.74 μg/L, respectively (USEPA 2017c). Pickford et al. (2018) reported a thiamethoxam NOEC of 0.3 μg/L for a 35-day outdoor mesocosm exposure with mayflies (*Cloeon dipterum*). A similar 28-day LOEC for larval growth and emergence rate (1.6 μg/L) was reported for *C. xanthu*s midges based on a laboratory partial life-cycle test (Ferreria-Junior et al. 2018). A 30-day NOEC (emergence) of 10 μg/L was also reported for *C. riparius*, confirming its relative sensitivity (Finnegan et al. 2017). Cavallaro et al. (2017) reported a 40-day EC50 (emergence) value for *C. dilutus* of 4.13 μg thiamethoxam/L compared to 0.28 μg clothianidin/L. The 96-h behavioural EC50 values for mayfly *Hexagenia* spp. were 630 μg/L for thiamethoxam and

24 µg/L for clothianidin in a water-only test conducted by Bartlett et al. (2018), which were well below the reported LC50 values of >10,000 and 2000 µg/L, respectively. Five crustacean species exposed to thiamethoxam in 48-h assays had EC50 values ranging from 84 to 3,000 µg/L (Finnegan et al. 2017). For nymphs of another species of mayfly (*Deleatidium* spp.), the IC50 for immobility and EC50 for impairment were both >4 µg/L following 28-day thiamethoxam exposure. In contrast, the median concentrations of clothianidin causing immobility and impairment were 1.24 and 1.02 µg/L, respectively, on Day 28 (Macaulay et al. 2019). Concentrations of thiamethoxam and clothianidin ≤4 µg/L also had transient effects on moulting propensity over the 28-day exposure duration (Macaulay et al. 2019). The mysid shrimp (*Mysidopsis bahia*) was less sensitive to thiamethoxam, with 96-h LC50 and chronic NOAEC values of 6,900 µg/L and 1,100 µg/L, respectively (USEPA 2017c). In the context of shrimp aquaculture, Butcherine et al. (2019) suggested that more acute and chronic data were needed to characterize effects of neonicotinoids on different developmental stages of shrimp and more broadly, sub-lethal responses (e.g., biochemical) of commercially harvested crustaceans.

Based on the available acute toxicity data, PMRA calculated an HC5 for clothianidin of 1.5 µg/L for all invertebrate taxa (PMRA 2018a). This is consistent with acute HC5 values reported by Raby et al. (2018a) – 0.14 µg/L for immobilization and 4.13 µg/L for EC50 and LC50 endpoints for clothianidin, and 6.09 µg/L and 12.29 µg/L, respectively, for thiamethoxam. Basley and Goulson (2018) also reported reduced colonization of microcosms by invertebrate populations when treated with clothianidin or thiamethoxam at up to 15 µg/L. The chronic PMRA reference value for clothianidin is 0.0015 µg/L based on the HC5 approach (PMRA 2018a), reflecting the highly toxic nature of this active ingredient towards sensitive invertebrates. In prairie wetlands, a mean total neonicotinoid concentration of 0.131 µg/L resulted in lower overall emergence and a shift towards more disturbance-tolerant insect species (Cavallaro et al. 2019). From a 56-day mesocosm study, a time-weighted average concentration of 0.281 µg/L was considered a reasonable NOEC for community-level effects following a single application of clothianidin (PMRA 2018a).

Clothianidin and thiamethoxam are practically non-toxic towards fish on an acute exposure basis (USEPA 2017a), with reported 96-h LC50 values of >91,400 µg/L to 117,000 µg/L for clothianidin (USEPA 2017b; Anderson et al. 2015) and ≥ 80,000 µg/L for thiamethoxam (Anderson et al. 2015; USEPA 2017c; Finnegan et al. 2017). Whiteside et al. (2008) estimated the HC5 values for fish species at 10,500 and 10,900 µg/L, respectively, for clothianidin and thiamethoxam. However, Baldissera et al. (2018) reported oxidative stress and disruption of gill biochemistry following 96-h exposure of silver catfish (*Rhamdia quelen)* to 3.75 µg/L of thiamethoxam, and exposure to 0.15 µg clothianidin/L significantly increased whole body 17β-estradiol in swim-up sockeye salmon (*Oncorhynchus nerka*) fry (Marlatt et al. 2019).

Clothianidin and thiamethoxam have very low octanol-water coefficients (low K_{ow} values of 1.12 and − 0.13, respectively; Table 4) and are not expected to bioaccumulate (USEPA 2017b, c; PMRA 2018a, b, c).

Exposure Risks for Aquatic Organisms

By 2010, neonicotinoid constituted 27% of insecticides used globally (Casida and Durkin 2013), but the European Union instituted a ban on nearly all uses of imidacloprid, thiamethoxam, and clothianidin as of 2018 due to potential risks to honeybees and other pollinators (Jactel et al. 2019). Thiamethoxam is also on the 2019 European Union watch list and is one of the most frequently detected pesticides in surface water, groundwater, and wastewater treatment plant influent sampling data collected from 21 countries (Pietrzak et al. 2019). The proposed interim decision from the USEPA includes application rate reductions, cancelling certain uses of clothianidin, restricting certain uses of thiamethoxam, and label changes in an effect to mitigate the potential risks to aquatic invertebrates and terrestrial pollinators (USEPA 2020b), consistent with the outcome of the Special Review in Canada (PMRA 2021a, b).

In the literature review by Anderson et al. (2015), it was noted that the interim water quality guideline of 0.23 μg/L for imidacloprid (and used as a surrogate for clothianidin and thiamethoxam) would likely not be protective of the most sensitive aquatic invertebrates. The USEPA benchmarks are 0.05 μg/L of clothianidin and 0.74 μg/L of thiamethoxam, each of which was surpassed by its respective active ingredient in water samples from Canadian waters (Fig. 2,). However, Finnegan et al. (2017) calculated 5% hazard concentrations for freshwater invertebrates based on acute toxicity data and found the likelihood of thiamethoxam exceeding this level in North American waters to be <1%. Pickford et al. (2018) also concluded that mayflies and similarly sensitive aquatic insects would be unlikely to experience effects of thiamethoxam exposure, based on the 95th percentile of reported concentrations in surface waters (0.054 μg/L) falling below the 35-day NOEC of 0.3 μg/L. Likewise, Raby et al. (2018b) compared measured concentrations of neonicotinoids from Ontario waters with species-specific EC10 values and concluded clothianidin and thiamethoxam posed little to no hazard. Given the low demonstrated toxicity of clothianidin and thiamethoxam towards fish, direct effects would not be expected, but indirect food web-mediated effects are possible. Monitoring efforts should continue as the Special Review Decision label changes and new spray buffer zones are put into practice to evaluate the effectiveness of the proposed mitigations in preventing unintended consequences of clothianidin and thiamethoxam use in aquatic invertebrates.

Permethrin

Permethrin is a broad-spectrum synthetic pyrethroid insecticide used to control insect pests in a variety of agricultural crops (e.g., legumes, tobacco, grains, oilseeds), as well as for public health applications (e.g., mosquito, bedbug, and/or flea control) (PMRA 2017; USEPA 2007, 2020c). Permethrin acts by disrupting sodium channel proteins in neural cells, which alters membrane polarization (USEPA 2007).

Presence in the Aquatic Environment

Permethrin is slightly to moderately persistent, degrading slowly from the environment with aquatic half-lives ranging from 38 to 175 days (USEPA 2007; PMRA 2017). It is expected to reach the aquatic environment via spray drift or runoff, after which it adsorbs strongly to soils, sediments, and suspended solids. While this binding reduces bioavailability, there is potential for increasing concentrations of permethrin in sediments and consequent risks for benthic communities (USEPA 2007).

Relatively few monitoring data were located for permethrin (which was also noted by PMRA 2017), but for those samples collected and analysed, detection rates were typically quite low ($\leq$2%). However, many studies had a reported limit of detection (LOD) that was greater than the CWQG-PAL value of 0.004 μg/L (CCME n.d.), suggesting that concentrations present in water could exceed guideline values without being detected. The maximum reported concentrations were 1.1 μg/L, measured in Quebec rivers by Giroux (2019), and 5.04 μg/L in a sample from New Brunswick (reported by PMRA 2017) (Fig. 2). PMRA (2017) also suggested that surface water monitoring programs might be missing peak concentrations due to the location and timing of sampling.

Toxicity Towards Aquatic Organisms

Permethrin toxicity data for freshwater vascular aquatic plants were not available in the risk assessments performed by USEPA (2007) or PMRA (2017), but data were available for several algal species. Acute LC50 values ranged from 12.5 μg/L (72-h, growth inhibition, *Chlamydomonas reinhardtii)* to >100 μg/L (12-days growth inhibition and biomass reduction, *Chlorella pyrenoidsa* and *Scenedesmus quadricaudata*; PMRA 2017, Stratton and Corke 1982). For the marine alga *Dunaliella tertiolecta*, EC50 values for growth inhibition ranged from 68 to 124 μg/L. These endpoints are considerably greater than endpoints for fish or invertebrates, consistent with the assumption made by USEPA (2007) that algae and macrophytes would be less susceptible to permethrin based on its mode of action (i.e., nervous system disruption).

Permethrin can be very toxic towards other aquatic organisms, as demonstrated by its low freshwater CWQG-PAL (0.004 μg/L; CCME n.d.). As of late 2015, the USEPA had received a total of 27 reports of fish kill incidents associated with permethrin since its registration, most of which occurred prior to label changes instituting a requirement for vegetative filter strips bordering areas of application to reduce runoff (PMRA 2017). Generally, fish and invertebrates are less sensitive to transformation products of permethrin than the parent compound, so risk assessment focuses on permethrin (PMRA 2017).

For the mayfly *Hexagenia bilineata,* a 48-h EC50 of 0.1 μg/L was reported, and in a life-cycle test with *D. magna,* the NOAEC and LOAEC for reproduction and growth were 0.0047 μg/L and 0.084 μg/L, respectively (USEPA 2007, PMRA 2017). Permethrin was also very highly toxic towards the marine mysid shrimp

(*A. bahia*) resulting in a reported 96-h LC50 value of 0.019 μg/L and 30-day life-cycle LOAEC for reduced survival at 0.024 μg/L (USEPA 2007); while the LOAEC value would be expected to be lower than the 96-h LC50, these data remain among the few calculated for a marine invertebrate and thus are worth reporting for comparison. Aquatic invertebrate HC5 values were calculated using data for freshwater ($n = 25$ acute endpoints) and estuarine/marine ($n = 11$ acute endpoints) invertebrates; these were 0.019 μg/L and 0.002 μg/L, respectively (PMRA 2017). In the benthic invertebrates *C. dilutus* and *H. azteca,* reported 10-day LC50 values for permethrin in sediments were 24.5 $\mu g/g_{oc}$ (Maul et al. 2008) and 4.88 $\mu g/g_{oc}$ (Amweg et al. 2005), respectively. However, given the tendency for permethrin to sorb strongly to sediment, toxicity testing and monitoring of sediments for permethrin remain a relative knowledge gap specific to this active ingredient.

Beyond survival, exposure to permethrin caused changes in other endpoints, particularly growth, in benthic invertebrates. The EC50 for chironomid immobilization was 11.5 $\mu g/g_{oc}$ and IC50 values for significant reductions in ash-free dry mass and instantaneous growth rate were 27.4 and 27.2 $\mu g/g_{oc}$, respectively (Maul et al. 2008). Growth of *H. azteca* was significantly inhibited following 10-day exposure to concentrations ranging from 0.68 to 5.3 $\mu g/g_{oc}$ (Amweg et al. 2005).

An in-situ exposure was conducted in a Wyoming stream to investigate effects on non-target invertebrates of permethrin application via typical municipal fogging for mosquito control. Measured concentrations in the stream were <0.25 μg/L (<LOD), but resulted in a significant increase in drifting aquatic invertebrates and decrease in benthic invertebrate biomass downstream of the application site (Wurzel et al. 2020). The authors noted that a high number of taxa were included in the drifting biomass, so it was not only the traditionally "sensitive" species that were affected, but also the community assemblage (Wurzel et al. 2020).

Acute toxicity data are available for a number of fish species, including greenback cut-throat trout (*Oncorhynchus clarkistomias)*, white sucker (*Catostomus commersonii*), largemouth bass, and rainbow trout (PMRA 2017). Among the most sensitive endpoints used for risk assessment were the reported 96-h LC50 for bluegill sunfish was 0.79 μg/L and the marine Atlantic silverside (*Menidia menidia*) value of 2.2 μg/L (USEPA 2007). Reduced survival was observed in a fathead minnow full life-cycle test at an LOEC of 0.41 μg/L and in a 28-day early-life-stage test with sheepshead minnow at an LOEC of 10 μg/L (USEPA 2007, PMRA 2017). Sufficient data were available to derive HC5 values for freshwater ($n = 30$ acute endpoints) and estuarine/marine fish ($n = 10$ acute endpoints); these were 1.2 μg/L and 2.38 μg/L, respectively (PMRA 2017).

The octanol-water partition coefficient for permethrin is relatively high (log K_{ow} of 6.1), suggesting that permethrin would bioaccumulate in aquatic organisms (USEPA 2007, PMRA 2017). Field- and lab-derived bioaccumulation or bioconcentration factors range from 114 to 2,714 and 30 to 1,100, respectively. Additionally, there is evidence of both bioaccumulation in benthic invertebrates and biomagnification in marine wildlife (PMRA 2017). The current marine CWQG-PAL is 0.001 μg/L (CCME n.d.), which is consistent with the calculated HC5 values, but no North American sediment benchmarks are currently available.

Exposure Risks for Aquatic Organisms

Permethrin is among the most commonly applied pyrethroids currently used in Canada, with sales quantities <100,000 kg a.i. ((Health Canada 2017, 2020). Permethrin was deemed among the top five pesticides posing risks to the aquatic environment in the UK, based on measured concentrations and toxicity profiles (Johnson et al. 2017). It the recent re-evaluation of permethrin, PMRA (2017) concluded that concentrations in Canadian waters did occur at levels that could pose risks to invertebrates, fish, and amphibians (shown in Fig. 2), though infrequently. As such, spray buffer zones and 10 m vegetative filter strips were proposed as new mandatory requirements to protect aquatic environments (PMRA 2017), which would be expected to reduce concentrations in Canadian aquatic environments.

However, there is still a paucity of water and sediment monitoring data with appropriate detection limits for permethrin. In addition, the HC5 values calculated by PMRA for aquatic invertebrates (0.019 and 0.002 μg/L for freshwater and estuarine/marine, respectively) suggest that the current CCME marine guideline of 0.001 μg/L might not be protective of the most sensitive ~5% of non-target invertebrate species. As concluded by USEPA (2020c), the primary risks of permethrin to the aquatic environment are for aquatic invertebrates, but under certain use patterns, fish could also be affected, particularly in the context of cumulative risks from pyrethroid and pyrethrin insecticides as a class with a common mode of action. The data in Fig. 2 also demonstrate that reported effects endpoints for fish could be surpassed in Canadian waters, and effects to fish could occur both directly and via indirect effects on food. As discussed in further detail in Sect. 4.4, monitoring of permethrin in the Canadian aquatic environment requires additional considerations and methodological improvements.

3.3.3 Fungicides

Chlorothalonil

Chlorothalonil is used as both a contact fungicide for a wide range of agricultural crops (including stone fruits, highbush blueberries, potatoes) and on turf, and as a material preservative in paint (PMRA 2018b). Chlorothalonil acts by deactivating the antioxidant co-enzyme glutathione through chemical reduction which inhibits spore formation in fungi (USEPA 2012).

Presence in the Aquatic Environment

Generally, environmental fate data suggest that chlorothalonil is rapidly transformed under both aerobic and anaerobic water/sediment systems (USEPA 2012). Chlorothalonil readily degrades in the aquatic environment, with reported half-lives ranging from 0.18 to 8.8 days but there is potential for adsorption to sediment

or suspended materials (ECCC 2011). Soil half-lives (estimated between 33 and 81 days) suggest that chlorothalonil could remain available for runoff for weeks to months after application (USEPA 2012). However, the fate dataset was found to be of insufficient quality for risk assessment for many of the environmental transformation pathways and additional studies are needed (USEPA 2012).

In national surface water monitoring, chlorothalonil was among the top 5 active ingredients most likely to exceed CCME guideline values, particularly in British Columbia and the Atlantic region (ECCC 2011). It has also been detected in Arctic lakes at concentrations up to 2.8 ng/L (Hoferkamp et al. 2010).

Toxicity Towards Aquatic Organisms

Few data are available for aquatic plants, but acute toxicity EC50 values for freshwater diatoms and vascular plants (duckweed, *L. gibba*) submitted to UESPA for registration review were 12 and 640 µg/L, respectively, while NOAEC values were 3.9 and 290 µg/L (USEPA 2012). Chlorothalonil was classified as acutely very highly toxic towards fish and invertebrates in a USEPA ecological risk assessment (USEPA 2012, 2017a). A weight-of-evidence Tier 1 screening concluded that chlorothalonil does not exert toxicity via interactions with oestrogen, androgen, or thyroid pathways in fish or mammals (USEPA 2015b).

Overall, for invertebrates, crustaceans, and molluscs were sensitive to chlorothalonil at concentrations ranging from 1.8 µg/L to >10,000 µg/L (CCME 1999c). Acute (48-h EC50) and chronic (21-day NOAEC) toxicity endpoints for *D. magna* were 54 and 0.6 µg/L, respectively. The shell deposition of Eastern oyster (*C. virginica*) was affected at even lower exposure thresholds, with a reported 96-h EC50 of 3.6 µg/L (USEPA 2012). A laboratory study of field-collected soft-shell clams (*Mya arenaria*) reported a chronic LC50 of >100 µg/L, and no significant induction of haemic neoplasia at this concentration after 35 days (Pariseau et al. 2009). As reported for chlorpyrifos and phorate, exposure of molluscs to chlorothalonil resulted in significant inhibition of AChE activity. A LOEC of 10 µg/L was reported for gill AChE activity inhibition in two marine species, Pacific oyster (*Magallana gigas*) and bay mussel *M. edulis* (Haque et al. 2019). Exposure to 100 µg/L of chlorothalonil induced an eight-fold reduction in egestion rates in the aquatic gastropod *P. acuta*, but had no significant effects on another freshwater snail species (Elias and Bernot 2017). Likewise, 100 µg/L significantly induced AChE activity in the estuarine polychaete *Laeonereis acuta*, as well as increased lipid peroxidation (da Silva Barreto et al. 2018).

Acute and chronic toxicity data were available for a number of fish species. Reported literature values for acute toxicity (96 h-LC50) in rainbow trout ranged from 10.5 to 195 µg/L, and chronic effects on survival and behaviour occurred at concentrations above 2.3 µg/L (CCME 1999c). A freshwater NOEC of 1.3 µg/L was reported from a study with fathead minnow (USEPA 2012). Consistent with this, a more recently published standard full life-cycle study conducted with fathead minnow reported a reproductive NOEC of 1.4 µg/L (Hamer et al. 2019). In addition, pulsed exposures (up to 3 pulses, 6 h to 11 days in duration) at concentrations up to

15.5 µg/L did not result in significant effects on fish fecundity (Hamer et al. 2019). A recent study with zebrafish embryos reported 21.9% mortality after 96-h exposure to 50 µg/L chlorothalonil and 57.3% mortality for the same concentration of 4-hydroxychlorothalonil, suggesting that the metabolite is more acutely toxic to fish than the parent (Zhang et al. 2016). For the marine three-spine stickleback (*Gasterosteus aculeatus*), chlorothalonil 96-h LC50 concentrations ranged from 27 to 4,700 µg/L (CCME 1999c). However, USEPA deemed acute and chronic toxicity of marine fish a data gap for which there were not acceptable studies available (USEPA 2012). Since the 2012 assessment, a study of early-life stage Pacific sockeye salmon (*Oncorhynchus nerka*) was conducted to investigate effects of chlorothalonil on development timing and success. Exposure to 5 µg/L reduced survival to hatch and increased incidence of finfold deformities and delayed hatch (Du Gas et al. 2017). Treatments of both 0.5 and 5 µg/L resulted in premature emergence (Du Gas et al. 2017). Sperm motility in estuarine guppy *(Poecilia vivipara*) was similarly sensitive, with significant effects observed after 96-h exposure to 1 or 10 µg/L of chlorothalonil (Chaves et al. 2020).

The CCME guidelines for protection of aquatic life are 0.18 µg/L in freshwater and 0.36 µg/L in marine environments for chlorothalonil total (including its 4-hydroxy transformation product) (CCME 1999c, Fig. 3). These were derived from the most sensitive chronic endpoints, a 22-day LOEC of 1.8 µg/L in *D. magna*, and 96-h EC50 of 7.3 µg/L in Eastern oyster (*C. virginica*), with safety factors of 0.1 and 0.05 applied (CCME 1999c).

The reported range of octanol-water coefficients for chlorothalonil (log K_{ow} of 2.88 to 3.8, Table 4) suggests some potential for bioaccumulation (PMRA 2011). Bioconcentration studies in fish and oysters reported bioconcentration factors (BCF) of 9 to 5,812 and 2,600, respectively, suggesting that these organisms can adsorb chlorothalonil into their tissues to some extent (USEPA 2012; PMRA 2011). However, depuration from fish tissues was fairly rapid (31–35% in the first day) following cessation of exposure (USEPA 2012) and parent chlorothalonil is not expected to bioconcentrate appreciably (PMRA 2011).

Exposure Risks for Aquatic Organisms

Sales in Canada in 2017 exceeded 1,000,000 kg of chlorothalonil and 500,000 kg in 2020 (Health Canada 2017, 2020), and concentrations of chlorothalonil have been measured in Canadian water bodies above the CCME freshwater guideline, as well as above effects concentrations reported in sensitive taxa (Fig. 3). Canadian incident reports collected by PMRA provide evidence of heavy rainfall events resulting in significant runoff of chlorothalonil and concentrations reaching levels of concern for fish (PMRA 2018b). In 2016, there were three environmental pesticide incidents reported to PMRA, including one major incident, that were attributed to runoff of chlorothalonil that resulted in fish mortality (PMRA 2016). It was found that two of these incidents related to runoff from Prince Edward Island potato fields following application of chlorothalonil according to label directions (PMRA 2018b). In response, PMRA initiated a Special Review regarding the environmental fate and

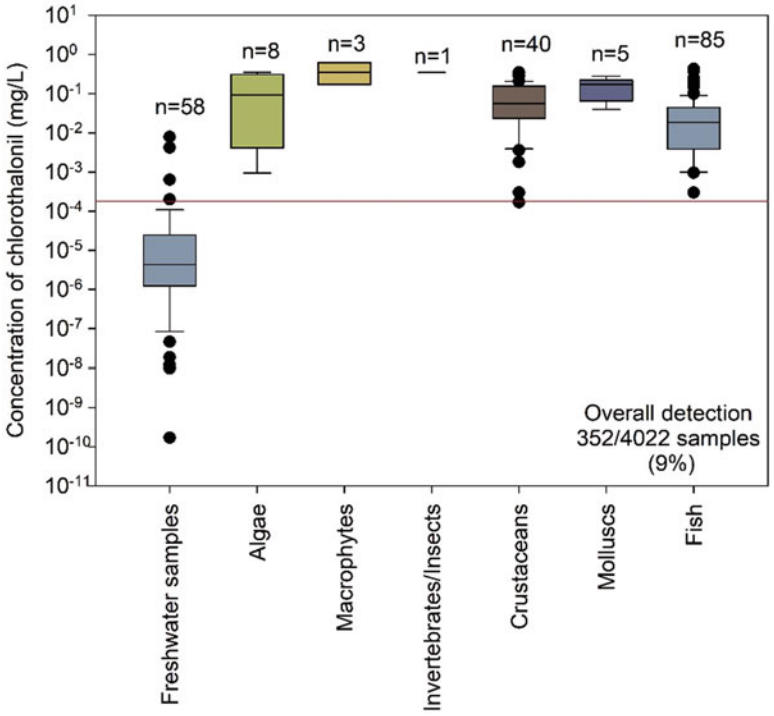

Fig. 3 Comparison of detectable concentrations of the fungicide chlorothalonil measured in Canadian freshwater samples with effective concentrations (LCXX, ECXX, LOEL, LOEC values, where XX can be any number, e.g., LC10, EC50) reported in the ECOTOX database for aquatic toxicity tests using algae, invertebrates/insects, fish, molluscs, and crustaceans. Horizontal lines within each box indicate the 25th, 50th, and 75th percentiles of measurements reported, while the tenth and 90th percentiles are indicated by the whiskers (note: concentrations <LOD are not included, and values reflect data available in raw and summary form. The *n*-value reflects the number of measured concentrations >LOD or the number of toxicity data records). The red line represents the Canadian Water Quality Guideline for the Protection of Aquatic Life (CWQG-PAL). The overall detection is the per cent of samples in which chlorothalonil was detected. The difference between *n* and the total number of samples used in the calculation of the overall detection is due to studies reporting a summary statistic of concentration, e.g., mean, the frequency of detection, and the total number of samples collected without providing the raw data

ecotoxicology of chlorothalonil with regard to agricultural and turf uses (PMRA Re-evaluation Decision RVD2018-11). A separate review of the use in paint coatings is currently underway (REV2018-02).

The risk assessment by PMRA found that there could be risks of chlorothalonil to aquatic organisms, particularly fish (PMRA 2018b). As a result, label and registration risk mitigations have been updated, including reducing the number of allowable applications per year for potatoes (from 12 to 3), in an effort to reduce risks to aquatic organisms (PMRA 2018b). Continued collection of monitoring data will

support PMRA in future assessments of the success of this approach in preventing adverse effects to receptors in Canadian aquatic habitats.

4 General Knowledge Gaps and Recommendations

For well-studied pesticides such as atrazine and chlorpyrifos, continued monitoring of both concentrations in the receiving environment and responses of communities there is required, not necessarily more research to fill data gaps. For the other active ingredients reviewed in this exercise, additional measured concentrations in water and/or sediment are needed to provide coverage across the broad expanse of receiving waters in Canada. In addition, a number of broader issues came to light that would not necessarily be specific to Canada alone or any one active ingredient. However, given the specific geographical, regulatory, and biophysical context of this country, addressing these higher-level knowledge gaps would improve our confidence in pesticide risk assessment and future refinement of the presented prioritization.

4.1 Baseline Fish and Fish Habitat Data

Monitoring of aquatic communities for abundance, diversity, and community-level variability is needed to establish baseline conditions for Canadian fisheries and place environmental chemistry and ecotoxicology data in context (Johnson et al. 2020; Johnson and Sumpter 2016). Without a strong understanding of typical conditions and natural fluctuations that can be expected within populations of fish, invertebrates, zooplankton, phytoplankton, and aquatic plants, it is not possible to detect changes as a result of pesticide exposure. This is particularly relevant in regions where agricultural pressures are strong, and thus, presence of pesticides is more likely, and where those pressures coincide with sensitive life stages (e.g., hatching and/or populations). Toxicity assays seek to, under controlled conditions, predict the concentrations of a pesticide that could induce significant changes to non-target receptors; however, these are not representative of real-world conditions. As such, ground-truthing of toxicity endpoints with field monitoring of water (and sediment, as relevant) is an important piece. While some studies have correlated measured concentrations of pesticides with observed changes in non-target aquatic invertebrate populations (e.g., Bartlett et al. 2016; Bashnin et al. 2019), this remains an important data gap for managing risks to fish, as noted previously by others (e.g., Scholz et al. 2012).

4.2 Pesticide Monitoring Data

Monitoring of surface waters for pesticides in Canada by provincial and federal agencies is a challenging undertaking requiring intentionality to address the existing gaps. For example, there is limited "on the ground" presence in the provinces of Manitoba or Saskatchewan of the federal department of Environment and Climate Change. For context, these are prairie regions with extensive agricultural areas, and Manitoba receives waters from across the Canadian and U.S. prairies/Midwest into some of the world's largest lakes (Environment Canada and Manitoba Water Stewardship 2011). While federal monitoring is limited, there is a strong ENGO-run community-based water monitoring network for Lake Winnipeg that could help to bridge the gap (Lake Winnipeg Data Stream 2021). To do so effectively, we propose that there needs to be clear communication, data-sharing understandings, and "apples to apples" sampling and reporting so that larger data products can be developed smoothly.

In another example, in the province of Ontario, the Ontario Ministry of the Environment, Conservation, and Parks is doing their best with the resources they have, but their monitoring program consists of taking 4–10 water grab samples per year from 18 to 20 sites across Ontario. The federal government has conducted pesticide monitoring in surface waters through the National Water Quality Pesticides Surveillance Program (Government of Canada 2016). However, the number of sites monitored across the country, the frequency of sampling at each site in a year, and the availability of the data is not clear (Government of Canada 2016). In contrast, the German Federal Environment Agency (Umweltbundesamt) conducts surveillance and operational monitoring (Arle et al. 2016). Surveillance monitoring assesses long-term changes in water quality over a relatively large scale, i.e., within a river catchment or sub-catchment (up to 2,500 km^2). Germany's surveillance monitoring includes more than 500 monitoring stations located in major rivers or major tributaries across the country. These sites are sampled 4–13 times in a year every 6 years (Arle et al. 2016). Operational monitoring involves more intensive sampling of water bodies that may be at greater risk of exceeding water quality guidelines. In Germany, the operational monitoring programs involve 10,000 stations along river and streams that are sampled 4–13 times in a year every 3 years (Arle et al. 2016).

The shortcomings of pesticide monitoring in Canada can be illustrated in Health Canada's PMRA listing monitoring data as a source of uncertainty in their recent risk assessment of the two neonicotinoid insecticides thiamethoxam and clothianidin to aquatic invertebrates (PMRA 2018a, c). In order to understand the risk that pesticides could pose to Canadian fisheries and aquatic ecosystems, comprehensive open-access data on exposure of Canadian aquatic ecosystems to pesticides is needed. A centrally managed, bilingual (reflective of the English and French official languages of operations in federal and provincial governments and academic institutions in Canada), up-to-date repository for pesticide data would help to integrate results from different sampling programs and allow the cumulative data to be used by all interested parties.

Canada would benefit from a collaborative and sustained monitoring program that incorporates knowledge of land use, agronomic practices, seasonal variation, pesticide fate, and sensitivity of aquatic species or communities to decide when and where to sample a representative variety of receiving water bodies. There is also a need for such programs to consider monitoring surface waters following heavy precipitation, irrigation, and/or snowmelt events, as these events have been shown to increase the probability of pesticide movement from agriculture areas into surface water (Waite et al. 1992; Guo et al. 2007; Davis et al. 2013).

4.3 Marine and Sediment Benchmarks

For many of the pesticide analytes of interest, Canadian benchmarks (freshwater and/or marine) do not yet exist to help researchers and policy makers put measured environmental concentrations into context (PMRA 2019c; Metcalfe et al. 2019; Johnson et al. 2020). In the present review, freshwater CWQG-PALs were only found for five of the seven important priority active ingredients; of these, only two (atrazine and chlorothalonil) also had a marine CWQG-PAL, and none had sediment guidelines (CCME n.d.). There are locations in Canada where coastal agriculture is established, and pesticide concentrations in these areas may be important for marine species.

Johnson et al. (2020) posited that there are gaps in terms of chronic toxicity, persistence, and bioconcentration for most registered chemicals in Europe and North America, which is consistent with the findings of the ECOTOX database review and regulatory findings for many of the active ingredients highlighted by the current exercise. This is particularly true for marine waters and for sediment, although only some current-use pesticides will be expected to partition into sediments, and only some compounds have been analysed for in sediments. In an attempt to address this gap, Nowell et al. (2016) recently developed proposed sediment-toxicity benchmarks for 129 current-use pesticides using the model amphipod *H. azteca* and insect *C. dilutus* as benthic invertebrate models. This work should continue, as appropriate for the specific physicochemical properties and use patterns for individual active ingredients.

4.4 Mixture Toxicity

Pesticides are frequently detected as mixtures in surface waters and sediments (e.g., ECCC 2011; Harris et al. 2008; Metcalfe et al. 2016, 2019), indicating that aquatic biota can be exposed to more than one active ingredient simultaneously, as well as other environmental contaminants. For example, Baldwin et al. (2016) collected water samples ($n = 709$) from 57 tributaries of the Great Lakes between 2010 and 2013 for analysis of organic contaminants. At 35% of sites and in 34% of samples,

there were ten or more compounds detected within a single sample, typically a combination of PAHs, flame retardants, caffeine, detergents, and/or pesticides. Atrazine was the most frequently detected pesticide and exceeded aquatic toxicity benchmark values at some sites, as did dichlorvos and carbaryl (Baldwin et al. 2016). Similarly, sampling in the Niagara Peninsula in 2004 to 2006 revealed frequent presence of atrazine, metolachlor, simazine, 2,4-D, mecoprop, dicamba, and clopyralid (Bartlett et al. 2016). In corn and soybean-dominated regions of Quebec, glyphosate, nicosulfuron, imazethapyr, bentazon, and dicamba were detected in over 60% of river water samples, while atrazine and metolachlor were present in nearly all samples collected (Giroux 2010).

Further compounding this issue, it is also common for pesticides to be applied as mixtures; for example, MCPA is typically applied in combination with other chemicals such as 2,4-D (USEPA 2014). Neonicotinoids are also often detected in mixtures due to widespread use and the degradation of thiamethoxam to clothianidin (Maloney et al. 2018). Concentrations of pesticides can also be very seasonally driven (i.e., by precipitation patterns and application schedule, Baldwin et al. 2016, Giroux 2015, 2019), so timing of sampling in the context of mixtures is important. Additionally, samples have also often indicated the presence of other stressors, including excess nutrients, metals, and/or pharmaceuticals and personal care products (Bartlett et al. 2016) and these multiple stressors can have additive, synergistic or even antagonistic effects on aquatic biota (Liess et al. 2019).

Several field and laboratory studies have examined potential effects of mixtures on aquatic non-target organisms. For invertebrates, for example, using *C. dilutus*, Maloney et al. (2018) demonstrated weak synergism of neonicotinoid mixtures and deviation from the concentration additive reference model. Chlorpyrifos (0.17 μg/L) and terbuthylazine (8.5 μg/L) had no effects on feeding rates of the planktonic crustacean *D. magna* during individual 28-day exposures, but when applied as a mixture, feeding rates were reduced by over 50% compared to controls (Pereira et al. 2017). In-situ caging studies with the amphipod *H. azteca* revealed effects of pesticide mixtures on survival and AChE activity. Organophosphate insecticides were deemed to be the likely drivers of toxicity, though excess nutrients and metals may have also acted in conjunction since these exceeded guideline values at some sites (Bartlett et al. 2016). At a community level, the Albemarle-Pimlico Estuarine System in the USA experienced substantial losses in submerged aquatic vegetation community which could be attributed to herbicide mixtures of atrazine, alachlor, and metolachlor (Powell et al. 2017).

While Canadian guidelines for the protection of aquatic organisms are available for some of these compounds, there remains a monumental challenge to assess the potential toxicity of mixtures, which can include pesticides, and approaches are needed to consider total pesticide burden (Metcalfe et al. 2019; Cruzeiro et al. 2017; Bopp et al. 2019; Kienzler et al. 2016). Mixture toxicity and risk assessment of multiple stressors or toxicants was universally highlighted as a top research priority at workshops held with scientists in North America (Fairbrother et al. 2019), Europe (Van den Brink et al. 2018), and Latin America (Furley et al. 2018), and represents a substantial gap in our understanding of the potential effects of current-use pesticides

on Canadian aquatic biota. One proposed response has been to determine those compounds that pose the greatest risk (or "drivers of toxicity") and test mixtures for those that would reasonably be expected to co-occur (Johnson et al. 2017; Van den Brink et al. 2018). A number of initiatives and studies have been undertaken to address chemical mixtures and their assessments in the environment (Bopp et al. 2018; PMRA 2019a, Verbruggen and Van den Brink 2010, Maazouzi et al. 2016) but further work is needed to identify mechanistically how combinations of active ingredients could have synergistic effects and under what specific field conditions. It should be noted here that all 55 pesticides that were screened into the present long list of current-use compounds, and particularly the 29 top-priority ones, may be important components of mixtures based on their use volumes and presence in the environment.

4.5 Study Design and Analytical Methods for Compounds with Low Benchmarks

Pesticides can be both present in the environment and biologically active at very low concentrations, necessitating sensitive analytical methods as part of the monitoring and risk assessment of these compounds. In the 2018–2019 annual report from PMRA, high limits of detection were among the key challenges identified (PMRA 2019a). The need for sensitive and reliable analytical chemistry methods to support contaminants of emerging concern (including pesticides and their metabolites and degradation products) was also one of the top priorities identified by Fairbrother et al. (2019) and Furley et al. (2018) in global surveys of environmental scientists.

Permethrin is one active ingredient that has posed a challenge for water quality monitoring programs and regulatory risk assessment as a result of inadequate method detection limits. In the recent re-evaluation review performed by PMRA, it was stated that, "*available Canadian water monitoring data are not robust enough to fully characterize the risks to aquatic invertebrates because 2405 of 2600 samples (93%) of the samples collected and analyzed for permethrin had limits of detection that were higher than the toxicity endpoint for aquatic invertebrates (HC5 = 0.019 µg/L). The analytical methods were not sensitive enough to capture detections of permethrin in water that could potential be a concern to aquatic invertebrates*" (PMRA 2017). Without scientifically rigorous and defensible monitoring data, true risks for environmental receptors for permethrin (and other active ingredients) cannot be determined.

Giroux (2015) noted that chlorpyrifos and diazinon presented particular challenges for achieving appropriate method detection limits due to their relatively low guideline values and potential for toxicity at fractions of a microgram per litre. For example, in Baldwin et al. (2016), the method detection limits reported for chlorpyrifos and diazinon were both 0.16 µg/L and the lab reporting limits were up to 0.32 µg/L, while the EPA Aquatic Life Benchmarks (maximum concentration) for

these compounds are 0.083 μg/L and 0.17 μg/L, respectively (USEPA 2019a), and the short-term CCME water quality guideline for chlorpyrifos is 0.02 μg/L (CCME 2008). With potential for acute toxicity of chlorpyrifos towards invertebrates at concentrations as low as 0.05 μg/L (Giddings et al. 2014), analytical methodologies need to be appropriate and sufficient to support these compounds with very low concentrations and correspondingly low toxicity endpoint concentrations.

There is a need to consider which target compounds will be analysed for and how, when sampling will take place, and the way in which samples will be collected, as these can all affect aquatic sampling results and the broader interpretation of potential risks for non-target aquatic organisms (Metcalfe et al. 2016, 2019). Grab samples typically have relatively small volumes of water, presenting a challenge to detect very low concentrations of target analytes. By comparing calculated concentrations of CECs obtained using three different passive sampling devices, Alvarez et al. (2014) concluded that a combination of samplers would provide the most useful characterization of contaminants in aquatic environments. However, the authors also noted that the use of biota for CEC monitoring (i.e., body burdens) would not be particularly informative, given the hydrophilic nature of many of these compounds (Alvarez et al. 2014).

Timing and location of sampling are important considerations for study design. For example, limited monitoring data were available for phorate from federal monitoring programs, and most results were below the limit of detection (ECCC 2011; Government of Canada 2016). However, data were absent for the Atlantic region, despite phorate being among the top pesticides sold in P.E.I. (PEI EWCC 2015; Lichtenberger 2017). While it is sold at relatively low volumes, a science-based benchmark was proposed by ECCC (2011) for phorate at 0.03 μg/L, reflecting the relatively high toxicity towards aquatic organisms. A PMRA re-evaluation review is scheduled to begin in 2020–2021, for which monitoring data for evaluating exposure risks under current-use patterns and label conditions, as well as toxicity data to fill any gaps, will be necessary.

Several studies have noted that greater concentrations of pesticides were measured in tributaries and wetlands compared to mainstem waterways (e.g., Sheedy et al. 2019; Montier-León et al. 2019), necessitating consideration of where samples should be collected from within a system. Also, it can be necessary to consider inputs from the USA or other provinces. For example, the Lake Winnipeg watershed integrates inputs from agriculturally intensive regions of the USA and Canada. Challis et al. (2018) reported that the USA seemed to be a major source of atrazine into the Red River in Manitoba. Neonicotinoid loadings also suggested inputs from both sides of the border. Like the Great Lakes, a large portion of the Red River watershed (nearly 70%) is located in the USA, but less work has been done to characterize pesticide inputs in this watershed (Challis et al. 2018).

Recommendations developed for regulatory risk assessment and monitoring of pesticides in Northern Europe by Stenrød et al. (2016) could perhaps apply to the diverse geographical, agricultural, and sociopolitical landscapes present across Canada, particularly with regard to interprovincial or international cooperation. Specifically, the authors call for establishing streamlined information sharing

platforms, evaluating current studies for their utility in risk assessment (and modifying accordingly in future studies), and characterizing the conditions present in each region to adapt local sampling programs within the umbrella of a larger coordinated program (Stenrød et al. 2016). Better cooperation and coordination in monitoring efforts across government, academic, and grass-roots organizations will improve the quality and availability of pesticide data, helping to optimize use of limited resources across the vast expanse of Canadian waters.

4.6 Habitat and Food Web-Mediated Effects on Fish

For active ingredients that are not acutely toxic to fish but instead exert greater toxicity towards plants and insects, there is generally a need to better understand whether impacts to primary producers and invertebrates will translate to indirect effects on fish populations. These indirect effects are more difficult to attribute to pesticide exposure. Given that trends in pesticides are moving towards more targeted chemistries, often with plant or invertebrate targets, greater toxicity towards habitat structural species (aquatic plants), and prey species including phytoplankton, insects, crustaceans, and/or molluscs compared with fish may be expected for many active ingredients. This was observed often in the review, but potential impacts to fish populations as a result of impacts to lower trophic levels are unclear.

The pulsed nature of pesticide use and thus input into local receiving waters necessitates consideration of chronic or sub-chronic endpoints in these sensitive organisms, as well as integrating an evaluation of recovery (Alvarez et al. 2019; Kattwinkel et al. 2015; Raby et al. 2018c). Repeated applications, mixtures, and timing (e.g., are sensitive life stages present?) should also be considered in study design to replicate conditions in the field, and models represent potential tools to help elucidate indirect effects to fish.

4.7 Current-Use and Legacy Pesticides in the Arctic

Recent studies suggest that current-use pesticides can be detected in Arctic media, but concentrations are typically relatively low compared to legacy compounds (e.g., DDT, chlordane, PCBs; Balmer et al. 2019, Brown et al. 2018, Cabrerizo et al. 2018, 2019). Generally, the physical-chemical properties common among the current-use pesticides measured in the Arctic are: high octanol-air partitioning, intermediate lipid solubility, low air-water partitioning (allowing long-range transport, perhaps some movement via ocean currents), and moderate to low water solubility (Balmer et al. 2019; summarized for currently discussed pesticides in Table 4). Modelling exercises reported by Balmer et al. (2019) suggest that nitrapyrin, picloram, nitrofen, 2,4,6-trichlorophenol, and dinoseb have the potential to reach the Arctic via long-range transport, but these have not yet been investigated in Arctic media. Balmer

et al. (2019) also reported that seven new current-use pesticides have been measured in Arctic media since 2010 – MCPA (2-methyl-4-chloro-phenoxyacetic acid), metribuzin, pendimethalin, phosalone, quizalofop-ethyl, tefluthrin, and trillate. Of these, MCPA, pendimethalin, and trillate are considered "high production volume chemicals" or those that are produced or imported at >1,000 t per year (Balmer et al. 2019). Sea-ice in the Arctic is a unique environmental compartment requiring additional consideration; it behaves as a lid over the ocean, potentially collecting pesticides which are released in a pulse when it melts (Bigot et al. 2017). In a study by Pućko et al. (2017), concentrations of dacthal, a pre-emergence herbicide used for control of grasses and some broad-leafed weeds, were deemed to pose a potential risk to Arctic marine organisms. Specifically, measured concentrations of dacthal in melt-pond water were much greater than those in seawater under ice, and the entry of the pulse into seawater was observed to coincide with spring blooms of under-ice phytoplankton, potentially posing a risk. To monitor which current-use pesticides may become contaminants in the Arctic, strategic environmental monitoring should be ongoing and increased effort in modeling which pesticides may reach the Arctic would be beneficial.

5 Conclusions

The specific active ingredients reviewed represent some of the most widely applied and detected pesticides in Canadian waters based upon the available sales and monitoring information. As would be expected, pesticide classes generally exhibited aquatic toxicity consistent with their uses and targets: herbicides were typically most toxic to algae or macrophyte species, insecticides were highly toxic to invertebrate species, and fungicides were toxic across taxa. As such, monitoring for effects in the aquatic environment should also be strategic to determine baseline conditions and changes in those organisms or classes most likely to be affected by the active ingredient(s) of interest. Generally, we found that toxicity data were available to support regulatory review, but gaps exist in our understanding of fate, species sensitivity distribution, and/or surface water concentrations for many of the active ingredients identified as among the top-priority active ingredients. It should be noted that the top-priority pesticides highlighted in this review represent a snapshot in time, and this exercise can and should be revisited to reflect changing use patterns, toxicity and monitoring data availability, and regulation. In addition, our selection of the top 7 national priority pesticides does not preclude consideration of the balance of the 55 active ingredients screened into the review, especially those scoring in the top half or third of the list. Some of these may be particularly relevant under mixture scenarios or where their local or regional use may be high. Through this review, it became clear that there are many opportunities for collaborations across Canadian provincial and federal agencies, as well as with academic and industry partners, to fill important data gaps that have been identified here and elsewhere. Doing so will support informed pesticide use in Canada and ongoing efforts to avoid unintended impacts to the Canadian aquatic environment.

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