Preliminary Assessment

Triclosan

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Health Canada
Environment Canada

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Synopsis

Triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol) is used as a material preservative and as an antimicrobial ingredient in a variety of consumer products to stop the growth of bacteria, fungi and mildew and to deodorize.

The potential sources of exposure to triclosan for Canadians include consumer products treated with or containing triclosan (including, but not limited to, cosmetic products, treated textiles and food contact materials, such as cutting boards and countertops), drinking water contaminated with triclosan, breast milk and contaminated household dust.

Exposure of the general population to triclosan was characterized using the available biomonitoring data for triclosan from the US National Health and Nutrition Examination Surveys (NHANES). In the absence of Canadian-specific data for the general population, the biomonitoring data for the US population were used. These data encompass exposures to triclosan from all potential sources and routes, and are considered the most accurate estimates of total exposure of the general population in Canada to triclosan given the similarities in registered uses under the Pest Control Products Act (PCPA) and Food and Drugs Act and the availability of products treated with or containing triclosan on the US and Canadian markets. Additional Canadian biomonitoring data were used to characterize the exposure of children under the age of 6 years to triclosan.

Risk to human health from exposure to triclosan is estimated by comparing mean and upper-bounding exposure estimates in humans with critical effect levels in health effects studies conducted in laboratory animals in order to derive margins of exposure (MOEs). For the general population, comparison of the estimated mean and upper-bound daily intakes with critical effect levels in mice (based on liver effects) resulted in MOEs between 700 and 13 000. Children under the age of 6 years were not included in NHANES; therefore, exposure for this subpopulation was derived separately and included potential exposures via breast milk, household dust and mouthing of triclosan-treated plastic products. Comparison of exposure estimates with the critical effect levels resulted in MOEs greater than 988. These MOEs were considered adequate to address uncertainties in the health effects and exposure databases for triclosan.

Due to its use in many consumer products, triclosan reaches wastewater treatment plants (WWTPs), where it is partially removed from wastewater. It is released to aquatic ecosystems as part of WWTP effluents. Since some triclosan partitions to sludge during the wastewater treatment process, triclosan also reaches terrestrial ecosystems when sewage sludge is spread on land.

Triclosan is not persistent in air, water, soil or sediment under aerobic conditions. It does not meet any of the criteria for persistence under the Persistence and Bioaccumulation Regulations of the Canadian Environmental Protection Act, 1999 (CEPA 1999) or the Toxic Substances
Management Policy. However, its continual input to surface water through WWTP effluents is likely to result in its continuous presence in receiving aquatic ecosystems. Based on bioconcentration data in fish, triclosan is bioaccumulative and meets the criteria for bioaccumulation under the *Persistence and Bioaccumulation Regulations* and the Toxic Substances Management Policy. There is also evidence of accumulation in algae, macrophytes and invertebrates.

Since triclosan is expected to be continuously present in certain aquatic ecosystems, organisms that live in these environments are likely to be exposed to this substance on a chronic basis. Triclosan has a high inherent toxicity to a variety of aquatic organisms, such as algae, macrophytes, invertebrates, amphibians and fish. Adverse effects on these organisms include reduction in growth, reproduction and survival. Based on the numerous toxicity data available, a predicted no-effect concentration of 115 ng/L was derived. Triclosan may also interfere with the action of thyroid hormones in amphibians at environmentally relevant concentrations.

Measured data for concentrations of triclosan at WWTPs as well as in receiving surface water were used to estimate exposure of aquatic organisms. Measured concentrations of triclosan in surface water and a nationwide exposure scenario based on concentrations of triclosan in the influent of numerous WWTPs indicate that triclosan may have harmful effects on aquatic organisms, especially in the vicinity of certain WWTPs.

While triclosan does not seem to accumulate in terrestrial organisms, there is some potential for adverse effects on soil organisms exposed to it through the spreading of sewage sludge on agricultural soils.

**Proposed Conclusions under CEPA 1999**

Based on the adequacy of the MOEs between estimates of aggregated exposure to triclosan and critical effect levels, it is proposed that triclosan is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Based on the information presented in this preliminary assessment, it is proposed that triclosan is entering or may enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity. Therefore, it is proposed that triclosan meets the criterion set out under paragraph 64(a) of CEPA 1999. It is also proposed that triclosan meets the criterion for bioaccumulation but not the criteria for persistence as set out in the *Persistence and Bioaccumulation Regulations*.

**Proposed Conclusions under the PCPA**

Based on the preliminary risk assessment, the Pest Management Regulatory Agency (PMRA) proposes to conclude that the use of pest control products containing triclosan in Canada does not pose an unacceptable risk to human health. While use of these products may contribute to
environmental exposure to triclosan, given the registered uses and the life cycle of triclosan-treated products (e.g., treated plastics, textiles, leather, paper and rubber), pest control products are not expected to contribute significantly to the risks to aquatic organisms identified in the preliminary assessment. Therefore, PMRA proposes to conclude that the use of pest control products containing triclosan does not pose an unacceptable risk to the environment. No further risk mitigation measures will be required at this time, as the current registrant of triclosan has chosen not to maintain its Canadian registration. Should a registrant seek to re-enter the Canadian market, further data may be required to supplement the current risk assessment.

Next Steps

This preliminary assessment of triclosan is both a consultation statement for the purposes of subsection 28(2) of the PCPA and a screening assessment for the purposes of section 74 and subsection 77(1) of CEPA 1999. It summarizes the science assessment for triclosan and presents the basis for these proposed conclusions. A proposed Risk Management Scope under both these Acts is being published at the same time as this preliminary assessment. The proposed Risk Management Scope is a preliminary outline of the options being examined for the management of triclosan based on the proposed conclusions of this preliminary assessment, and it briefly describes the sources of release and exposure, uses and sectors for which risk management is being considered.

Health Canada and Environment Canada will accept written comments on this preliminary assessment and the proposed Risk Management Scope up to 60 days from the date of publication of these documents. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).
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1. Introduction

Triclosan (5-chloro-2-(2,4-dichlorophenoxy) phenol) is used as a material preservative and as an antimicrobial ingredient in a variety of consumer products to stop the growth of bacteria, fungi and mildew and to deodorize. In Canada, triclosan can be regulated under the Pest Control Products Act (PCPA) (Canada 2002), the Food and Drugs Act (Canada 1985) and the Canadian Environmental Protection Act, 1999 (CEPA 1999) (Canada 1999).

CEPA 1999 requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that meet the categorization criteria set out in the Act to determine whether the substances present or may present a risk to the environment or to human health. A screening assessment involves an analysis of a substance using available information to determine whether the substance is harmful to human health or the environment as defined in section 64 of CEPA 1999. Based on the results of a screening assessment, the Ministers can propose taking no further action with respect to the substance, adding the substance to the Priority Substances List for further assessment or recommending that the substance be added to the List of Toxic Substances in Schedule 1 to CEPA 1999 and, where applicable, the implementation of virtual elimination.

Triclosan is a substance on the Domestic Substances List and was included in the pilot project launched in 2001 to refine the process for conducting screening assessments. Triclosan was identified as a priority since it met the ecological categorization criteria set out in the Act. Triclosan as a pest control product was also scheduled for re-evaluation under Health Canada’s Pest Management Regulatory Agency (PMRA) pesticide re-evaluation program that considers potential risks, as well as value, of pesticide products to determine whether they meet modern standards established to protect human health and the environment.

Health Canada and Environment Canada conducted a scientific assessment of available information relevant to the assessment of triclosan. This preliminary assessment provides the basis for proposed conclusions under CEPA 1999 and the PCPA.

The assessment of human health effects was informed by foreign reviews conducted by the:

- US Environmental Protection Agency (US EPA 2008a,b,c,d);
- European Union (EU) Scientific Committee on Consumer Products (SCCP 2009) and Scientific Committee on Consumer Safety (SCCS 2011);
- Australian Department of Health and Ageing National Industrial Chemicals Notification and Assessment Scheme (NICNAS 2009).

Exposure of the Canadian population to triclosan was assessed by Health Canada using the available biomonitoring data for triclosan from the US National Health and Nutrition
Examination Surveys (NHANES). In the absence of Canadian-specific data for the general population, the biomonitoring data for the US population was used. These data encompass exposures to triclosan from all potential sources and routes, and are considered the most accurate estimates of total exposure of the general population in Canada to triclosan given the similarities in registered uses and availability of consumer products on the US and Canadian markets. Additional assessments were conducted by Health Canada to fully characterize the human health effects and exposure of the general population of Canada. Data obtained as of September 2011 were considered in this document.

Data relevant to the ecological assessment of triclosan were identified in original literature, review documents, and commercial and government databases and indices. In addition to retrieving the references from reviews and a literature database search, efforts were made to contact researchers, academics, industry and other government agencies to obtain relevant information on triclosan. Data obtained as of November 2011 were considered in this document.

The critical studies that form the basis for 1) proposing whether the substance meets the criteria under section 64 of CEPA 1999 and 2) the proposed conclusion under the PCPA have been critically evaluated by Health Canada and Environment Canada. The preliminary assessment does not present an exhaustive review of all available data; rather, it presents the most critical studies and lines of evidence pertinent to the conclusions.

This preliminary assessment examines technical information and develops proposed conclusions as required under CEPA 1999 and the PCPA. The human health portions of this assessment have undergone external written peer review or consultation. Comments on the technical portions relevant to human health were received from scientific experts selected and directed by Toxicology Excellence for Risk Assessment, Risk Sciences International Inc. and ToxEcology - Environmental Consulting Ltd. The ecological portions of this assessment have been subject to an external review by Canadian and international experts selected from government organizations, academia and stakeholders. The conclusions presented in this document are those of Health Canada and Environment Canada and do not necessarily reflect the opinions of the external reviewers.

The preliminary assessment for triclosan includes the proposed conclusion as to whether triclosan meets any of the criteria in section 64 of CEPA 1999 as required for substances that met the categorization criteria under CEPA 1999. Further, this document contains the proposed conclusion regarding the acceptability of current pest control products containing triclosan regulated under the PCPA.
2. Substance Identity, Properties and Uses

2.1 Substance Identity

Phenol, 5-chloro-2-(2,4-dichlorophenoxy), commonly known as triclosan, is a chlorinated aromatic compound that has functional groups representative of both ethers and phenols. Information on its identity, including names and chemical structure, is presented in Table 1.

Table 1. Substance identity for triclosan

<table>
<thead>
<tr>
<th>CAS RN</th>
<th>3380-34-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCPA RN (technical-grade active ingredient)</td>
<td>28553</td>
</tr>
<tr>
<td>DSL name</td>
<td>Phenol, 5-chloro-2-(2,4-dichlorophenoxy); triclosan</td>
</tr>
<tr>
<td>IUPAC</td>
<td>2,4,4’-Trichloro-2′-hydroxydiphenyl ether</td>
</tr>
</tbody>
</table>

Inventory names¹

- Phenol, 5-chloro-2-(2,4-dichlorophenoxy) (AICS, ASIA-PAC, NZIoC, PICCS, SWISS, TSCA)
- Triclosan (EINECS, PICCS, SWISS)
- 2,4,4’-Trichloro-2′-hydroxydiphenyl ether (ENCS)
- 5-Chloro-2-(2’,4’-dichlorophenoxy) phenol (ENCS)
- 5-Chloro-2-(2,4-dichlorophenoxy)phenol (ECL)
- 2’,4’,4-Trichloro-2-hydroxydiphenyl ether
- 2’,4’,4-Trichloro-2-hydroxydiphenyl ether
- 2-Hydroxy-2,4,4′-trichlorodiphenyl ether
- 2,2′-Oxybis(1′,5′-dichlorophenyl-5-chlorophenol)
- 2-Hydroxy-2′,4,4′-trichlorodiphenyl ether
- 3-Chloro-6-(2,4-dichlorophenoxy)phenol
- 4-Chloro-2-hydroxyphenyl 2,4-dichlorophenyl ether

Other names

- Amicor; Aquasept; Bacti-Stat soap; Bactonix; Biofresh; Cansan TCH; CH 3565; CH 3635; DP 300; Cloxifenolum; Endure 200; Gamophen; Irgacare CF 100; Irgacare MP; Irgacide LP 10; Irgaguard B 1000; Irgaguard B 1325; Irgasan; Irgasan CH 3565; Irgasan DP 30; Irgasan DP 300; Irgasan DP 3000; Irgasan DP 400; Irgasan PE 30; Irgasan PG 60; Lexol 300; Microban Additive B; Microban B; NM 100; Oletron; Sanitized XTX; Sapoderm; SterZac; TCCA; THDP; Tinosan AM 100; Tinosan AM 110; Ultra Fresh NM 100THDP; Vinyzene DP 7000; Yujiexin; ZerZac; Zilesan UW

Chemical group

- Organic

Chemical subgroup

- Phenols

Chemical formula

\( \text{C}_{12}\text{H}_7\text{Cl}_3\text{O}_2 \)
2.1.1 Impurities of Human Health and Environmental Concern

Triclosan contains low levels of Toxic Substances Management Policy (TSMP) Track 1 contaminants: polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs).

In Canada, triclosan is included on Health Canada’s List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as the Cosmetic Ingredient Hotlist or simply the Hotlist). The Hotlist is an administrative tool that Health Canada uses to communicate to manufacturers and others that certain substances, when present in a cosmetic at a certain concentration level, may contravene the general prohibition found in section 16 of the Food and Drugs Act. Under Canadian legislation, cosmetics that contain substances that are harmful to the user cannot be sold. The Hotlist recommends that manufacturers of oral cosmetic products containing triclosan must ensure that polychlorinated dibenzo-p-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF) impurities should not exceed 0.1 ng/g (0.1 part per billion [ppb]) for 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) and 2,3,7,8-tetrachlorodibenzofuran and 10 µg/g (10 parts per million [ppm]) for total other PCDD/PCDF impurities, with no individual impurity greater than 5 µg/g (5 ppm).

The presence of TSMP Track 1 substances in pest control products is managed in accordance with Health Canada’s strategy to prevent or minimize releases, with the ultimate goal of virtual elimination, as described in Regulatory Directive DIR99-03 (PMRA 1999). It should be noted that PCDDs and PCDFs were the subject of an assessment as part of the Priority Substances List of CEPA 1999. These substances are considered both persistent and bioaccumulative as well as “toxic” as defined under paragraphs 11(a) and 11(c) of CEPA 1988 (Canada 1990). The relative importance of triclosan as an environmental source of PCDDs is expected to be low compared
with other sources on a national scale. These other sources include large-scale burning of municipal and medical waste, production of iron and steel, backyard burning of household waste, fuel burning (including diesel), wood burning (especially if the wood has been chemically treated), electrical power generation and tobacco smoke (Health Canada 2005).

### 2.2 Physical and Chemical Properties

Triclosan is soluble in water and has low volatility (Table 2). It is not expected to volatilize from a water surface, as indicated by its Henry’s Law constant. It should ionize to some extent at environmentally relevant pH values (i.e., pH 6–9 for water bodies in Canada), as indicated by its acid dissociation constant (pKₐ) of 8.1.

### Table 2. Physical and chemical properties of triclosan

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Data type</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting point (°C)</td>
<td>54–57</td>
<td>Experimental</td>
<td>Sax and Lewis 2000</td>
</tr>
<tr>
<td></td>
<td>54–57.3</td>
<td>Experimental</td>
<td>O’Neil 2001</td>
</tr>
<tr>
<td>Boiling point (°C)</td>
<td>374</td>
<td>Modelled</td>
<td>MPBPWIN 2008</td>
</tr>
<tr>
<td>VP at 20°C (Pa)</td>
<td>$5.33 \times 10^{-4}$ (4 \times 10^{-6}$ mmHg)</td>
<td>Experimental</td>
<td>O’Neil 2001</td>
</tr>
<tr>
<td>WS at 20°C (mg/L)</td>
<td>10</td>
<td>Experimental</td>
<td>Yalkowsky and He 2003</td>
</tr>
<tr>
<td>Solubility in other solvents</td>
<td>Readily soluble in alkaline solutions and many organic solvents</td>
<td>Experimental</td>
<td>O’Neil 2001</td>
</tr>
<tr>
<td>HLC at 25°C (Pa·m³/mol)</td>
<td>$1.54 \times 10^{-2}$ (HLC = VP/WS)</td>
<td>Experimental</td>
<td>O’Neil 2001; Yalkowsky and He 2003</td>
</tr>
<tr>
<td></td>
<td>($1.52 \times 10^{-7}$ atm·m³/mol)</td>
<td>Modelled</td>
<td>HENRYWIN 2008</td>
</tr>
<tr>
<td></td>
<td>$5.05 \times 10^{-4}$ (Bond method)</td>
<td>Experimental</td>
<td></td>
</tr>
<tr>
<td></td>
<td>($4.99 \times 10^{-9}$ atm·m³/mol)</td>
<td>Modelled</td>
<td></td>
</tr>
<tr>
<td>log $K_{ow}$</td>
<td>4.76</td>
<td>Experimental</td>
<td>NITE 2006</td>
</tr>
<tr>
<td>log $K_{oa}$</td>
<td>9.97</td>
<td>Modelled</td>
<td>KOAWIN 2008</td>
</tr>
<tr>
<td>log $K_{oc}$</td>
<td>3.34–4.67</td>
<td>Experimental</td>
<td>Singer et al. 2002; Wu et al. 2009; Xu et al. 2009; Karnjanapiboonwong et al. 2010</td>
</tr>
<tr>
<td>log $K_d$</td>
<td>1.00–2.45</td>
<td>Experimental</td>
<td>Wu et al. 2009; Xu et al. 2009; Karnjanapiboonwong et al. 2010</td>
</tr>
<tr>
<td>pKₐ</td>
<td>8.1 (acid form)</td>
<td>Experimental</td>
<td>Reiss et al. 2002</td>
</tr>
</tbody>
</table>

Abbreviations used: HLC, Henry’s law constant; $K_d$, soil/water partition coefficient; $K_{oa}$, octanol/air partition coefficient; $K_{oc}$, soil organic carbon/water partition coefficient; $K_{ow}$, octanol/water partition coefficient; pKₐ, dissociation constant; VP, vapour pressure; WS, water solubility

### 2.3 Triclosan Use Patterns in Canada

Triclosan is used as a medicinal ingredient in drug products and as a non-medicinal ingredient in cosmetics, natural health products and drug products (CNS 2011; DPD 2011; LNHPD 2011;
2011 personal communication from Therapeutic Products Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). Triclosan is also registered as a pest control product for use as a material preservative.

2.3.1 Cosmetic Products

Approximately 1600 cosmetic products containing triclosan have been notified to Health Canada, including face cream, face and eye makeup, hand cream (barrier cream), deodorant sticks/sprays, fragrances, body lotion, tanning products, skin cleansers, shaving preparations and shampoos (CNS 2011; 2009 personal communication from Consumer Product Safety Directorate, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced).

In Canada, triclosan is included on Health Canada’s Cosmetic Ingredient Hotlist, which indicates concentrations limits of triclosan in mouthwash (0.03%) and in other cosmetic products (0.3%). This is consistent with limits set by the EU, which allows triclosan in cosmetic products at 0.3% as a preservative (European Commission 2010). Furthermore, by virtue of section 24 of the Cosmetic Regulations (Canada 2007) of the Food and Drugs Act, the Cosmetic Ingredient Hotlist indicates that oral cosmetic products containing triclosan should include a label statement indicating that children under the age of 12 years should not use the products and that mouthwashes should include a label statement to the effect of “Avoid swallowing”.

2.3.2 Natural Health Products

Triclosan is listed in the Natural Health Products Ingredients Database as an acceptable non-medicinal ingredient in natural health products where it functions as an antimicrobial preservative, provided that it does not contribute to the claim of the overall product (NHPID 2011). The Natural Health Products Ingredients Database lists concentrations of less than or equal to 0.03% in mouthwashes and 0.3% in topical products, as per concentrations indicated in the Cosmetic Ingredient Hotlist (Health Canada 2011; NHPID 2011). As a non-medicinal ingredient, triclosan is listed in the Licensed Natural Health Products Database and is present in approximately 13 licensed natural health products (e.g., toothpaste, foot gel, acne treatment, body spray, skin cleanser and lotion) (LNHPD 2011; 2009 personal communication from Natural Health Products Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced).

2.3.3 Drug Products

Approximately 130 drug products with an assigned Drug Identification Number, primarily antiseptic skin cleansers, were listed on Health Canada’s Drug Product Database as of December 2011 (DPD 2011). Health Canada’s antiseptic skin cleanser monograph states that the permitted concentration of triclosan as an active ingredient can range from 0.1% to 1.0% (Health Canada 2006). In drug products, triclosan has a maximum concentration of 1% as an active ingredient.
Triclosan is also present as a medicinal ingredient in some toothpastes at a concentration of 0.3% and functions as an anti-gingivitis agent (DPD 2011).

**2.3.4 Pest Control Products**

In Canada, there are six triclosan pest control products (i.e., one technical and five commercial end-use products) registered for use as a material preservative to control the growth of microorganisms (Appendix 1). Domestic-class pest control products containing triclosan are not registered in Canada.

Triclosan end-use products can be applied as material preservatives during the manufacturing process to textiles (including leather) and paper at a maximum rate of 0.375% active ingredient (a.i.) by weight of final product. According to the current Canadian end-use product label, triclosan can also be applied to textiles by padding or spray (in the picker) at a rate of 0.056% a.i. by weight of final product and to plastic, rubber material, textiles, leather and paper by spraying a 0.7% a.i. solution until thoroughly wet.

**2.4 Triclosan Use Patterns in the United States**

In the United States, triclosan uses are regulated by both the US Food and Drug Administration (US FDA) and the US EPA.

The US FDA regulates the use of triclosan when incorporated into soaps, toothpastes, deodorants, laundry detergents, fabric softeners, facial tissues, antiseptics for wound care and medical devices.

The US EPA regulates the antimicrobial uses of triclosan when used as a material preservative in 1) consumer products, including textiles (clothing, mattresses, footwear, upholstery fabrics), plastic (toys and toothbrushes), floor wax emulsions, polyethylene, polyurethane, polypropylene, paper, rubber materials, paints, adhesives and caulks; 2) commercial, institutional and industrial premises (conveyor belts, fire hoses, dye bath vats and ice-making machines); and 3) residential and public access premises, including direct applications to heating, ventilating and air conditioning coils, but also as a material preservative in insulations, concrete mixtures, grouts, brooms, toilet bowls and urinals.

As per the *Federal Insecticide, Fungicide, and Rodenticide Act* (FIFRA) requirements, the US EPA re-evaluated triclosan to determine whether it met current scientific and regulatory standards. A risk management decision was published by the US EPA in the 2008 Reregistration Eligibility Decision (RED). Triclosan was found to be eligible for reregistration as a pesticide provided that the recommended mitigation measures were implemented (US EPA 2008a).

The 2008 RED included a human health risk assessment based on the 2003–2004 biological monitoring data for triclosan from the US NHANES. The biomonitoring data measuring the concentration of triclosan in urine provided a good indication of total exposure of an individual
to triclosan resulting from all potential sources of triclosan in residential settings. Following the publication of the RED, a comprehensive review of additional information regarding the effects of triclosan on thyroid hormone homeostasis (US EPA 2011a) as well as the updated estimates of human exposure based on the 2007–2008 biomonitoring data (US EPA 2011b) were published by the US EPA in 2011.

Considering registered uses and availability of consumer products on the US and Canadian markets, it was concluded that the US exposure assessments would be representative of the Canadian situation and would appropriately inform the Canadian human exposure assessment.
3. Human Health

3.1 Toxicology Profile of Triclosan

Reviews of the triclosan toxicological database conducted by the US EPA (2008b), the Australian Department of Health and Ageing (NICNAS 2009), which was adopted by the Organisation for Economic Co-operation and Development at the Screening Information Data Set (SIDS) Initial Assessment Meeting (SIAM) 30 in April 2010 (OECD 2011), and the EU SCCP (2009) and SCCS (2011) were used to inform Health Canada’s human health hazard evaluation. Where appropriate, secondary review references are cited. Additional review of pivotal toxicological studies was undertaken by Health Canada when deemed necessary. A review of additional US EPA Office of Research and Development toxicological studies investigating the effects of triclosan on thyroid hormones, presented by the US EPA to the US FIFRA Scientific Advisory Panel (US EPA 2011a), was also considered. Furthermore, more recently published studies and reviews were considered and incorporated into the assessment when determined relevant for risk assessment purposes.

3.1.1 Metabolism and Toxicokinetics

Data available on the absorption, distribution, metabolism and elimination of triclosan in mice, rats, hamsters, rabbits, dogs and baboons suggest that there are differences in the clearance profile between species.

Oral metabolism studies conducted in hamsters with radiolabelled triclosan showed that 60–80% of the radioactivity was excreted in the urine, while 12–35% was excreted with feces. Intravenous and oral administration at low doses resulted in similar patterns of elimination in male and female hamsters. The major urinary metabolite detected after oral and intravenous administration in hamsters was the glucuronide conjugate of triclosan, while the major fecal metabolite was parent triclosan in all oral dose groups. Distribution patterns in the orally and intravenously dosed animals were similar between the single- and repeated-dose groups, with the highest residual radioactivity found in the kidney, liver, lung and plasma. Urinary excretion was also found to be a major route of elimination following oral, intravenous and intraduodenal administration in rabbits and oral administration in baboons. The major urinary metabolite in the baboon was a glucuronide conjugate (US EPA 2008b).

Following oral administration of radiolabelled triclosan in mice, rats and dogs, triclosan was rapidly absorbed and eliminated primarily through the feces via biliary excretion. Urinary excretion was secondary to that in the gastrointestinal tract. This excretory pattern was consistent following intravenous and intraduodenal administration in these species. Following repeated oral administration in the mouse, the concentrations were higher in the liver than in plasma, indicating that the liver was the target organ. Triclosan was found to be metabolized to both glucuronide and sulfate conjugates. Although different ratios of the individual glucuronide and
sulfate conjugates were observed among species, no unique species-specific metabolites have been identified to date. Repeated high-dose administration of triclosan was also shown to change the ratio of these two metabolites in hamsters, mice and monkeys, with the sulfate shown to predominate following chronic oral administration (SCCP 2009). Primary excreted compounds in the urine following single oral exposures in mice included the unmetabolized parent compound and two parent conjugates (sulfate and glucuronide conjugates of triclosan); fecal excretion was primarily that of the free parent compound, as only small amounts of glucuronide were detected, and no sulfate was detected. In addition, four conjugated metabolites (M5, M6, M8 and M9) accounting for 5% of the administered dose were detected in kidney, plasma and liver extracts in the mouse. The major biliary product in the rat was the glucuronide conjugate, with some unmetabolized parent compound. The major urinary metabolite in the rat after oral and intravenous administration was the glucuronide conjugate of triclosan. In the rat, the parent compound could be detected in the brain, indicating that triclosan can cross the blood–brain barrier (US EPA 2008b). Whole-body autoradiography studies in the mouse and rat showed the presence of two peak concentrations in the plasma following single or repeated dosing, indicating enterohepatic circulation. As such, these species would experience an enhanced local exposure to triclosan in the liver and gastrointestinal tract (SCCP 2009).

In humans, triclosan is rapidly absorbed and distributed, with plasma levels increasing rapidly within 1–4 hours. Following all routes of administration, absorbed triclosan is nearly totally converted to glucuronic and sulfuric acid conjugates due to a pronounced first-pass effect, with only trace amounts of the parent compound detected in the plasma. Elimination is rapid, with a terminal plasma half-life of 21 hours (SCCP 2009). Similar to baboons, hamsters, monkeys and rabbits, the major route of excretion is via urine (24–83%, according to Sandborgh-Englund et al. 2006), with the majority of the compound appearing as the glucuronide conjugate. Excretion of triclosan in the feces represents a smaller portion of the administered dose (10–30%), and triclosan is present as the free unchanged compound. The human oral and dermal data provide no evidence of bioaccumulation potential (SCCP 2009).

There is evidence that the toxicokinetics of triclosan are different in humans and rodents; however, the interspecies differences are difficult to quantify based on the available toxicokinetic data. Data examining area under the plasma concentration versus time curve (AUC) and maximum concentrations in plasma ($C_{\text{max}}$) in rodents were typically generated with doses 10-fold higher or more than those doses used in humans. In general, $C_{\text{max}}$ values were lower in humans than in rodents, but AUC data were more variable, depending on the dosing regime:

- For a single oral dose of 2 mg/kg body weight (bw) per day in rats and mice, AUC values ranged from 63.9 µg·h/mL (rats) to 166 µg·h/mL (mice), and $C_{\text{max}}$ values ranged from 4.77 µg/mL (rats) to 19.48 µg/mL (mice); single oral doses ranging from 0.017 to 0.17 mg/kg bw per day in adult humans yielded AUC values from 0.2 to11.2 µg·h/mL and $C_{\text{max}}$ values from 0.023 to 0.974 µg/mL (SCCP 2009).
- For repeated doses of 2 mg/kg bw per day (14 days) in rats, an AUC value of 77.4 µg·h/mL and a $C_{\text{max}}$ value of 4.49 µg/mL were reported. In adult humans, an AUC value of 219
µg·h/mL and a $C_{\text{max}}$ of 0.878 µg/mL were reported after daily swallowing of a dental slurry containing 0.3 mg/kg bw per day for 14 days. Similar doses in toothpaste (expelled after brushing) resulted in an AUC of 34 µg·h/mL and a $C_{\text{max}}$ of 0.146 µg/mL in adult humans (SCCP 2009).

In dermal absorption studies, triclosan was shown to be relatively well absorbed through the skin in all tested species. In vivo absorption in humans following dermal application of products containing triclosan ranged from 11% to 17%, depending on the formulation, applied dose, duration of exposure, type of skin and skin occlusion (Maibach 1969; Stierlin 1972; Queckenberg et al. 2010). In vitro dermal absorption studies using human skin and various formulations containing triclosan showed dermal absorption values ranged from 7% to 30% (Moss et al. 2000; SCCP 2009).

In the in vivo dermal absorption studies in rats, the extent of dermal absorption ranged from 4% to 93%, depending on formulation, applied dose and duration of exposure (Black and Howes 1975; Chun Hong et al. 1976; Ciba-Geigy 1976a; Moss et al. 2000; SCCP 2009). Lower absorption ranging from 4% to 28% was reported with triclosan in shampoo, soap suspension or a cream formulation. Higher absorption was observed with triclosan in an aqueous solution or in petroleum jelly (SCCP 2009).

In addition, the US EPA reported that an in vivo dermal absorption study in the rabbit showed absorption of up to 48% of an applied dose (US EPA 2008b). The EU SCCP noted that a dermal absorption study with diapers washed in a solution containing triclosan indicated that the absorption of triclosan through the skin was very low in rabbits (SCCP 2009).

### 3.1.2 Acute Toxicity

Technical triclosan was non-toxic via oral and dermal routes and of moderate toxicity via the inhalation route in rats. It was moderately irritating to the rabbit eye and mildly to moderately irritating to the rabbit skin. Triclosan is not considered a skin sensitizer based on the results from a guinea pig test (US EPA 2008b).

### 3.1.3 Subchronic Toxicity

In a 28-day dietary study, exposure of MAGf[SPF] mice (five of each sex per dose) to technical triclosan at a dose of 6.48 or 135.59 mg/kg bw per day in males and 8.25 or 168.78 mg/kg bw per day in females resulted in no effects on mortality, body weight or feed consumption. A no-observed-adverse-effect level (NOAEL) of 6.48 mg/kg bw per day (males) and 8.25 mg/kg bw per day (females) was established based on changes in clinical chemistry (increases in alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase activities; significant decrease in globulin fraction) and liver pathology (an increased incidence of liver cell necrosis, hemosiderosis of Kupffer cells in the vicinity, cytoplasmic vacuoles in hepatocytes, liver cell hypertrophy) observed at the lowest-observed-adverse-effect level (LOAEL) of 135.59 mg/kg bw per day for males and 168.78 mg/kg bw per day for females (US EPA 2008b).
In a 90-day toxicity study, CD-1 mice (15 of each sex per dose) were exposed to triclosan (99.7% a.i.) in the diet at a dose of 0, 25, 75, 200, 350, 750 or 900 mg/kg bw per day. Treatment-related effects were observed at all dose levels in a dose-related manner, as evidenced by clinical pathology, organ weight changes and increased incidence or severity of histopathological lesions (especially of the liver). A statistically significant and generally dose-related reduction in measures of oxygen-carrying capacity, including reduced red blood cells, hemoglobin and hematocrit, was noted in all dose groups, reaching a level of adversity at a dose of 200 mg/kg bw per day. Lower dose groups demonstrated adaptive changes in measures of red blood cells, with deficits less than 10% change from control values. Supporting evidence of a toxicological effect on the hematopoietic system was noted as a regenerative response in the spleen by an increased severity (but not incidence) of splenic hematopoiesis at doses of 200 mg/kg bw per day and greater in males and 750 mg/kg bw per day and greater in females. Statistically significant but not dose-related increases in enzymes indicative of liver injury included aspartate aminotransferase at 750 mg/kg bw per day and above, alanine aminotransferase at 350 mg/kg bw per day and above (males) and 750 mg/kg bw per day and above (females) and alkaline phosphatase (not dose related) at 200 mg/kg bw per day and above (males) and 900 mg/kg bw per day (females). An increase in triglyceride level was observed in males at 350 mg/kg bw per day and above and in females at 750 mg/kg bw per day and above. A decrease in cholesterol level (statistically significant, but not dose related) was reported at 25 mg/kg bw per day and above (NICNAS 2009; SCCP 2009). Given the known increase in peroxisomal fatty acid β-oxidation in mice exposed to triclosan, this is not unexpected (SCCP 2009). At 25 mg/kg bw per day, a slight increase in liver/gallbladder weights in females (7% and 9%, absolute and relative to brain, respectively) was not considered significant; no change in liver/gallbladder weights in males was reported at this dose. Absolute and relative liver/gallbladder weights increased 1.3- to 3.0-fold at 75 mg/kg bw per day and above in both sexes, and the increases were statistically significant. A slight increase in the number of animals with liver lesions (vacuolization observed in 2/15 males and 1/15 females; individual cell necrosis observed in 3/15 females) was observed at 25 mg/kg bw per day (Trutter 1993). This dose level was considered a LOAEL by other agencies (NICNAS 2009; SCCP 2009). Based on the observation that there was no increase in the severity of liver lesions when compared with the control group at this dose level, but a further increase in the incidence of liver lesions (including an increase in both incidence and severity of vacuolization) observed at 75 mg/kg bw per day and above, a NOAEL of 25 mg/kg bw per day was established by Health Canada for this study.

In a 90-day oral study, Sprague-Dawley rats (25 of each sex per dose) received triclosan (purity not reported) at a dietary concentration of 0, 1000, 3000 or 6000 ppm, equivalent to 0, 65, 203 and 433 mg/kg bw per day in males and 0, 82, 259 and 555 mg/kg bw per day in females. A statistically significant decrease in relative spleen weight (11–12%) and increase in relative kidney weight (12–17%) were seen at the middle dose and above in males and females, respectively. A statistically significant and dose-dependent decrease in cholesterol level in the presence of mild centrilobular cytomegaly was observed in males at the middle dose and above. A NOAEL of 1000 ppm (equivalent to 65 and 82 mg/kg bw per day for males and females, respectively) was established based on histopathological changes in the liver observed at the
LOAEL of 3000 ppm, equivalent to 203 and 259 mg/kg bw per day in males and females, respectively (US EPA 2008b; NICNAS 2009).

In a 91-day study, Beagle dogs (three of each sex per group) were administered daily gelatin capsules containing triclosan at a dose of 0, 25, 50, 100 or 200 mg/kg bw per day. Limited hematology, clinical biochemistry and urinalysis investigations were undertaken, together with a limited histopathological examination. One female died at 25 mg/kg bw per day, two males at 100 mg/kg bw per day and four animals (two females and two males) at 200 mg/kg bw per day. Diarrhea was seen in animals at 25 mg/kg bw per day and above, and the severity and frequency increased with dose. Emesis was also seen in some animals at all doses. Body weight changes were not determined. Hematology and clinical chemistry assessment revealed a number of “abnormal” values in individual animals at 25 mg/kg bw per day and above suggestive of liver dysfunction, as were urinalysis findings of bile salts and polymorphonuclear leukocytes in the urine at all doses. Statistically significant and dose-related increases in combined male and female relative organ weights were seen only in the pancreas (35–50%), kidneys (38–44%) and adrenals (12–29%) at 100 mg/kg bw per day and above. However, histopathological changes were seen in only one of these organs, the kidney. At necropsy, focal interstitial nephritis (a kidney disorder in which the spaces between the kidney tubules become swollen or inflamed) was seen in one female at 100 mg/kg bw per day and in one male and one female at 200 mg/kg bw per day. Additionally, “unusual” Kupffer cell activation, bile retention and/or necrosis were seen in the liver of one female, two males and two animals of each sex at 25, 100 and 200 mg/kg bw per day, respectively. In addition, pathological fat was seen in the liver of one or more male and female animals at all doses. Severe liver damage was associated with bone marrow hyperplasia and was seen in one female at 25 mg/kg bw per day, one male and one female at 50 mg/kg bw per day, two males and two females at 100 mg/kg bw per day and two females at 200 mg/kg bw per day. All of these histopathological changes were absent in control animals. Since clinical signs of toxicity, liver damage and enhanced hematopoietic activity were observed at the lowest dose tested (LOAEL of 25 mg/kg bw per day), a NOAEL was not established (NICNAS 2009; SCCP 2009).

In a 90-day study, Beagle dogs (four of each sex per group) were administered triclosan in the diet at a dose equivalent to 0, 5, 12.5 or 25 mg/kg bw per day. No deaths or effects on body weight gain, feed consumption or water consumption were seen. Pasty to thin feces were observed occasionally in all groups and were considered not treatment related. Compared with controls, no treatment-related effects were seen in hematology, clinical chemistry or urinalysis parameters at the top dose, the only dose level examined. No treatment-related histological findings or effects on organ weight were seen at any dose level. Thus, the NOAEL was determined to be 25 mg/kg bw per day in this 90-day study (NICNAS 2009). SCCP (2009) did not establish a NOAEL for this study, as the highest dose did not produce any treatment-related effects.

In a 90-day oral toxicity study, Beagle dogs were administered daily gelatin capsules containing triclosan at a dose of 0, 12.5, 25, 50 or 100 mg/kg bw per day. Body weight gain in females at 12.5 mg/kg bw per day was significantly lower in relation to untreated controls, but body weight
decimals were not observed at higher doses in either sex. There were treatment-related morphological changes in the livers (including focal acidophilic to granular degeneration of the cytoplasm of hepatocytes) of most animals in the 25, 50 and 100 mg/kg bw per day dose groups. One male receiving 100 mg/kg bw per day died after 23 days on test, and another 100 mg/kg bw per day male was sacrificed in extremis after 26 days. One female receiving 50 mg/kg bw per day was sacrificed in extremis after 57 days. Each of the three animals that died or was sacrificed during the study displayed weight loss, anorexia, lethargy and symptoms of jaundice 3–5 days prior to death. Upon autopsy, histopathological examination of tissues revealed that the jaundice was a result of hepatotoxicity. A NOAEL of 12.5 mg/kg bw per day was established based on treatment-related liver morphology changes observed at the LOAEL of 25 mg/kg bw per day (US EPA 2008b).

In a 13-week study, Syrian Golden hamsters (15–20 of each sex per group) were administered triclosan in the diet at a dose equivalent to 0, 75, 200, 350, 750 or 900 mg/kg bw per day. Additional groups of 10 animals of each sex receiving 0, 75, 350 or 900 mg/kg bw per day were sacrificed at week 7 of exposure. No treatment-related deaths were reported in the study. Polyuria (increased urination; statistically significant and dose related) was observed at 350 mg/kg bw per day and above. A slight to moderate increased incidence of blood in urine, which was statistically significant, was reported at 200 mg/kg bw per day and above, along with statistically significant decreases in urine specific gravity (2–3%) and osmolarity (31–65%). Increased coagulation times and statistically significant changes in red blood cell morphology were reported at 750 mg/kg bw per day and above. Statistically significant increases in relative liver (21–36%) and brain weights (14–38%) were observed at 750 mg/kg bw per day in the absence of histopathological changes. Dose-related nephrotoxicity (tubular casts, basophilia and dilation) was reported at 350 mg/kg bw per day and above. Significant increases in the incidence and severity of erosion to the stomach were seen at 750 mg/kg bw per day and above. Consequently, a NOAEL of 75 mg/kg bw per day was established, based on effects on urinalysis parameters together with blood in the urine in both sexes at the LOAEL of 200 mg/kg bw per day (NICNAS 2009). The SCCP considered 75 mg/kg bw per day to be a no-observed-effect level (NOEL) (SCCP 2009).

In a 90-day dermal toxicity study, Sprague-Dawley rats (10 of each sex per group) were exposed to triclosan in propylene glycol by dermal application at a dose level of 10, 40 or 80 mg/kg bw per day for 6 hours/day during the study. An additional group of 10 animals of each sex per group received 80 mg/kg bw per day for 90 days followed by a 28-day recovery period. Dermal irritation was observed at the application site in all treated animals. Minor adaptive changes in hematology parameters (decrease in red blood cells, hemoglobin and hematocrit) in males and decreased triglyceride (males) and cholesterol levels (males and females) were noted at 80 mg/kg bw per day. Also, an increased incidence of occult blood in the urine (2/9 males vs. 0/10 controls, 3/9 in recovery males, 1/10 in recovery females) and a slight focal degeneration of cortical tubules (3/10 males vs. 1/10 controls) were observed at 80 mg/kg bw per day (Trimmer 1994). The NOAEL of 40 mg/kg bw per day established by the US EPA (2008b) was accepted by Health Canada. A NOAEL of 80 mg/kg bw per day (excluding dermal irritation) was determined by other agencies (NICNAS 2009; SCCP 2009).
In a 21-day inhalation toxicity study, rats (nine of each sex per dose) were exposed (nose only) to triclosan (purity not reported) 5 days/week for 2 hours/day at a dose level of 0, 3.21, 7.97 or 24.14 mg/kg bw per day for males and 0, 4.51, 9.91 or 30.81 mg/kg bw per day for females. Twelve high-dose animals (five males and seven females) died during the course of the study. For females, a NOAEL of 4.51 mg/kg bw per day was established based on treatment-related effects, including slightly decreased body weight, body weight gain, feed consumption and thrombocytes, as well as increased leukocytes and alkaline phosphatase activity and a slightly increased incidence of respiratory irritation, observed at the next dose (LOAEL of 9.91 mg/kg bw per day). In males, treatment-related effects (decreased thrombocytes and total serum proteins, increased alkaline phosphatase activity) were observed at the lowest dose tested (Ciba-Geigy 1974). Although the US EPA established a LOAEL of 3.21 mg/kg bw per day based on the above-mentioned effects in males, Health Canada determined that the observed effects were minor, and a NOAEL of 3.21 mg/kg bw per day was established.

3.1.4 Reproductive Toxicity

In a two-generation reproduction study in the rat, triclosan (purity not reported) was administered to Sprague-Dawley rats (25 of each sex per dose) in the diet at a dose of 15, 50 or 150 mg/kg bw per day for 10 weeks prior to mating and through postnatal day (PND) 21 for both generations. No treatment-related effects were seen on mortality, clinical signs or estrous cyclicity. In the F₀ generation, there were no significant decreases in parental body weight during pre-mating. Body weight in high-dose F₀ females during lactation was significantly decreased on PND 7 (statistically significant). An increased incidence of liver discoloration in 50 and 150 mg/kg bw per day parental F₀ males was observed at necropsy, but no histopathological assessment was undertaken. No effects on reproductive performance were found in the F₀ generation. Pups of the F₀ generation (F₁ pups) showed statistically significant decreases in mean body weight on PNDs 14 and 21 at the 150 mg/kg bw per day dose. Slightly increased pup mortality was observed on PNDs 0–3 in high-dose pups, resulting in a decreased viability index (82% compared with 90% in controls), as well as an increased incidence of dilated renal pelvis at the 150 mg/kg bw per day dose in F₁ pups. In F₁ parental animals, significantly lower group mean body weights were observed during pre-mating at the 150 mg/kg bw per day dose (statistically significant). Gestational body weights in high-dose F₁ females were significantly decreased by 12% during the period of gestation, with a significant negative trend for gestational days 1, 7, 14 and 20. There were no differences in number of pregnant animals, mean gestation duration or mean precoital (pairing to insemination) interval in F₁ females. In pups of the F₁ parental generation (F₂ pups), a slight increase in number of pups found dead or missing was observed at 150 mg/kg bw per day (84% compared with 87% in controls), as well as a statistically significant, but slight (less than 10%), decrease in mean body weights in both sexes compared with controls. The weaning index was decreased at the high dose in F₂ pups, and total litter deaths were increased. A parental NOAEL of 50 mg/kg bw per day was established based on reduced mean body weight observed at the LOAEL of 150 mg/kg bw per day. A reproductive/developmental NOAEL of 50 mg/kg bw per day was established based on reduced
pup weights and reduced pup viability in both generations at the LOAEL of 150 mg/kg bw per day) (US EPA 2008b). Similar findings were reported by NICNAS (2009) and SCCP (2009).

3.1.5 Developmental Toxicity

In a prenatal developmental toxicity study in rabbits, triclosan (100% a.i.) was administered by gavage to pregnant female New Zealand White rabbits (18 per group) on gestational days 6–18 at a dose level of 0, 15, 50 or 150 mg/kg bw per day. Signs of maternal toxicity at the high dose (150 mg/kg bw per day) consisted of statistically significant decreases in body weight and feed consumption and statistically significant decreases in body weight gain over the period of treatment. A maternal NOAEL of 50 mg/kg bw per day was established based on decreased body weight gain and feed consumption during treatment observed at the LOAEL of 150 mg/kg bw per day. There were no statistically significant differences in the mean number of resorptions or the resorption/implant ratio between the control and treatment groups. Fetal body weights of both sexes were comparable between the control and treatment groups. No treatment-related external, visceral or skeletal malformations or variations were observed in fetuses. A developmental NOAEL of 150 mg/kg bw per day, the highest dose tested, was established (US EPA 2008b; NICNAS 2009; SCCP 2009).

In a prenatal developmental toxicity study in rats, triclosan (99.8% a.i.) was administered by gavage to pregnant female Wistar rats (30 rats per group, 60 per group in controls) on days 6–15 of gestation at a dose level of 30, 100 or 300 mg/kg bw per day. At 300 mg/kg bw per day, maternal toxicity was evident and consisted of transient diarrhea, statistically significant decreases in body weight gain during treatment, and reduced feed consumption and increased water consumption from onset of treatment through gestation. Based on these findings, a maternal NOAEL of 100 mg/kg bw per day (LOAEL of 300 mg/kg bw per day) was established. There was no evidence of prenatal toxicity at any dose level in this study; therefore, a developmental NOAEL of 300 mg/kg bw per day, the highest dose tested, was established (US EPA 2008b; NICNAS 2009; SCCP 2009).

In a developmental toxicity study in mice, triclosan (99% a.i.) was administered via the diet to 25 CD-1 (ICR)BR female mice at a target dose level of 0, 10, 25, 75 or 350 mg/kg bw per day from day 6 to day 15 of gestation. The maternal toxicity appeared to be minor, with liver weight increases (7% and 17% absolute and relative to brain weight, respectively; statistically significant) and 1 out of 25 dams with a tan-coloured liver at 75 mg/kg bw per day. The NOAEL of 25 mg/kg bw per day for maternal toxicity may represent a marginal NOAEL in view of these findings. Developmental effects were noted at 350 mg/kg bw per day as a statistically significant increased incidence of variations (characterized as irregular ossification of the phalanges). Irregular ossification of interfrontal bones (an extra bone between the frontal bones of the skull) was reported at 75 mg/kg bw per day; however, the biological significance of this finding was unclear, and incidences were within historical control ranges (NICNAS 2009). Fetal weight was decreased by 14% and 18%, respectively, at the 75 and 350 mg/kg bw per day target dose levels. The decreased fetal body weight at 75 mg/kg bw per day was considered treatment related, and a
developmental NOAEL of 25 mg/kg bw per day was established (US EPA 2008b). NICNAS (2009) determined the NOAEL to be 75 mg/kg bw per day.

### 3.1.6 Chronic Toxicity

In a 1-year toxicity study, triclosan was administered to baboons (seven of each sex per dose) by capsule at a dose level of 0, 30, 100 or 300 mg/kg bw per day. Signs of vomiting were reported at 100 mg/kg bw per day (one female on day 196, one male on day 341) and at 300 mg/kg bw per day (one male on day 17). Failure to eat was reported at 100 mg/kg bw per day and above. Dose-related increases in incidences of diarrhea (4–6 hours after dosing or during the night) occurred within the first 90 days of exposure in 1 out of 14 animals at 30 mg/kg bw per day, in 7 out of 14 animals at 100 mg/kg bw per day and in all animals at the top dose. Statistically significant increases in mean relative kidney and liver weights were reported at 300 mg/kg bw per day and in mean absolute brain weight from 30 mg/kg bw per day (no treatment-related histopathological changes observed) (NICNAS 2009). At necropsy, an effect on the lining of the stomach was observed at the high dose. As seen with other studies, administration of triclosan via gavage or capsule appears to cause irritation and/or enteritis, which confounded the interpretation of the results. A systemic NOAEL of 30 mg/kg bw per day was established based on clinical signs of toxicity observed at the LOAEL of 100 mg/kg bw per day (US EPA 2008b; NICNAS 2009). The SCCP considered 30 mg/kg bw per day to be a NOEL (SCCP 2009).

In a chronic toxicity/carcinogenicity study conducted in male and female Sprague-Dawley rats (85 of each sex per dose), triclosan (99% a.i.) was administered for 104 weeks in the diet at a dose of 0, 300, 1000 or 3000 ppm (equivalent to 0, 15.3, 52.4 or 168.0 mg/kg bw per day in males and 0, 20.0, 66.9 or 217.4 mg/kg bw per day in females, according to US EPA 2008a). An additional group of animals (20 of each sex) received triclosan in the diet at 415.0 mg/kg bw per day (males) or 519.3 mg/kg bw per day (females) for 52 weeks. No treatment-related effects on mortality, clinical toxicity, ophthalmology, urinalysis or gross pathology were observed at any dose level tested. No carcinogenic potential was demonstrated for triclosan in this study. Slightly but significantly decreased erythrocyte counts were observed in males at the middle (8%) and high doses (11%) at week 78 and at all doses (10%, 14% and 11%) by the end of the study (week 104). Hemoglobin concentrations at the high dose level (6%) and hematocrit at the middle and high dose levels (9%) were decreased in males at week 78, but these effects were not statistically significant at week 104 and were below 10%, and they were therefore considered adaptive. Erythrocyte counts were decreased in females at 66.9 mg/kg bw per day and above at week 78 (8% at the middle dose and 6% at the high dose), but were not statistically significant at week 104 and were below 10%, and they were therefore considered adaptive. It should be noted that hematology parameters in control animals (both male and female) dropped by 8–23% from week 13 to week 104. Minor increases or decreases in alanine aminotransferase and aspartate aminotransferase activities were noted in males, but the changes never reached levels of biological significance. Slight changes in clinical chemistry (triglycerides, blood urea nitrogen and glucose) were noted (females only) at the earliest test period of week 13. From week 26 onward, the female clinical chemistry results were comparable to those for controls, suggesting that effects noted in subchronic testing may be transient and that animals can compensate...
adequately with prolonged dosing. Histopathology was limited to 7 out of 85 males with hepatocellular hypertrophy and 12 out of 85 males with chronic progressive renal calculi (kidney stones), a common aging disease in rats. Between two and five males or females (out of 85 per group) demonstrated hepatocellular necrosis, determined to be not related to treatment by a pathology working group. The SCCP (2009) considered the NOAEL to be 12–17 mg/kg bw per day based on changes in hematology. However, these changes were considered toxicologically insignificant, and a NOAEL of 52.4 mg/kg bw per day was established based on significant decreases in body weight in male and female rats and non-neoplastic changes of the liver in males at the LOAEL of 168.0 mg/kg bw per day (US EPA 2008b). Similar findings were reported by NICNAS (2009).

In an 18-month carcinogenicity bioassay, triclosan was administered to CD-1 mice (50 of each sex per dose) in the diet at a dose level of 0, 10, 30, 100 or 200 mg/kg bw per day. An additional group of mice (20 of each sex per dose) was exposed for 6 months. There were no significant signs of clinical toxicity at any dose level and no significant effects of treatment on group mean body weight, feed consumption, ophthalmology or urinalysis. A dose-related increase in the activities of alanine aminotransferase and alkaline phosphatase was observed in male and female mice at 100 mg/kg bw per day and above in both the 6-month and 18-month dose groups. Significant decreases in both albumin and total protein levels were observed in males at 6 months and in females at 18 months at doses of 100 mg/kg bw per day and above. Serum cholesterol level was markedly reduced at all doses, including the 10 mg/kg bw per day dose, but the decrease was not considered to be adverse at this dose in the absence of frank liver toxicity. Treatment-related hematological effects included increased reticulocyte count in males and platelet count in males and females at 200 mg/kg bw per day. Mean liver weights (absolute and relative) were increased in both male and female mice at 30 mg/kg bw per day and above at 18 months and at 100 mg/kg bw per day and above at the 6-month interim sacrifice. A dose-related increase in severity of hepatocellular hypertrophy was observed in both male and female mice at 30 mg/kg bw per day and above. A statistically significant increase in the incidence of hepatocellular adenoma and/or carcinoma was observed in male and female mice at 100 mg/kg bw per day and above. The incidence was dose related in both sexes. The combined incidence of adenoma and carcinoma was 12%, 20%, 34%, 64% and 84% for males and 0%, 2%, 6%, 12% and 40% for females at 0, 10, 30, 100 and 200 mg/kg bw per day, respectively. The incidence of adenoma/carcinoma combined exceeded the historical control incidence at 10 mg/kg bw per day (17% for males, 1% for females) but became statistically significant at 30 mg/kg bw per day for males and at 100 mg/kg bw per day for females. Consequently, a NOAEL of 10 mg/kg bw per day was established, based on an increased incidence of liver neoplasms in males and females at the LOAEL of 30 mg/kg bw per day (US EPA 2008b). The SCCP did not establish a NOAEL for this study based on findings of liver effects at all doses and considered triclosan a peroxisome proliferator in mouse liver (SCCP 2009).

In a chronic toxicity/carcinogenicity study in the Bio F1D Alexander Syrian hamster, triclosan (99.5% a.i.) was administered in the diet to 70 animals of each sex per group at a target dose level of 0, 12.5, 75 or 250 mg/kg bw per day for up to 90 weeks. No treatment-related clinical signs of toxicity were observed during the first 80 weeks of the study. After this time, high-dose
males showed deterioration in their general clinical condition, with signs of lethargy, hunched posture, pallor, thin appearance and unsteady gait. High-dose males had an increase in mortality after week 80, which correlated with their deteriorating condition. A statistically significant decrease was seen in body weight gain in males receiving 250 mg/kg bw per day at the end of the study (compared with controls), and a slight, although statistically significant, decrease (3%) was seen in feed consumption in females at 250 mg/kg bw per day (NICNAS 2009). At terminal sacrifice, no dose- or treatment-related gross findings were observed in males. However, in the control, low-dose, mid-dose and high-dose female groups, white nodules in the forestomach, pale kidneys and irregular cortical scarring of the kidney were observed in some animals. Microscopically, a statistically significant increase in the incidence of nephropathy was observed in high-dose males and females as compared with control animals and was considered the main factor contributing to death in animals that died before study termination. In males tested with the high dose of triclosan, statistically significant increases in the incidences of absent spermatozoa and abnormal spermatogenic cells and reduced numbers of spermatozoa were observed. An increased incidence of partial depletion of one or more generations of germ cells within the testis was also observed. Lesions in the stomach were significantly increased in high-dose males and females at termination (focal atypical hyperplasia of the fundic region in males, statistically significant increases in distended gastric glands with or without debris in females). No evidence of potential carcinogenicity of triclosan was observed in this study. A NOAEL of 75 mg/kg bw per day was established, based on decreased body weight gain, increased mortality (males), nephropathy and histopathological findings in the stomach and testes at the LOAEL of 250 mg/kg bw per day (US EPA 2008b; NICNAS 2009).

No chronic dermal toxicity study is available. In 2008, the US FDA determined that, taking into consideration the long-term dermal exposure resulting from application of products containing triclosan, the carcinogenic potential of triclosan following dermal application is unknown. Since the only repeated-exposure dermal study, a 90-day rat study, showed dose-dependent signs of severe dermal irritation, such as erythema (redness of the skin), edema (swelling), desquamation (skin peeling) and eschar formation, the US FDA made a recommendation to the US National Toxicology Program for a dermal carcinogenicity study (US FDA 2008).

3.1.7 Genotoxicity

Triclosan has been tested for mutagenic activity in several assays, including two bacterial reverse mutation tests, an in vitro mammalian cell gene mutation test, in vitro mammalian chromosomal aberration tests, a mammalian bone marrow chromosomal aberration test and an unscheduled deoxyribonucleic acid (DNA) synthesis assay in mammalian cells in culture.

Triclosan was negative at all doses in both bacterial reverse mutation tests (dose levels ranging from 0 to 5 µg/plate) and the in vitro mammalian cell gene mutation test (dose levels ranging from 0 to 20 µg/mL), with and without metabolic activation. Triclosan was found to induce a dose-related increase in the yield of cells with abnormal chromosome morphology in the in vitro mammalian chromosomal aberration test with dose levels ranging from 0 to 250 µg/mL for 18–20 hours. The most frequently observed type of chromosome damage was exchange figures.
However, no signs of structural chromosomal aberrations were observed in the *in vivo* bone marrow chromosomal aberration test. Triclosan was also negative in an unscheduled DNA synthesis assay in rat primary hepatocytes at the concentrations tested (US EPA 2008b).

### 3.1.8 Carcinogenicity Potential in Humans

The US EPA’s Cancer Assessment Review Committee of the Office of Pesticide Programs reviewed the carcinogenic potential of triclosan based on a chronic toxicity/carcinogenicity study in hamsters, carcinogenicity studies in mice and rats, metabolism and mutagenicity studies, as well as additional documentation regarding the significance of the mouse study results for human health. The Cancer Assessment Review Committee determined that there was a sufficient weight of evidence supporting activation of peroxisome proliferator-activated receptor alpha (PPARα) as the primary mode of action (MOA) for triclosan-induced hepatocarcinogenesis in the mouse. Mutagenic and cytotoxic MOAs were ruled out based on the overall negative *in vivo* genotoxicity database for triclosan and the lack of evidence supporting a sustained regenerative cellular proliferative response, respectively.

The proposed MOA for liver tumours in mice was found to be theoretically plausible in humans. Although human cells contain PPARα, its activity is approximately 10 times lower than that of mouse hepatocytes. Thus, the human liver would be less susceptible to peroxisome proliferation than the mouse liver. Further, peroxisome proliferators (including hypolipidemic drugs) that are known carcinogens in rodents have not been shown to be carcinogenic in other species, including humans. Consequently, based on quantitative species differences in PPARα activation and differences in toxicokinetics, triclosan-induced carcinogenicity by the proposed MOA was considered by the US EPA to be quantitatively implausible and unlikely to take place in humans. In accordance with the US EPA Final Guidance for Carcinogen Risk Assessment, the US EPA’s Cancer Assessment Review Committee classified triclosan as “Not likely to be carcinogenic to humans” (US EPA 2008c).

### 3.1.9 Neurotoxicity

In a 14-day neurotoxicity study in rats exposed to triclosan at a dose level of 0, 100, 300, 1000 or 2000 mg/kg bw per day, a slight inhibition of movement, decreased muscular tone, polydypsia (excessive thirst) and polyuria (increased urination) were observed at 300 mg/kg bw per day, with more pronounced signs at 1000 mg/kg bw per day. No changes in brain weights or histopathology and no changes in peripheral nerves were observed at any dose level tested (US EPA 2008b).

### 3.1.10 Thyroid Effects

In a published short-term (4-day) study by Crofton et al. (2007), weanling female Long-Evans rats (27–29 days old) were exposed via oral gavage to triclosan at a dose of 0, 10, 30, 100, 300 or 1000 mg/kg bw per day. Decreased serum total thyroxine (T₄) concentrations and increased liver weights were reported in exposed animals. Serum T₄ concentrations were reduced in a dose-
dependent manner by 28%, 34% and 53% at 100, 300 and 1000 mg/kg bw per day, respectively. No significant changes were seen at 10 or 30 mg/kg bw per day. The study authors did not report thyroid-stimulating hormone (TSH) levels. The study NOEL was 30 mg/kg bw per day, and the lower 95% confidence limit on the benchmark dose (BMDL) (calculated by the study authors) for a 20% reduction in T4 was 35.6 mg/kg bw per day.

In a published study by Zorrilla et al. (2009), the effect of triclosan on the thyroid was investigated using the pubertal assay. Weanling male rats were dosed via oral gavage for 30 days starting on PND 23. Animals were exposed to 0, 3, 30, 100, 200 or 300 mg/kg bw per day. Mean serum T4 concentrations were decreased in a dose-dependent manner by 47%, 50%, 80% and 81% at 30, 100, 200 and 300 mg/kg bw per day, respectively. Triiodothyronine (T3) was affected only at 200 mg/kg bw per day, while TSH was not affected statistically significantly at any dose. Mean liver weight in male rats was increased significantly at 100 mg/kg bw per day and above, suggestive of hepatic enzyme induction and increased clearance of thyroid hormones. However, the study noted no induction of liver uridine diphosphate-glucuronyl transferase at 3 or 30 mg/kg bw per day. In the same study, decreased serum testosterone was observed at 200 mg/kg bw per day only, although the onset of puberty (balano-preputial separation) and growth of androgen-dependent reproductive tissues (including epididymides and testis) were not altered. At the highest dose, a few animals showed testicular degeneration (multinucleated giant cells within the semiferous tubule epithelium); however, this change was minimal and not correlated with decreased testosterone or testis weight in the individual animals. The study NOEL was 3 mg/kg bw per day, and the BMDL (calculated by the study authors) for a 20% reduction in T4 was 7.23 mg/kg bw per day.

In a published study by Paul et al. (2010a), exposure of weanling female Long-Evans rats by oral gavage to triclosan at a dose of 10, 30, 100, 300 or 1000 mg/kg bw per day for 4 days starting on PND 27 resulted in dose-dependent decreases in thyroid hormones, more pronounced for serum T4 than for T3. Total T4 decreased to 43% of control at 1000 mg/kg bw per day, and total T3 decreased to 89% and 75% of control at 300 and 1000 mg/kg bw per day, respectively, while TSH levels remained unchanged. The study authors speculated that triclosan-induced hypothyroxinemia was likely due to the observed upregulation of hepatic enzymes (i.e., induction of cytochrome P450 2B1/2 [CYP2B1/2] and pentoxyresorufin O-depentylase activity) and increased glucuronidation and sulfation of thyroid hormones. In contrast, the lack of CYP1A1 (ethoxyresorufin O-deethylase) induction indicated that the minor dioxin contaminants found in the triclosan sample used in this study (2,8-dichlorodibenzo-p-dioxin [2,8-DCDD] and 2,4,8-trichlorodibenzo-p-dioxin [2,4,8-TriCDD]) did not induce aryl hydrocarbon receptor–mediated effects on phase I and phase II hepatic enzymes. The NOEL was 30 mg/kg bw per day, and the BMDL (calculated by the study authors) for a 20% reduction in T4 was 65.6 mg/kg bw per day.

Two additional studies investigated the effects of triclosan on thyroid hormone levels in pubertal and maternal animals, as well as offspring.
In a published study by Stoker et al. (2010), the effects of triclosan on thyroid hormones were investigated in a 21-day female pubertal assay and an immature rat uterotrophic assay (3-day exposure). Wistar rats were dosed orally by gavage after weaning with triclosan doses up to 300 mg/kg bw per day (PNDs 22–42 in the prepubertal assay; for 3 days in the uterotrophic assay, either alone or co-treated with ethinylestradiol at 3 mg/kg bw per day). A dose-dependent decrease in thyroid hormone levels was observed at doses of 37.5–150 mg/kg bw per day following the 21-day exposure, and free serum T₄ was decreased at 75 and 150 mg/kg bw per day. There was no significant difference in the mean serum TSH concentration following a 21-day exposure. In the pubertal exposure study, the highest dose of triclosan (150 mg/kg bw per day) resulted in a significant earlier age of onset of vaginal opening and increased uterine weight, which, according to the authors, was indicative of an estrogenic effect. There was also a non-significant decrease in age of first estrus at the highest dose. In the uterotrophic assay measuring the estrogenicity of the compound, triclosan enhanced the uterine response to ethinylestradiol, but did not alter uterine weight or histopathology when tested alone at doses as high as 300 mg/kg bw per day. The NOEL for the decrease in total serum T₄ level was 9.4 mg/kg bw per day; the lowest-observed-effect level (LOEL) was 18.75 mg/kg bw per day in this study (no BMDL was calculated).

In a published study by Paul et al. (2010b), pregnant Long-Evans rats were exposed to triclosan at a dose of 0, 30, 100 or 300 mg/kg bw per day by oral gavage from gestational day 6 through PND 22. Perinatal maternal exposure to triclosan resulted in hypothyroxinemia in dams and young neonates and a 31% and 27% decrease in serum T₄ levels in dams (PND 22) and pups (PND 4) at 300 mg/kg bw per day, respectively. No changes in serum T₄ levels were reported in pups on PND 14 or PND 21 at any dose level. TSH levels were not reported by the study authors. At 300 mg/kg bw per day, triclosan concentrations in fetal and neonatal serum as well as liver were observed to decrease with animal age from PND 4 to PND 21, suggesting that the lack of effect on T₄ at PND 14 and PND 21 is due to lower exposures at these ages (US EPA 2011a). According to the authors, toxicokinetic and/or toxicodynamic factors were likely to contribute to a reduced exposure or a reduced toxicological response during the lactation period. The NOEL was 100 mg/kg bw per day for both dams and pups. The BMDLs calculated by the study authors for a 20% reduction in T₄ were 104 mg/kg bw per day and 58 mg/kg bw per day for dams and pups, respectively.

The proposed adverse outcome pathway for the effects of triclosan on the thyroid hormone system includes the activation of the pregnane X receptor (PXR) and/or the constitutive androstane receptor (CAR) in rat liver by triclosan as an initiating event, leading to the effect on the circulating free T₄. The activation of these receptors was shown to result in upregulation of hepatic phase I and phase II enzymes and hepatic transporters, leading to an increased catabolism of thyroid hormones in rats (US EPA 2011a). To compensate for the movement of free T₄ into the liver, a compensatory mechanism is activated, and T₄ moves from the protein-bound state into the free pool. Due to the constant removal of T₄ from the free fraction into the liver, free T₄ concentrations remain decreased, and T₄ storage in the serum (i.e., protein-bound T₄) decreases, as manifested by a decrease in total T₄, with a subsequent potential impact on neurological development (Figure 1).
Figure 1. Proposed adverse outcome pathway for the effects of triclosan on the thyroid hormone system [TR = thyroid receptor]

While the proposed adverse outcome pathway identifies key events for triclosan-induced hypothyroxinemia, a number of uncertainties remain as to whether the magnitude of the observed thyroid hormone alteration is sufficient to affect brain development in rats. In the existing animal database for triclosan, no neurodevelopmental effects were reported following triclosan exposure. However, these in vivo screens and tests were originally designed to evaluate effects of the test material on reproduction and development, and not alterations in cognitive or behavioural function. Further, a developmental neurotoxicity study with triclosan is not available. Thus, there is uncertainty associated with whether triclosan-induced alterations in T4 levels may have an effect on brain development in rats.

In general, triclosan-induced hypothyroxinemia would be expected to manifest itself in several systemic effects. One of the early indications of a reduction of T4 in the rat is an increase in serum cholesterol. In the rodent database with triclosan, animals were shown to demonstrate decreases in cholesterol level. Hypothyroxinemia would also have an effect on the reproduction system. In human and rodent males, thyroid hormones regulate testis development through promotion of Sertoli cell differentiation. The effect is proposed to occur through activation of thyroid receptor alpha 1 (TRα1) in both species. In general, hypothyroxinemia-induced alterations in the reproductive system, such as decreased sperm count and decreased libido, are observed in adult male laboratory animals and humans (Bourget et al. 1987; Jannini et al. 1995). Prepubertal hypothyroxinemia is associated with precocious sexual development (enlargement of the testes without virilization) and absence of libido and ejaculate in rats (Jannini et al. 1995; Longcope 2000). In adult female rats, hypothyroxinemia is generally associated with altered menstrual and estrous cycles (Fisher and Brown 2000; Krassas 2000). Fetal hypothyroxinemia in female rats alters reproductive tract development, but a similar effect is not seen in human females. Hypothyroxinemia in the prepubertal period is associated with delayed sexual maturity in female rats and humans. However, in the rodent database with triclosan, alterations in the reproductive system either were not noted or were observed at high doses of triclosan (e.g., chronic toxicity study with hamsters, the Stoker et al. 2010 study with rats). Thus, the paucity of clear indicators of hypothyroid function in the rat with triclosan exposure suggests that decreases in T4 may not be sufficient to cause overt hypothyroxinemia in the animal model.

Extrapolation of thyroid hormone data obtained in rats to human risk should be tempered by toxicodynamic and toxicokinetic differences in thyroid hormone homeostasis between humans and rats. In general, humans are considered less sensitive than rats to chemical-induced perturbation in thyroid hormone homeostasis due to the presence of high-affinity binding proteins (thyroxine-binding globulin) in human serum, which results in a longer serum T4 half-life in humans (5–9 days in humans compared with 0.5–1 day in rats) (Glinoer 1997; Choksi et
al. 2003). In rats, most T$_4$ in serum is bound to transthyretin, which has a lower binding affinity for T$_4$, resulting in a higher rate of T$_4$ clearance in adult rats compared with humans (Savu et al. 1987; Rouaze-Romet et al. 1992; US EPA 2011a). The increased clearance of thyroid hormones results in a higher rate of production of T$_4$ per unit of body weight in rats to maintain normal concentrations of T$_4$ (US EPA 2011a). These differences have been linked to increased susceptibility of rats to thyroid follicular tumours compared with humans (US EPA 2011a). Thus, it is likely that humans will be less responsive to triclosan-induced changes in serum T$_4$ levels. As well, less than 1% of T$_4$ in humans is freely circulating and available for destruction by liver enzymes, resulting in humans having a greater resistance than the rat model to thyroid toxicity, which occurs secondary to liver enzyme activation.

In a published short-term (14-day) study by Allmyr et al. (2009), the effect of triclosan on thyroid hormone status was measured in 12 adult humans following exposure to triclosan-containing toothpaste. The plasma triclosan concentrations increased from 0.009–0.81 to 26–296 ng/g upon exposure. The highest serum concentration was determined to be equivalent to a triclosan dose of 0.1 mg/kg bw per day. Despite this, there were no significant changes in plasma levels of either 4β-hydroxycholesterol (indicative of CYP3A4 induction) or thyroid hormones during the exposure (Allmyr et al. 2009), demonstrating that triclosan-induced alterations in T$_4$ levels are unlikely to occur in healthy adult humans.

In 2011, both the EU SCCS and the US FIFRA Scientific Advisory Panel considered the effects of triclosan on thyroid hormone homeostasis in rats and their relevance to humans. In light of the rat being more sensitive to chemically induced alterations in thyroid hormone levels, the SCCS regarded a decrease in T$_4$ levels following exposure to triclosan as a biochemical marker that is not linked to an adverse effect (SCCS 2011). In consideration of the fact that the observed triclosan toxicity does not fit the typical pattern expected from perturbations of thyroid homeostasis, the FIFRA Scientific Advisory Panel recommended further revisions and refinements to the proposed adverse outcome pathway for triclosan before it could be used predictively. Although subtle perturbations of the T$_4$ level may have little or no effect due to the operation of homeostatic processes, the FIFRA Scientific Advisory Panel noted that additional data are needed “to determine the magnitude of perturbation of T$_4$ alone or in combination with other thyroid hormones that would lead to adverse neurodevelopmental effects” (US EPA 2011a).

In summary, given 1) the paucity of indications of adverse effects on thyroid function in the animal database as discussed above, 2) the suggestion that the reductions in T$_4$ levels were attributed to enzymatic destruction following increases in liver enzymes and 3) the fact that humans have a much greater capacity to adapt to deviations in T$_4$ levels, the overall weight of evidence does not currently support effects of triclosan on thyroid function as a critical effect for risk characterization in humans.
3.1.11 Immunotoxicity

A recent study by Udoji et al. (2010) examined the ability of triclosan to suppress human natural killer cell function in vitro. Triclosan was able to inhibit natural killer cell lytic function by 87% within 24 hours. These negative effects persisted following a brief (1-hour) exposure, indicating that the impairment of function cannot be eliminated by removal of triclosan under in vitro conditions. Clayton et al. (2011) investigated the association of triclosan with markers of immune function using 2003–2006 NHANES data by comparing triclosan levels with serum cytomegalovirus antibody levels and diagnosis of allergies or hay fever in US adults and children 6 years of age and older. Triclosan showed a positive association with hay fever diagnosis in the less than 18 year age group (p < 0.01), although triclosan levels were not associated with cytomegalovirus antibody levels. These studies have multiple limitations, but the ability of triclosan to affect the immune system should be further studied.

3.2 Toxicological Endpoints for the Human Health Risk Assessment

3.2.1 Completeness of the Database

There is high confidence in the health effects database. The database for triclosan consists of the full array of toxicity studies currently required for hazard assessment purposes and is therefore adequate to define the majority of the toxic effects that may result from exposure to triclosan.

In examination of the database as a whole, the principal toxicity in rodents and dogs following ingestion of triclosan is mainly hepatic in nature, as demonstrated by hepatocellular necrosis, vacuolization, inflammation and other morphological changes in the liver, with the mouse being the most sensitive species. Triclosan produced hepatic effects and hepatic tumours in mice, but only limited hepatic effects and no tumours in rats. There is evidence that liver effects observed in mice were typical of a PPAR agonist.

A FIFRA Scientific Advisory Panel convened in 2003 reviewed the issue of PPARα agonist–mediated hepatocarcinogenesis in rodents and its relevance to human health risk assessment (SAP 2004). Overall, the majority of the Panel felt that there was adequate evidence in support of the proposed MOA for PPARα agonist–induced rodent hepatocarcinogenesis and that there are relevant data indicating that humans are less sensitive than rodents to the hepatic effects of PPARα agonists, although the opinions of the experts ranged from full agreement to complete disagreement. The basis for the disagreement was the lack of human data and the evidence that would be necessary to fully support the proposed MOA and its relevance to humans.

More recently, two different transgenic PPARα-humanized mouse models have been generated, demonstrating that while peroxisome proliferators can activate human PPARα expression, the mitogenic and hepatocarcinogenic effects do not occur (Cheung et al. 2004; Morimura et al.)
2006). It was suggested that the difference in species response may be due to species-specific regulation of a micro-ribonucleic acid (RNA) (Shah et al. 2007; Peters 2008).

Although it is generally accepted that hepatocarcinogenesis in rodents by a PPAR agonist is irrelevant to humans, the same cannot be concluded for activation of PPARα, which alters the expression of genes involved in lipid metabolism that induce hypolipidemia (SAP 2004). Further, it cannot be excluded that non-cancer liver effects observed in rodent studies may also be a result of other modes of triclosan toxicity, such as CAR and PXR activation.

Toxicity in hamsters and baboons was different from that observed in rodents and dogs. Hamsters showed no increased liver toxicity and no tumours following chronic exposure (US EPA 2008b). Chronic toxicity was characterized by urinary and stomach lesions, which is consistent with the rapid conjugation and urinary excretion of triclosan. Chronic oral administration of triclosan via capsule to baboons did not lead to systemic toxicity, with the exception of clinical signs of vomiting and diarrhea occurring 4–6 hours after dosing, consistent with stomach irritation (US EPA 2008b). Similar to hamsters, liver toxicity was absent. Limited subchronic studies in rabbits also showed no clinical signs of toxicity from triclosan exposure (SCCP 2009).

Minor changes in hematology were considered adaptive, and alterations in biochemical parameters observed following short-term (mice), subchronic and chronic oral exposures to triclosan in rats and mice were considered secondary to liver toxicity in these species.

The data from the reproductive study in rats provide evidence of reduced viability of the offspring in the early postnatal days and a reduced weaning index in both generations. In a developmental toxicity study in mice, an irregular ossification was reported in fetuses (US EPA 2008b). These effects in rodents were observed at doses that also caused maternal toxicity. Increased liver weights in adult mice and increased incidence of liver discoloration in adult rats were observed in these studies; however, no histopathological assessment was undertaken (US EPA 2008b).

As indicated above, there is uncertainty as to whether the magnitude of triclosan-induced alterations in T₄ levels is sufficient to affect brain development in rats. For that reason, even in light of the possibility that changes in thyroid function may occur only at dose levels resulting in liver effects, as well as the fact that humans are likely to be less sensitive to chemically induced changes in thyroid homeostasis, the lack of a developmental neurotoxicity study is considered by Health Canada as a gap in the triclosan database. Consequently, an additional 3-fold uncertainty factor for database deficiency is proposed by Health Canada to be applied to all exposure scenarios.

3.2.2 PCPA Hazard Characterization

For assessing risks from exposure to chemicals in products used in or around homes or schools, the PCPA requires the application of an additional 10-fold factor to threshold effects to take into
account completeness of the data with respect to the exposure of and toxicity to infants and children and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate based on reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database for triclosan contains the full complement of required studies, including developmental toxicity studies in rats, mice and rabbits and a two-generation reproductive toxicity study in rats. The lack of a developmental neurotoxicity study was accounted for through the use of an uncertainty factor for database deficiency.

With respect to identified concerns relevant to the assessment of risk to infants and children, in the developmental toxicity study in mice, a decrease in fetal weight was observed at a dose that also caused maternal toxicity. No treatment-related developmental effects were observed in developmental toxicity studies in rats and rabbits (US EPA 2008b). No evidence of increased susceptibility was observed in offspring in the available two-generation reproductive toxicity study conducted with rats. Effects in offspring, including reduced pup weight and viability in both generations, were observed following in utero and/or lactational exposure at a dose that was also associated with maternal toxicity (NOAEL of 50 mg/kg bw per day, LOAEL of 150 mg/kg bw per day; US EPA 2008b).

Reduced pup viability is considered a serious endpoint and, if selected for risk assessment purposes, would be subject to the application of the PCPA factor. As concern for this endpoint is tempered by the occurrence of maternal toxicity at the same dose level, the PCPA factor would be reduced from 10-fold to 3-fold for scenarios involving in utero and lactational exposure; however, when a point of departure less than or equal to the NOAEL of 50 mg/kg bw per day is utilized for risk assessment, the concerns identified under the PCPA 3-fold factor are considered to be subsumed by the 3-fold uncertainty factor for database deficiency, to temper compounding conservatism. Accordingly, the PCPA factor was reduced to 1-fold, since uncertainties with respect to the completeness of the data were accounted for through application of the database deficiency factor, and there was a low level of concern for prenatal and postnatal toxicity, given the endpoints and uncertainty factors selected for risk assessment.

It should be noted that the submission of a developmental neurotoxicity study could result in the potential removal of the uncertainty factor for database deficiency, pending the results of the study. However, reference doses would need to be reconsidered in totality to determine whether they remain protective of all vulnerable populations.

3.2.3 Acceptable Daily Intake (All Populations)

A number of studies were considered in the selection of the acceptable daily intake (ADI), an estimate of a daily intake of a substance over a lifetime that is considered to be without appreciable health risk, for the general population. Subchronic oral studies in the dog were not considered suitable for endpoint selection due to a number of factors, including study deficiencies, limited reporting, the age of the studies and the inconsistent results obtained (i.e.,
capsule studies demonstrated a LOAEL of 25 mg/kg bw per day, whereas a dietary study demonstrated no effects at this same level; US EPA 2008b). The results of the 1-year baboon study (NOAEL of 30 mg/kg bw per day, LOAEL of 100 mg/kg bw per day) were similarly disregarded, as the effects observed (i.e., diarrhoea and vomiting) following administration by capsule were thought to reflect the irritant properties of triclosan rather than systemic toxicity (US EPA 2008b).

In the remaining species tested, the mouse exhibited a NOAEL of 25 mg/kg bw per day (LOAEL of 75 mg/kg bw per day) in the 90-day and developmental toxicity studies for non-cancer effects (liver effects and decreased fetal body weight), compared with NOAELs of approximately 50 mg/kg bw per day in the rat (reduced pup weights and reduced pup viability in a reproductive toxicity study and liver effects in a 2-year oral toxicity study) and 75 mg/kg bw per day in the hamster (kidney effects in a 90-week study) (US EPA 2008b). Liver effects observed at the NOAEL in the mouse studies (e.g., increased liver weights, hypertrophy) were typical of a PPAR agonist. However, it cannot be excluded that the observed liver effects may also be the result of other triclosan modes of toxicity, such as PXR and CAR activation. Additional effects on hematology (mild decreases in erythrocyte parameters in the 90-day study), clinical chemistry parameters (decreased cholesterol) and liver pathology (vacuolization) were observed at the NOAEL that progressed to adversity at higher dose levels. It is well recognized that humans are generally less sensitive to PPARα agonist–induced hepatocarcinogenesis, primarily due to a reduced quantity of functional receptors in the human liver (compared with the mouse). That said, humans are at least as sensitive to activation of PPARα, which alters the expression of genes involved in lipid metabolism that induce hypolipidemia (SAP 2004).

Considering the overall weight of evidence, a NOAEL of 25 mg/kg bw per day was obtained from a 90-day oral toxicity study in the mouse, with a LOAEL of 75 mg/kg bw per day, based on liver pathology, increased liver weights and a statistically significant reduction in total cholesterol. The selected endpoint is considered protective of potential liver effects in humans, independent of the mode of toxicity. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. An additional uncertainty factor of 3-fold has been applied to account for database deficiency (i.e., lack of a developmental neurotoxicity study). For the reasons outlined in Section 3.2.2, the PCPA factor was reduced to 1-fold for risk assessment purposes. This results in a composite assessment factor (CAF) (or target margin of exposure [MOE]) of 300.

The ADI for all populations is calculated according to the following formula:

\[
\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{25 \text{ mg/kg bw per day}}{300} = 0.08 \text{ mg/kg bw per day}
\]

This ADI provides a margin of greater than 600 to the NOAEL for reduced pup viability (50 mg/kg bw per day) and is considered protective for pregnant women and their fetuses as well as nursing infants.
Further, even though there is uncertainty regarding the significance of the effects of triclosan on thyroid hormone homeostasis in rats and their relevance to humans, characterizing risk based on liver effects in the most sensitive species (i.e., mouse) is considered to address uncertainties in the thyroid effects database.

3.2.4 Toxicological Endpoints for Residential and Occupational Risk Assessment

3.2.4.1 Incidental Oral Exposure (Directly Exposed Children)
For short-term incidental oral exposure (object-to-mouth and hand-to-mouth scenarios) of all children, the NOAEL of 25 mg/kg bw per day from the mouse studies was considered the most appropriate endpoint (as per the ADI). Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. An additional uncertainty factor of 3-fold has been applied to account for database deficiency (i.e., lack of a developmental neurotoxicity study). For the reasons outlined in Section 3.2.2, the PCPA factor was reduced to 1-fold for risk assessment purposes. This results in a target MOE (or CAF) of 300.

3.2.4.2 Dermal Exposure
For dermal exposure of all durations for all populations, the NOAEL of 40 mg/kg bw per day from a 90-day dermal toxicity study in rats was considered the most appropriate endpoint. Treatment-related effects at the LOAEL of 80 mg/kg bw per day included minor hematological changes (males), reduced triglyceride (males) and cholesterol levels (males and females), occult blood in urine and a slight focal degeneration of cortical tubules (males) (US EPA 2008b). Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. An additional uncertainty factor of 3-fold has been applied to account for database deficiency (i.e., lack of a developmental neurotoxicity study). For the reasons outlined in Section 3.2.2, the PCPA factor was reduced to 1-fold for risk assessments pertaining to residential scenarios. This results in a target MOE (or CAF) of 300 for the general population.

3.2.4.3 Inhalation Exposure
For inhalation exposure assessments, the NOAEL of 3.21 mg/kg bw per day from a 21-day inhalation toxicity study in rats was considered the most appropriate endpoint for all populations. Effects at the LOAEL of 7.97 mg/kg bw per day included changes in body weight, hematology and clinical chemistry and a slight increase in respiratory irritation (US EPA 2008b). The selected NOAEL is considered protective of effects observed in other species. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. An additional uncertainty factor of 3-fold has been applied to account for database deficiency (i.e., lack of a developmental neurotoxicity study). For the reasons outlined in Section 3.2.2, the PCPA factor was reduced to 1-fold for risk assessments pertaining to residential scenarios. This results in a target MOE of 300 for the general population. The target MOE (or CAF) for all inhalation scenarios and populations is therefore 300.
3.2.5 Aggregate Exposure Scenarios

Aggregate exposures of adults and children to triclosan in consumer products (e.g., treated clothing, cosmetics, toothpaste and toys) are expected in residential settings. Exposures are expected to occur via the oral and dermal routes; inhalation exposure to triclosan is expected to be a negligible contributor to the aggregate exposure due to its low volatility.

For assessing aggregate exposure of the general population, the assessment can be performed using the endpoints and assessment factors selected for the ADI for the general population. Both oral and dermal studies have shown minor, but consistent, effects on hematology parameters at the LOAEL, as well as effects on cholesterol. Consequently, the NOAEL of 25 mg/kg bw per day, selected from the mouse studies, was considered the most appropriate endpoint for assessing aggregate risks for all populations (US EPA 2008b). Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. An additional uncertainty factor of 3-fold has been applied to account for database deficiency (i.e., lack of a developmental neurotoxicity study). For the reasons outlined in Section 3.2.2, the PCPA factor was reduced to 1-fold for risk assessments pertaining to residential scenarios. This results in a target MOE (or CAF) of 300 for the general population.

3.2.6 Cancer Risk Assessment

Hepatic adenomas and carcinomas were observed in both sexes of mice in an 18-month dietary study; however, there was no evidence of carcinogenicity in long-term dietary studies in rats or hamsters (US EPA 2008b). Based on the weight of evidence, triclosan was not considered genotoxic, suggesting that the mouse tumours occurred as a result of a non-genotoxic MOA. It was determined that the hepatic tumours in mice were the consequence of a species-specific response to the peroxisome-proliferating properties of triclosan. This specificity has been demonstrated both morphologically and biochemically. Notably, mouse livers have shown dose-dependent increases in the numbers of peroxisomes and sensitivity to biochemical indicators of peroxisome proliferation, such as peroxisomal fatty acid β-oxidation, 11- and 12-hydroxylation of lauric acid and levels of CYP4A proteins. In comparison, effects in rats and hamsters are less pronounced (i.e., no increases in numbers of peroxisomes and biochemical indicators either unaffected or affected at high doses only) (Klaunig et al. 2003). It is generally accepted in the scientific community that mouse liver tumours induced through the MOA of peroxisome proliferation are of little relevance to humans. While PPAR can be activated in humans following exposure to known agonists with resulting hypolipidemia, there is little evidence to indicate that hepatocellular proliferation and clonal expansion of initiated hepatocytes (required for tumour development) occur in humans. Accordingly, no quantitative cancer risk assessment is warranted for triclosan.

Endpoints of toxicological concern selected for use in the human health risk assessment are summarized in Appendix 2.
3.3 Human Health Exposure and Risk

Assessments of general population exposure conducted by the US EPA (2008a) based on the available biomonitoring data for triclosan from the US NHANES (CDC 2011) were used as an important source of information to determine the level of Canadian general population exposure to triclosan. In the absence of Canadian-specific data for the general population, the biomonitoring data for the US population were used. These data encompass exposures to triclosan from all potential sources and routes, and are considered the most accurate estimates of total exposure of the general population in Canada to triclosan given the similarities in registered uses and availability of consumer products on the US and Canadian markets. Additional exposure characterization was undertaken as appropriate.

3.3.1 General Population Exposure and Risk Assessment

The potential sources of exposure to triclosan for Canadians include consumer products treated with or containing triclosan (including, but not limited to, cosmetic products, treated textiles and food contact materials), drinking water contaminated with triclosan, breast milk and contaminated household dust. Domestic-class pest control products containing triclosan are not registered in Canada.

The NHANES is a series of US national surveys of the health and nutrition status of the non-institutionalized civilian population conducted by the US Centers for Disease Control and Prevention. The biomonitoring data for triclosan provide actual measures of exposure, not only because they include specific measurements of triclosan in urine, but also because they reflect actual use patterns of various consumer products containing triclosan as they co-occur in practice.

According to the NHANES data, approximately 82% of urine samples (general population ≥ 6 years of age) from the 2007–2008 survey had detectable levels of triclosan, indicating that the majority of the US population was exposed to this antimicrobial active ingredient. The NHANES biomonitoring data for the US population are considered representative of the Canadian population, given the registered uses and availability of products on the US and Canadian markets. On this basis, general population (≥ 6 years of age) daily dose estimates derived by the US EPA based on the 2007–2008 NHANES data were used to assess risks for the Canadian populations (≥ 6 years of age). Based on preliminary analysis of raw NHANES data for 2009–2010, levels of triclosan in urine were similar to those used in the current assessment.

It should be noted that Health Canada is currently involved in a number of research initiatives that will allow better characterization of exposure to triclosan in the Canadian population. One study, the Canadian Health Measures Survey, will permit direct comparisons with NHANES data. The survey has a biomonitoring component that includes the collection of urine samples with the aim of measuring potential exposure to a number of environmental chemicals, including triclosan, in Canadians aged 3–79 years. Samples were collected from September 2009 to August 2011, and the results are expected to be available in 2013.
Another study initiated by Health Canada in 2008, Plastic and Personal-Care Product Use in Pregnancy (referred to as the P4 study), recruited 80 pregnant women from the Ottawa, Ontario, area in order to collect multiple maternal urine samples, detailed consumer product/food packaging diaries, infant urine and meconium samples, and breast milk. Meconium is being evaluated as a potential matrix to measure in utero exposure. Biospecimens will be analyzed for a number of substances, including triclosan. Estimated daily doses for children are based on the available preliminary results from this study. Results for both infants and women are expected in 2013.

3.3.2 Estimation of the Daily Exposure Dose Based on the Spot Triclosan Urine Concentration

Given that the health effect levels are expressed in milligrams per kilogram body weight, it is necessary to convert the spot triclosan urine concentrations to estimates of daily exposure.

In order to derive the daily dose, the spot urine concentration was adjusted for the volume of urine that is typically excreted during a 24-hour period. Considering a variable urine dilution caused by wide fluctuations in fluid intake and excretion across the general population, the preferred option would be to use the total urine volume reported for each participant. However, these data are not available in the NHANES or the P4 study.

For the general population (≥ 6 years of age), the most conservative daily dose estimates were achieved by the US EPA when the spot urine concentration was adjusted for the mean and 95th percentile of daily urine volume in litres per kilogram per day, reported by Lentner (1981). The latter is considered a bounding estimate that leads to an overestimate of exposure. For infants in the P4 study, the maximum spot urine concentrations were adjusted by Health Canada for the range of mean urine volumes reported in the published literature (see Appendix 3).

In addition to correcting spot triclosan urine concentrations, corrections were also made for incomplete excretion of triclosan to account for exposures not captured in urine. Based on pharmacokinetic studies (Table 3) investigating the absorption, metabolism and excretion of triclosan in humans with several different routes of administration, including oral exposure to triclosan-containing products (e.g., toothpaste), oral ingestion of capsules, aqueous solutions and dental slurries (i.e., following brushing with triclosan-containing toothpaste) and percutaneous exposure (in vivo and in vitro), the SCCP (2009) concluded that ingested triclosan is almost completely absorbed, whereas oral cavity and percutaneous exposure to triclosan-containing products (e.g., toothpaste, soap, cream) results in limited absorption. The SCCP (2009) also concluded that following all routes of administration, absorbed triclosan is nearly totally converted to glucuronic and sulfuric acid conjugates (varied relative proportions), with only trace amounts of the parent compound detected in the plasma, and the predominant route of excretion was the urine, with the majority of the compound appearing as the glucuronide conjugate.
Table 3. Summary of triclosan excretion data in humans

<table>
<thead>
<tr>
<th>Type of administered dose</th>
<th>% of dose excreted in urine</th>
<th>% of dose excreted in feces</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single or multiple oral doses, capsule</td>
<td>57–87</td>
<td>10–33</td>
<td>Stierlin 1972; Ciba-Geigy 1976b; Lucker et al. 1990</td>
</tr>
<tr>
<td>Single oral dose, aqueous</td>
<td>24–83</td>
<td>—</td>
<td>Sandborgh-Englund et al. 2006</td>
</tr>
<tr>
<td>Dermal dose</td>
<td>2–14</td>
<td>0.5–2</td>
<td>Stierlin 1972; Caudal et al. 1974; Thompson et al. 1975; Queckenberg et al. 2010</td>
</tr>
<tr>
<td>Intravenous dose</td>
<td>65</td>
<td>21</td>
<td>Maibach 1969</td>
</tr>
</tbody>
</table>

Following single and multiple oral doses of triclosan, 57–87% of the administered dose was excreted in urine, with much smaller amounts appearing in the feces (10–33% of the administered dose), based on studies by Lucker et al. (1990), Stierlin (1972) and Ciba-Geigy (1976b). In a study using single doses of aqueous solutions containing triclosan, the major fraction was excreted within 24 hours of exposure, with between 24% and 83% (median 54%) of the oral dose excreted within the first 4 days after dosing (Sandborgh-Englund et al. 2006). For dermal dosing, the excretion profile was similar, with the predominant route of excretion in the urine (2–14%) based on studies by Stierlin (1972), Caudal et al. (1974) and Thompson et al. (1975), with much smaller amounts appearing in the feces (0.5–2% of the applied dose) (SCCP 2009). The SCCP (2009) also concluded that excretion data obtained from an intravenous study were consistent with those obtained from the oral studies, with the majority of the dose (approximately 65%) excreted in the urine, while approximately 21% was excreted in the feces (Maibach 1969).

To account for variability in urinary excretion of triclosan between individuals, a conservative median urinary excretion of 54%, as reported in the Sandborgh-Englund et al. (2006) study, was assumed for all individuals (i.e., 54% of triclosan is excreted in the urine). Consequently, all estimates were corrected by a factor of 0.54 to account for incomplete excretion following exposure via multiple routes. For children, although there are limited pharmacokinetic data, the SCCP (2009) concluded that the rate of elimination is comparable to that of adults; therefore, the same correction factor was applied to the assessment for children under the age of 6 years.

3.3.2.1 Uncertainties Associated with Dose Conversion

There are several uncertainties associated with using spot urine samples from NHANES to estimate human exposures to triclosan. Spot urine samples were used as a surrogate for 24-hour urine samples and were therefore corrected based on urine volumes specific to a given subpopulation (Lentner 1981; Prentice 1987; Water UK 2006). The 95th percentile urine volume was used to calculate an upper-bounding estimate of 24-hour urinary excretion volume for individuals 6 years of age and older, which likely leads to an overestimate of the dose. For conversion of infant spot urine samples from the P4 study, a range of mean infant urine volumes were used to provide a lower- and upper-bound range of exposures.
Another uncertainty in the dose conversion of spot urine samples for all age groups is the assumption that absorption, distribution, metabolism and elimination parameters are the same for all individuals and remain constant within individuals over time. There is uncertainty associated with the use of the median value of 54% to account for urinary excretion of triclosan for all individuals, as the values were highly variable (24–83%) and were based on oral dosing (Sandborgh-Englund et al. 2006). However, according to Krishnan et al. (2010), the data from the Sandborgh-Englund et al. (2006) study were considered to be fairly robust. In addition, the SCCP (2009) concluded that, although there are limited pharmacokinetic data for children and no direct comparisons with adults were possible given differences in doses and dosing formulations in various studies, elimination was determined to be essentially the same for children and adults based on an oral dosing study with toothpaste and dental slurry. Given the number of potential sources of exposure via the dermal route, there is uncertainty in correcting spot urine samples for incomplete excretion using an oral dosing study. However, given the high absorption of triclosan via the oral route and limited absorption via the dermal route combined with similar excretion noted via intravenous administration (65%), correction using a median of 54% via oral dosing is considered appropriate.

There is also some uncertainty with converting spot urine samples to a daily dose, as the routes of exposure and timing of exposure in relation to the timing of sampling are unknown. However, given the short half-life of triclosan in urine (11 hours) and the widespread daily use of triclosan-containing products, the spot urine samples from NHANES for triclosan represent a range of short- and long-term measurements of exposure. Since the dose estimation likely represents a range of exposure durations, and given that there is a high percentage (82%) of individuals with detectable levels of triclosan in urine (US EPA 2011b) and that triclosan is found in a number of consumer products that could be used more than once a day, it is reasonable to assume that the elimination of triclosan in urine of individuals in the NHANES study is at steady state.

### 3.3.3 Aggregate Risk Assessment for the General Population (≥ 6 Years of Age)

The NHANES data provide information on the total exposure to triclosan of individuals 6 years of age and older only. As such, exposure and risk for children less than 6 years of age were assessed separately (see below).

The risk for the Canadian population (≥ 6 years of age) was characterized by comparing the estimated daily dose for each population subgroup with the relevant health effect endpoint identified by Health Canada (Appendix 2).

The mean daily dose estimates based on the 2007–2008 NHANES (US EPA 2011b) are summarized below. To account for uncertainties with respect to the dose estimation (e.g., high variability between individuals’ pharmacokinetic data for triclosan) and potentially higher exposure of some individuals due to high use of consumer products containing triclosan or a single event such as swallowing toothpaste prior to sampling, aggregate exposure assessments were also determined based on an upper-bound exposure (Table 4).
Table 4. General population risk based on the mean and upper-bound daily dose estimates

<table>
<thead>
<tr>
<th>Group</th>
<th>Estimated daily dose¹ (mean urine volume) (mg/kg bw per day)</th>
<th>MOE²</th>
<th>Estimated daily dose¹ (95th percentile urine volume) (mg/kg bw per day)</th>
<th>MOE²</th>
<th>Target MOE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean daily dose estimates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (adults and children ≥ 6 years of age)</td>
<td>0.0029</td>
<td>8621</td>
<td>0.0045</td>
<td>5556</td>
<td></td>
</tr>
<tr>
<td>Children 6–11 years of age</td>
<td>0.0025</td>
<td>10 000</td>
<td>0.0035</td>
<td>7143</td>
<td></td>
</tr>
<tr>
<td>Adults 12–19 years of age</td>
<td>0.0038</td>
<td>6579</td>
<td>0.0058</td>
<td>4310</td>
<td></td>
</tr>
<tr>
<td>Adults 20–59 years of age</td>
<td>0.0029</td>
<td>8321</td>
<td>0.0046</td>
<td>5435</td>
<td></td>
</tr>
<tr>
<td>Adults ≥ 60 years of age</td>
<td>0.0024</td>
<td>10 417</td>
<td>0.0038</td>
<td>6579</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>0.0029</td>
<td>8621</td>
<td>0.0044</td>
<td>5682</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed non-pregnant</td>
<td>0.0034</td>
<td>7463</td>
<td>0.0054</td>
<td>4313</td>
<td></td>
</tr>
<tr>
<td>Confirmed pregnant</td>
<td>0.0043</td>
<td>5828</td>
<td>0.0069</td>
<td>3602</td>
<td></td>
</tr>
<tr>
<td>6–12 years of age</td>
<td>0.0033</td>
<td>7530</td>
<td>0.0047</td>
<td>5330</td>
<td></td>
</tr>
<tr>
<td>13–49 years of age</td>
<td>0.0035</td>
<td>7184</td>
<td>0.0056</td>
<td>4480</td>
<td></td>
</tr>
<tr>
<td>50 and above</td>
<td>0.0018</td>
<td>13 889</td>
<td>0.0029</td>
<td>8562</td>
<td></td>
</tr>
<tr>
<td>Upper-bound (95th percentile) daily dose estimates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (adults and children ≥ 6 years of age)</td>
<td>0.0144</td>
<td>1736</td>
<td>0.0222</td>
<td>1126</td>
<td>300</td>
</tr>
<tr>
<td>Children 6–11 years of age</td>
<td>0.0137</td>
<td>1825</td>
<td>0.0200</td>
<td>1250</td>
<td></td>
</tr>
<tr>
<td>Adults 12–19 years of age</td>
<td>0.0163</td>
<td>1534</td>
<td>0.0246</td>
<td>1016</td>
<td></td>
</tr>
<tr>
<td>Adults 20–59 years of age</td>
<td>0.0148</td>
<td>1689</td>
<td>0.0239</td>
<td>1046</td>
<td></td>
</tr>
<tr>
<td>Adults ≥ 60 years of age</td>
<td>0.0126</td>
<td>1984</td>
<td>0.0202</td>
<td>1238</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>0.0144</td>
<td>1736</td>
<td>0.0222</td>
<td>1126</td>
<td>300</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed non-pregnant</td>
<td>0.0178</td>
<td>1404</td>
<td>0.0287</td>
<td>871</td>
<td></td>
</tr>
<tr>
<td>Confirmed pregnant</td>
<td>0.0176</td>
<td>1420</td>
<td>0.0284</td>
<td>880</td>
<td></td>
</tr>
<tr>
<td>6–12 years of age</td>
<td>0.0244</td>
<td>1025</td>
<td>0.0356</td>
<td>702</td>
<td></td>
</tr>
<tr>
<td>13–49 years of age</td>
<td>0.0176</td>
<td>1420</td>
<td>0.0284</td>
<td>880</td>
<td></td>
</tr>
<tr>
<td>50 and above</td>
<td>0.0092</td>
<td>2717</td>
<td>0.0148</td>
<td>1689</td>
<td></td>
</tr>
</tbody>
</table>

² MOE = NOAEL (mg/kg bw per day) / exposure dose (mg/kg bw per day), where the NOAEL of 25 mg/kg bw per day with a target MOE of 300 was selected for all populations.

For all populations, the mean and upper-bound daily dose estimates (calculated assuming mean and 95th percentile urine volumes) resulted in MOEs above the target MOE, indicating that there are no risks of concern.
Consequently, based on the results of the aggregate risk assessment, it can be concluded that exposure of adults (including pregnant females) and children over the age of 6 years to triclosan residues is below the level of concern.

### 3.3.4 Aggregate Risk Assessment for Children Younger than 6 Years of Age

Among young children, infants 6–12 months of age are likely to have the highest exposure to triclosan, given that children in this age group display a number of additional behavioural activities that are not captured by the 6–11 years age category. These behaviours include nursing, “object-to-mouth” (e.g., mouthing plastic toy), “hand-to-mouth” (e.g., touching triclosan-impregnated products or crawling) and inhalation of contaminated dust (created as a result of children’s activities on the floor/carpet). Younger age groups (i.e., birth to < 1 month, 1 to < 3 months and 3 to < 6 months) are considered to have lower exposures relative to body weight due to less frequent contact with treated objects (i.e., hand-to-mouth and object-to-mouth activities). Older age groups (i.e., 1 to < 2 years, 2 to < 3 years, 3 to < 6 years of age) are expected to have lower exposures due to the cessation of nursing and a reduction in hand-to-mouth activities (US EPA 2011b).

Although NHANES did not sample children younger than 6 years of age, triclosan has been measured in the urine of infants and children younger than 6 years of age, as reported in the other studies. Preliminary results of the spot urine triclosan concentration are available from the Canadian P4 study for infants under 1 week of age and infants 2–3 months of age. Other biomonitoring data for children in the under 6 years of age group were identified, including a study that collected urine from 42 premature infants in Boston, Massachusetts (Calafat et al. 2009) and urine samples from 56 children 3–6 years of age collected in Guangzhou, China (Li et al. 2011). The results of these three studies are shown in Table 5.

#### Table 5. Concentrations of total triclosan in urine of children less than 6 years of age

<table>
<thead>
<tr>
<th>Location</th>
<th>Age</th>
<th>Number of Samples</th>
<th>Triclosan concentration (µg/L)</th>
<th>Limit of detection (µg/L)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>&lt; 7 days</td>
<td>44</td>
<td>86 (max)</td>
<td>&lt; 3</td>
<td>Preliminary results from P4 study¹</td>
</tr>
<tr>
<td></td>
<td>2–3 months</td>
<td>46</td>
<td>100 (max)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boston, MA</td>
<td>Premature infants</td>
<td>42</td>
<td>&lt; 2.3–16.7</td>
<td>2.3</td>
<td>Calafat et al. 2009</td>
</tr>
<tr>
<td>Guangzhou, China</td>
<td>3–6 years</td>
<td>56</td>
<td>5.04 (GM)</td>
<td>0.0005</td>
<td>Li et al. 2011</td>
</tr>
</tbody>
</table>

Abbreviations used: GM, geometric mean; max, maximum

¹ 2011 e-mail from Environmental Health Science and Research Bureau, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced.

Using the same method as was used for individuals 6 years of age and older to convert spot urine samples to dose, the estimated daily dose for 2- to 3-month-old infants ranged from 0.0064 to
0.0185 mg/kg bw per day based on the maximum concentration from the P4 study, a range of mean urine volumes (Appendix 3) and a factor of 54% to account for urinary excretion. Although there are limited pharmacokinetic data for children and no direct comparisons with adults, elimination of triclosan was determined to be essentially the same for children and adults based on an oral dosing study with toothpaste and dental slurry (SCCP 2009). Using the NOAEL of 25 mg/kg bw per day from a 90-day oral toxicity study in the mouse and estimated daily doses, the resulting MOEs ranged from 1351 to 3906 (target MOE of 300).

### 3.3.4.1 Infant-Specific Exposure Scenarios

#### Nursing

Triclosan has been measured in human breast milk in the United States, Europe and China (Adolfsson-Erici et al. 2002; Allmyr et al. 2006; Dayan 2007; Ye et al. 2008; Azzouz et al. 2011; Wang et al. 2011). A summary of the results of these studies is shown in Table 6.

#### Table 6. Concentration of total triclosan in human breast milk

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of Samples</th>
<th>Minimum (µg/kg lipid)</th>
<th>Maximum (µg/kg lipid)</th>
<th>LOD (µg/kg lipid)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>62</td>
<td>&lt; LOD</td>
<td>2100</td>
<td>0.150</td>
<td>Dayan 2007</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>&lt; LOD</td>
<td>353</td>
<td>24.3</td>
<td>Ye et al. 2008</td>
</tr>
<tr>
<td>Europe</td>
<td>36</td>
<td>&lt; LOQ</td>
<td>23.4</td>
<td>0.45</td>
<td>Allmyr et al. 2006</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt; 20</td>
<td>300</td>
<td>Not specified</td>
<td>Adolfsson-Erici et al. 2002</td>
</tr>
<tr>
<td>China</td>
<td>10</td>
<td>&lt; MQL</td>
<td>6.3</td>
<td>3.5</td>
<td>Azzouz et al. 2011</td>
</tr>
</tbody>
</table>

**Abbreviations used:** LOD, limit of detection; LOQ, limit of quantification; MQL, method quantification limit

Daily exposure of infants to triclosan in breast milk was estimated by Health Canada (Table 7), assuming the maximum concentration of triclosan in breast milk of 2100 µg/kg lipid (Dayan 2007), corresponding to 84 µg/kg whole milk (assuming 4% lipid in breast milk). Additional assumptions included mean breast milk intakes of 770 mL/day and 620 mL/day for infants under 6 months and 6–12 months of age, respectively, the specific gravity of milk of 1.03 g/mL, and the body weights of 6 kg and 9.2 kg for infants less than 6 months of age and 6–12 months of age, respectively (US EPA 2011c).

#### Table 7. Exposure of infants to triclosan in breast milk

<table>
<thead>
<tr>
<th>Exposure scenario</th>
<th>Triclosan concentration in milk (mg/kg)</th>
<th>Daily milk intake (mL/day)</th>
<th>Milk density (g/mL)</th>
<th>Body weight (kg)</th>
<th>Estimated daily dose(^1) (mg/kg bw per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6 months</td>
<td>0.084</td>
<td>770</td>
<td>1.03</td>
<td>6</td>
<td>0.011</td>
</tr>
<tr>
<td>6–12 months</td>
<td>0.084</td>
<td>620</td>
<td>1.03</td>
<td>9.2</td>
<td>0.006</td>
</tr>
</tbody>
</table>

\(^1\) Estimated daily dose (mg/kg bw per day) = triclosan concentration in milk (mg/kg) × daily intake (mL/day) × milk density (g/mL) × conversion factor (0.001 kg/g) / body weight (kg).
For infants under 6 months of age and 6–12 months of age, daily exposures to triclosan in breast milk were estimated to be 0.011 mg/kg bw per day and 0.006 mg/kg bw per day, respectively. Using these estimated daily exposures and the NOAEL of 25 mg/kg bw per day from the 90-day oral toxicity study in the mouse, the resulting MOEs are 2773 and 4167 (target MOE of 300) for infants under 6 months and 6–12 month of age, respectively.

**Object-to-Mouth Activity**

Incidental oral exposure of children to triclosan resulting from object-to-mouth behaviours was assessed for 6- to 12-month-old infants mouthing a plastic toy. The following assumptions were used in the assessment of a plastic toy being mouthed: maximum surface area of 50 cm$^2$ that can be mouthed, plastic weight of 5 g, application rate of 0.5% a.i., 0.5% a.i. available on the surface of the toy, a saliva extraction efficiency of 50% and an average infant body weight of 9.2 kg (US EPA 2011c). The exposure dose for children mouthing a plastic toy was estimated to be 0.0068 mg/kg bw per day (Table 8).
Table 8. Incidental oral exposure of a 6- to 12-month-old infant mouthing a toy made from plastic treated with triclosan

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Surface area mouthed (cm²)</th>
<th>Plastic weight (g)</th>
<th>% a.i. available on plastic surface</th>
<th>Maximum application rate (% a.i.)</th>
<th>Surface residue¹ (mg a.i./cm²)</th>
<th>Saliva extraction efficiency (%)</th>
<th>Estimated daily dose² (mg/kg bw per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child mouthing a plastic toy</td>
<td>50</td>
<td>5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.0025</td>
<td>50</td>
<td>0.0068</td>
</tr>
</tbody>
</table>

¹ Surface residue (mg a.i./cm²) = toy weight/toy surface (g/cm²) × % a.i./100 × % a.i. available on surface/100 × conversion factor (1000 mg/g) = 0.0025.

² Estimated daily dose (mg/kg bw per day) = surface residue (mg a.i./cm²) × saliva extraction efficiency (%) × 100 × surface area (cm²) / body weight (kg).

Using this estimated daily exposure and the NOAEL of 25 mg/kg bw per day from the 90-day oral toxicity study in the mouse, the resulting MOE is 3676 (target MOE of 300).

**Hand-to-Mouth Activity**

Children playing on a treated surface (e.g., floor or carpet) can be exposed to triclosan as a result of ingestion of triclosan residues in dust stuck to their hands. Triclosan has been measured in indoor dust in Canada, Belgium and Spain (Canosa et al. 2007a,b; Geens et al. 2009; Fan et al. 2010). A summary of the results of each study is shown in Table 9.

Table 9. Triclosan in household dust

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of Samples</th>
<th>Mean (ng/g)</th>
<th>Minimum (ng/g)</th>
<th>Maximum (ng/g)</th>
<th>Limit of detection (ng/g)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>63 homes</td>
<td>Median = 571 (fresh sample)</td>
<td>87</td>
<td>3040</td>
<td>8.7</td>
<td>Fan et al. 2010</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Median = 378 (composite sample)</td>
<td>82</td>
<td>4090</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>261</td>
<td>Median = 415</td>
<td>32</td>
<td>7849</td>
<td>8.7</td>
<td>Unpublished data¹</td>
</tr>
<tr>
<td>Belgium</td>
<td>18 homes</td>
<td>484</td>
<td>25</td>
<td>1828</td>
<td>0.5</td>
<td>Geens et al. 2009</td>
</tr>
<tr>
<td>Spain</td>
<td>10 homes</td>
<td>702</td>
<td>240</td>
<td>2200</td>
<td>Not specified</td>
<td>Canosa et al. 2007a</td>
</tr>
<tr>
<td></td>
<td>8 homes</td>
<td>1134</td>
<td>90</td>
<td>2444</td>
<td>1.2</td>
<td>Canosa et al. 2007b</td>
</tr>
</tbody>
</table>

¹ 2011 e-mail from Environmental Health Science and Research Bureau, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced.

Incidental oral exposure of children resulting from hand-to-mouth activities was assessed based on a representative scenario of a 6- to 12-month-old infant crawling on a floor or carpet and
ingesting triclosan-contaminated dust stuck to his or her hands. The assessment of potential oral exposure of children from hand-to-mouth activities was based on the modelled estimates for dust ingestion rates for children 3–6 years of age reported by Özkaynak et al. (2011) and the highest median and maximum dust concentrations from the Canadian studies (see Table 10).

Table 10. Incidental oral exposure of a 6- to 12-month-old infant from hand-to-mouth activities

<table>
<thead>
<tr>
<th>Exposure scenario</th>
<th>Triclosan dust residue¹ (ng/g household dust)</th>
<th>Dust ingestion rate² (mg/day)</th>
<th>Estimated daily dose³ (mg/kg bw per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum dust concentration</td>
<td>7849</td>
<td>20 (mean)</td>
<td>1.71 × 10⁻⁵</td>
</tr>
<tr>
<td></td>
<td></td>
<td>74 (95th percentile)</td>
<td>6.31 × 10⁻⁵</td>
</tr>
<tr>
<td>Median dust concentration</td>
<td>571</td>
<td>20 (mean)</td>
<td>1.24 × 10⁻⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td>74 (95th percentile)</td>
<td>4.59 × 10⁻⁶</td>
</tr>
</tbody>
</table>

¹ 2011 e-mail from Environmental Health Science and Research Bureau, Health Canada, to Existing Substances Risk Assessment Bureau, Health Canada; unreferenced.
² Özkaynak et al. (2011).
³ Estimated daily dose (mg/kg bw per day) = [(Dust residue, ng/g) × (ingestion rate of house dust, mg/day) × (conversion factor, 0.000 001 mg/ng) × (conversion factor, 0.001 g/mg)] / (body weight, 9.2 kg).

For 6- to 12-month-old infants, the daily exposure resulting from ingestion of triclosan-contaminated dust was estimated to be 0.00124 µg/kg bw per day (median dust concentration and mean dust ingestion rate). Using this estimated daily exposure and the NOAEL of 25 mg/kg bw per day from the 90-day oral toxicity study in the mouse, the resulting MOE is greater than 20 000 000 (target MOE of 300).

Inhalation of Triclosan-Contaminated Dust

Inhalation exposure of infants to triclosan in household dust was estimated using available dust standards (US EPA 2008d) and a mean triclosan concentration in dust of 733 ng/g from the Canadian unpublished study (see Table 9). Additional assumptions included an inhalation rate for a child < 1 year of age of 5.4 m³/day (US EPA 2011c) and the average body weight of a 6- to 12-month-old infant of 9.2 kg (Table 11).
Table 11. Inhalation exposure of a 6- to 12-month-old infant to triclosan-contaminated dust

<table>
<thead>
<tr>
<th>Exposure standard</th>
<th>Dust exposure level (mg/m³)</th>
<th>Triclosan concentration in dust¹ (mg a.i./mg dust)</th>
<th>Triclosan concentration in inhaled air² (mg/m³)</th>
<th>Estimated daily dose³ (mg/kg bw per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US EPA’s ambient air quality standard for dust exposure</td>
<td>0.15</td>
<td>7.33 × 10⁻⁷</td>
<td>1.1 × 10⁻⁷</td>
<td>6.45 × 10⁻⁸</td>
</tr>
<tr>
<td>ACGIH-TLV</td>
<td>10</td>
<td>7.3 × 10⁻⁶</td>
<td>4.30 × 10⁻⁶</td>
<td>6.45 × 10⁻⁶</td>
</tr>
<tr>
<td>OSHA PEL</td>
<td>15</td>
<td>1.1 × 10⁻⁴</td>
<td>6.45 × 10⁻⁶</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: ACGIH, American Conference of Governmental Industrial Hygienists; OSHA, Occupational Safety and Health Administration; PEL, permissible exposure level; TLV, threshold limit value

¹ Triclosan concentration in dust of 733 ng a.i./g dust = 7.33 × 10⁻⁷ mg a.i./mg dust.
² Triclosan concentration in inhaled air (mg/m³) = dust exposure level (mg/m³) × triclosan concentration in dust (mg/mg).
³ Estimated daily dose (mg/kg bw per day) = [triclosan concentration in inhaled air (mg/m³) × inhalation rate (m³/day) × exposure duration (1 day)] / body weight (9.2 kg).

For 6- to 12-month-old infants, the maximum daily exposure resulting from inhalation of triclosan-contaminated dust was estimated to be 0.006 45 µg/kg bw per day. Using this estimated daily exposure and the NOAEL of 3.21 mg/kg bw per day from the inhalation study in rats, the resulting MOE is greater than 497 000 (target MOE of 300).

3.3.4.2 Aggregate Exposure of Children Less than 6 Years of Age

The Canadian biomonitoring data available for children less than 6 years of age are limited to infants less than 1 week old and 2- to 3-month-old infants. No Canadian biomonitoring data are available for 6- to 12-month-old infants.

The aggregate risk for children was estimated by combining estimated daily doses from infant-specific scenarios with estimated daily doses derived from biomonitoring data for either children 6–11 years of age (NHANES) or 2- to 3-month-old infants (P4 study) (Table 12). A combined MOE approach is used to aggregate estimated daily exposures from scenarios with the same target MOE. According to information obtained for 2- to 3-month-old infants in the P4 study, the maximum urine concentration is from a breastfed infant; therefore, inclusion of exposure (and MOE) for 2- to 3-month-old infants is expected to account for all potential routes of exposure, including nursing. The following aggregation equation was used to aggregate “unitless” MOEs into a total MOE (MOET):

\[
\text{MOET} = \frac{1}{\text{MOE}_1} + \frac{1}{\text{MOE}_2} + \cdots + \frac{1}{\text{MOE}_n}
\]

where MOE₁, MOE₂, ..., MOEₙ represent route-specific scenarios (i.e., object-to-mouth, hand-to-mouth and P4 biomonitoring data for a 2- to 3-month-old infant or NHANES biomonitoring data for a 6- to 11-year-old child).
data for 6- to 11-year-old children). A total MOE greater than the target MOE of 300 indicates that risk is not of concern.

Table 12. Aggregate risk estimates for children less than 6 years of age

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Estimated daily dose (mg/kg bw per day)</th>
<th>MOE</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine data (NHANES data)</td>
<td>0.0025</td>
<td>10 000</td>
<td>NHANES urine data for children 6–11 years of age (mean concentration and mean urine volume)</td>
</tr>
<tr>
<td>Urine data (P4 biomonitoring data)</td>
<td>0.0185</td>
<td>1351</td>
<td>P4 urine data for infants 2–3 months of age (maximum exposure dose)</td>
</tr>
<tr>
<td>Nursing</td>
<td>0.006</td>
<td>4167</td>
<td>Infants 6–12 months of age</td>
</tr>
<tr>
<td>Hand-to-mouth</td>
<td>$1.24 \times 10^{-6}$</td>
<td>20 161 000</td>
<td>Infants 6–12 months of age (median concentration and mean ingestion rates)</td>
</tr>
<tr>
<td>Object-to-mouth</td>
<td>0.0068</td>
<td>3676</td>
<td>Infants 6–12 months of age</td>
</tr>
<tr>
<td>Combined MOE approach$^1$</td>
<td></td>
<td>988</td>
<td>P4 (infants 2–3 months old) + hand-to-mouth + object-to-mouth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1634</td>
<td>NHANES (children 6–11 years of age) + hand-to-mouth + object-to-mouth + nursing</td>
</tr>
</tbody>
</table>

$^1$ Combined MOE = $1/(1/MOE_1 + 1/MOE_2 + \ldots + 1/MOE_n)$, where MOE_1, MOE_2, \ldots, MOE_n represent route-specific scenarios.

The inhalation estimate was not included in the aggregate exposure assessment, since the contribution of inhalation exposure was considered negligible when compared with other potential routes of exposure (see above).

Using the combined MOE approach, aggregate exposure of 6- to 12-month-old infants resulted in combined MOEs ranging from 988 to 1634 (target MOE of 300), depending on the use of exposure estimates based on P4 and NHANES data, respectively. The results of this highly conservative risk assessment indicate that the aggregate risk for children less than 6 years of age, including breastfed infants, is below the level of concern.

3.3.4.3 Uncertainties Associated with Aggregate Risk Assessment for Children

There are uncertainties and conservatism in conducting an aggregate exposure and risk assessment for children, due to a lack of adequate data to fully characterize the exposure of young children to triclosan. These uncertainties are highlighted below.

There is an uncertainty with respect to the dose estimation for breastfed infants due to the high variability of triclosan measurements in breast milk. It is unknown if high levels of triclosan in some breast milk samples were the result of abundant use of consumer products or the result of an isolated event prior to sampling. For that reason, an assumption of the maximum triclosan concentration detected in breast milk for the nursing exposure scenario is considered conservative.
There is an uncertainty regarding the potential co-occurrence of all identified scenarios in practice. An assumption that a child will be exposed daily to high triclosan residues as identified for each scenario is considered conservative. The assumption that all potential exposure scenarios will co-occur also represents conservatism in the aggregate assessment for infants 6–12 months of age. Further, assumptions used in incidental oral exposure assessments (i.e., hand-to-mouth and object-to-mouth) are considered conservative, since it is unlikely that all plastic toys and carpets will be made with material treated with triclosan.

There is also an uncertainty regarding the inclusion of the NHANES estimate for children 6–11 years of age in the aggregate risk assessment for 6- to 12-month-old infants. The inclusion of the NHANES estimate is expected to err on the side of overestimating the potential aggregate dose, since additional sources of exposure that are not relevant to the infant scenario will also be captured (e.g., washing hand with antimicrobial soap).

3.3.5 Human Health Risk Assessment for Workers Exposed to Pest Control Products Containing Triclosan

Workers can be exposed to triclosan via inhalation and dermal contact with this active ingredient at workplaces where triclosan is produced or used. Workers can be exposed either when they are applying the chemical during the manufacturing process or when handling the manufactured goods.

3.3.5.1 Handler Exposure and Risk
There were no chemical-specific exposure studies available for triclosan. Health Canada’s PMRA assessed occupational exposure in industrial settings using exposure data from the Chemical Manufacturers’ Association (CMA) Antimicrobial Exposure Assessment Study (CMA 1990). The objective of the CMA study was to measure occupational exposure of industrial workers during mixing or transfer of antimicrobials to industrial systems. The study monitored workers’ exposure to chemicals used as preservatives in metal working fluids, paints and coatings, in wood, pulp and paper facilities and in cooling towers. Worker exposure was measured for different application methods, including a liquid pour (open mixing/transfer) and liquid pump (closed mixing/transfer).

Dermal and inhalation exposures of individuals involved in the transfer of the antimicrobial (as many transfers as are normally conducted in a workday) from the container to the production batch were monitored in the study. Dermal exposure was assessed by inside and outside gauze patch dosimeters through one layer of clothing. Exposure of the hands was measured using cotton fabric gloves. Inhalation exposure was measured by using a personal sampling pump. Due to the diversity of the products used, there was significant variability in the types of protective clothing worn. Most individuals wore long-sleeved shirts and long pants. Each replicate was representative of the time spent performing the antimicrobial-related task in 1 day; therefore, the data were not normalized. Laboratory and field recoveries were measured; however, recoveries were highly variable due to an insufficient number of spiked samples, poor collection efficiency
of sample media, difficulty in the analysis for the active ingredient and poor storage stability. This is considered a limitation of the CMA exposure study.

Monitoring times and the amount of active ingredient handled daily in plants manufacturing paints and coatings, in plants using metal working fluids and in cooling towers ranged from 2 to 285 minutes and from 0.006 to 265 kg, respectively. In all scenarios, exposure was primarily dermal. Total exposure for each replicate was calculated by summing the total dermal and inhalation doses for each replicate. Since applications of biocides in industrial processes are similar regardless of the use site (e.g., cooling towers, pulp and paper), it was considered appropriate to combine replicates based on the application method. Thus, the replicates with liquid pour and pump application in material preservatives, cooling towers and pulp and paper scenarios were combined to generate exposure estimates. Given the limitations of the exposure study (low and variable laboratory and field recoveries), the 90th percentiles generated from the input CMA data were used by Health Canada’s PMRA to estimate potential risks to operators handling industrial products containing triclosan. Dermal and inhalation exposure estimates represent the 90th percentile of exposure dose normalized to a 70 kg body weight (Table 13). Since most individuals in the CMA study wore long sleeves, long pants and cotton gloves, these data are considered representative of an individual wearing a single layer and gloves.

Table 13. Occupational risk assessment for industrial handler

<table>
<thead>
<tr>
<th>Application method</th>
<th>Dermal exposure(^1) (mg/kg bw per day)</th>
<th>Inhalation exposure(^1) (mg/kg bw per day)</th>
<th>MOE(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dermal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inhalation</td>
</tr>
<tr>
<td>Liquid, pour</td>
<td>0.1034</td>
<td>0.0010</td>
<td>387</td>
</tr>
<tr>
<td>Liquid, pump</td>
<td>0.0268</td>
<td>0.0032</td>
<td>1493</td>
</tr>
</tbody>
</table>

\(^1\) 90th percentile of the exposure dose normalized to a 70 kg body weight (CMA 1990).

\(^2\) MOE = NOAEL (mg/kg bw per day) / daily exposure dose (mg/kg bw per day), where the NOAEL of 40 mg/kg bw per day with a target MOE of 300 was selected for the dermal scenarios, while the NOAEL of 3.21 mg/kg bw per day with a target MOE of 300 was selected for the inhalation scenarios.

The results of the occupational risk assessment for workers applying triclosan in industrial settings via the closed delivery system or an open pour method indicate that risks are below the level of concern.

3.3.5.2 Occupational Post-application Exposure and Risk

Occupational post-application exposure of workers handling manufactured products is not expected to be of concern based on the registered use pattern, since triclosan is applied at low application rates during the manufacturing process and is expected to be embedded in the finished product.

3.3.5.3 Uncertainties in Worker Exposure Estimation

There are uncertainties and conservatisms in conducting occupational risk assessments due to a lack of adequate tools and data to fully characterize exposure from all possible routes. Some of these uncertainties are highlighted below.
Occupational exposure estimates are based on data from the CMA Antimicrobial Exposure Assessment Study. Even though there are a number of limitations associated with the study, it is currently the only occupational study available with which to assess potential exposure from antimicrobial uses of pest control products. Low and variable laboratory and field recoveries were obtained in this study, which may affect the validity of the reported exposure estimates. However, since the 90th percentile estimates from this study were used for risk assessment purposes, exposure estimates are not expected to be underestimated.

Exposure estimates from the CMA Antimicrobial Exposure Assessment Study were not normalized to the amount of active ingredient handled per day. The activities monitored in the study were considered representative of a typical workday; thus, no normalization was conducted. In addition, many of the activities do not involve direct handling of the biocide, but rather a change in coupling or hose from the biocide container. It is uncertain whether the amount of triclosan handled per day is within the range of kilograms of active ingredient handled in the study.

3.4 Cumulative Effects

In the 2008 RED for triclosan, the US EPA did not determine whether triclosan shares a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Consequently, the US EPA assumed that triclosan does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.5 Transformation Products

There are a number of potential environmental transformation products of triclosan to which the general population may be exposed, including methyl-triclosan, 2,4-dichlorophenol (2,4-DCP) and PCDDs (Section 4.2).

Methyl-triclosan is a major environmental transformation product formed as a result of biomethylation in soil and water systems (see Sections 4.1.2.2 and 4.2.5.2). It is also formed during the aerobic treatment of sewage and is discharged in effluents from wastewater treatment plants (WWTPs) with triclosan. Methyl-triclosan should not be considered a degradation product of triclosan, since it is the result of an addition of a methyl group to the triclosan parent molecule, and no degradation takes place. While there is limited monitoring information for methyl-triclosan in the environment and there is uncertainty regarding the observed half-lives and bioaccumulation estimates for this compound, the available laboratory and aquatic field evidence indicates that methyl-triclosan is likely to be both more persistent and more bioaccumulative than triclosan.

2,4-DCP and the lower chlorinated dioxins 2,7/2,8-DCDD are major photoprodusts of triclosan (see Section 4.2.3). In addition, 2,4-DCP as well as PCDDs (1,2,8-trichlorodibenzo-p-dioxin [1,2,8-TriCDD], 2,3,7-TriCDD and 1,2,3,8-TCDD) can form in natural water as a result of
further phototransformation of chlorinated triclosan derivatives (formed during the disinfection of wastewater). A SIDS Initial Report for 2,4-DCP (under the OECD High Production Volume [HPV] Chemicals Programme) indicated that human exposure to this chemical from the use of products containing 2,4-DCP and from the environment is expected to be low (OECD 2007). Dioxins usually enter and are present in the environment as complex mixtures. The toxicity of different dioxins is expressed on a common basis using the international toxicity equivalency factors that recognize and compare the similarities and differences between the toxic actions of the dioxins. The lower chlorinated dibenzodioxins (2,7/2,8-DCDD, 1,2,8-TriCDD, 2,3,7-TriCDD and 1,2,3,8-TCDD) are not listed on the list of 17 dioxins and furans that are of the greatest concern to human health based on international toxicity equivalency factors (NATO 1988), which means that they will be expected to contribute comparatively little to the toxicity of a complex mixture. On this basis, the potential for general population exposure to these dioxins is expected to be low.

Triclosan was also shown to react with chlorine ion in tap water to form chloroform (Rule et al. 2005). The 2001 Government of Canada Priority Substances List Assessment Report for Chloroform (Canada 2001) indicated that human exposure to chloroform from all potential routes and sources of exposure is expected to be considerably less than the level to which a person may be exposed daily over a lifetime without harmful effect.

3.6 Antimicrobial Resistance

Biocides and antibiotics are known to share some common characteristics; consequently, the resistance mechanisms developed by bacteria to such compounds can overlap (e.g., efflux pumps, permeability changes, biofilms, degradation pathways). It is possible that long-term exposure to biocides may create selection pressure that may favour the emergence of genes conferring cross-resistance to both biocides and antibiotics, and some of them could be encoded in mobile genetic elements.

In order to determine the potential of triclosan to induce antimicrobial resistance, recent assessments published by the Australian Department of Health and Ageing (NICNAS 2009) and the European Commission (SCENIHR 2009, 2010; SCCS 2010) were reviewed.

In 2009, the Australian Department of Health and Ageing NICNAS concluded, based on a comprehensive review of literature published in scientific journals between 2002 and 2005 and the 2002 EU Scientific Steering Committee review of triclosan antimicrobial resistance (European Commission 2002), that there was “no evidence that the use of triclosan is leading to an increase in triclosan-resistant bacterial populations or that there is any increased risk to humans regarding antibiotic resistance” (NICNAS 2009).

In 2009 and 2010, the European Commission also published comprehensive reviews of available scientific data on the antibiotic resistance effects of triclosan (SCENIHR 2009, 2010; SCCS 2010). The studies reviewed by the EU’s Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) indicated that triclosan-resistant bacteria can be found in
health care settings and in consumer products. Although laboratory studies showed that it is possible to develop bacterial mutants with reduced susceptibility to both triclosan and antibiotics, no notable selection of antibiotic resistance in bacteria exposed to triclosan was observed in the environmental studies. In addition, the lack of data on other biocide compounds prevented the SCENIHR from reaching a conclusion regarding the potential for triclosan to induce bacterial antibiotic resistance under field use conditions (SCENIHR 2009). The EU’s SCCS concluded that, based on the available scientific information, it is not possible to quantify the risk of development of antimicrobial resistance induced by triclosan applications, including its use in cosmetics (SCCS 2010).

Overall, the SCENIRH concluded that in order to clearly characterize potential risk, new data and methodologies are needed, including quantitative data on exposure to biocides, surveillance programs to evaluate the ability of a biocide to induce/select for resistance against biocides and antibiotics, as well as environmental studies to identify and characterize biocide-related resistance and cross-resistance to antibiotics (SCENIHR 2009, 2010). Consistent with these, more recent information also suggests that additional studies warrant further investigation of the significance of cross-resistance to antibiotics selected by triclosan/biocides (Dann and Hontela 2011; Saleh et al. 2011).
4. Environment

4.1 Releases of Triclosan to the Environment

There are no known natural sources of triclosan; its presence in the environment is due solely to human activity. The sections below present potential anthropogenic sources of triclosan for different environmental compartments—namely, air, water and soil. The possible pathways for releases of triclosan to the environment are presented in Figure 2; they are based on a conceptual diagram proposed by Bound and Voulvoulis (2005) for pharmaceuticals in the environment.

![Figure 2. Possible pathways for releases of triclosan to the environment (modified from Bound and Voulvoulis 2005)](image)

4.1.1 Releases to Air

Based on the documented uses of triclosan in Canada and on its physical/chemical properties (e.g., low volatility), this substance is not expected to be released to air.

4.1.2 Releases to Water

4.1.2.1 Releases from Industry/ Household to Wastewater Treatment Plants

Triclosan is used in a variety of consumer products. These products are for the most part released down the drain, discharged into sewers and carried to WWTPs. Industries that manufacture products that contain triclosan may also release some into sewers. The relative contribution of
households versus industries to releases of triclosan to WWTPs is unknown. In addition, triclosan that is present in products such as drugs and toothpaste can be absorbed orally by humans and then excreted (up to 83% of the oral dose; Sandborgh-Englund et al. 2006) or directly spit out into the sink, in the case of toothpaste. The excreted triclosan is then carried to WWTPs through sewers. Triclosan is also applied on textiles such as T-shirts to prevent emissions of undesirable odours. Based on published studies, it is estimated that the washing of these T-shirts during their use life can release to the sewers 1.5% of the mass of triclosan that they contain (22 mg per shirt) (Walser et al. 2011). Junker and Hay (2004) showed that only trace amounts of triclosan are desorbed from plastic when exposed to water in a laboratory setting. Treated plastics and textiles are not expected to contribute significantly to the total amount of triclosan released from households to sewers and WWTPs.

Data on concentrations of triclosan in the influent of a series of WWTPs (i.e. in sewage or wastewater at point of entry into WWTP) located across Canada were available from the literature and are shown in Table 14.

**Table 14. Concentration of triclosan in the influent and effluent of certain WWTPs in Canada**

<table>
<thead>
<tr>
<th>Location of WWTPs</th>
<th>Sampling year</th>
<th>Population served by WWTP (persons)</th>
<th>Concentration in influent (min–max or average, ng/L)</th>
<th>Concentration in effluent (min-max, ng/L)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quebec</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A municipal WWTP²</td>
<td>2010–2011</td>
<td>n/d²</td>
<td>351 (winter) 650 (summer)</td>
<td>315 (winter) 411 (summer)</td>
<td>Personal communication³</td>
</tr>
<tr>
<td><strong>Ontario</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamilton</td>
<td>2002</td>
<td>352 000</td>
<td>1150</td>
<td>520–740</td>
<td>Lee et al. 2003</td>
</tr>
<tr>
<td>Toronto (4 WWTPs)</td>
<td></td>
<td>75 000–1 750 000</td>
<td>380–1320</td>
<td>140–210</td>
<td></td>
</tr>
<tr>
<td>Burlington</td>
<td></td>
<td>144 130</td>
<td>790</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>Guelph</td>
<td></td>
<td>100 000</td>
<td>740</td>
<td>110–130</td>
<td></td>
</tr>
<tr>
<td>Dundas</td>
<td></td>
<td>27 800</td>
<td>2910</td>
<td>30–50</td>
<td></td>
</tr>
<tr>
<td>Waterdown</td>
<td></td>
<td>n/a</td>
<td>2260</td>
<td>120–150</td>
<td></td>
</tr>
<tr>
<td>Windsor</td>
<td>2003</td>
<td>78 500</td>
<td>n/a</td>
<td>Mean prior to UV disinfection: 80</td>
<td>Hua et al. 2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean after UV disinfection: 63</td>
<td></td>
</tr>
<tr>
<td>Location of WWTPs</td>
<td>Sampling year</td>
<td>Population served by WWTP</td>
<td>Concentration in influent (min–max or average, ng/L)</td>
<td>Concentration in effluent (min-max, ng/L)</td>
<td>Reference</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>---------------</td>
<td>---------------------------</td>
<td>--------------------------------------------------------</td>
<td>------------------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>12 municipal WWTPs along the Thames River (receiving a mix of residential and industrial wastewater)</td>
<td>2002</td>
<td>2475–182 000</td>
<td>410–3640 Mean: 108 Maximum: 324</td>
<td></td>
<td>Lishman et al. 2006</td>
</tr>
<tr>
<td>8 municipal WWTPs in southern Ontario</td>
<td>2004</td>
<td>77 225–1 750 000</td>
<td>870–1830</td>
<td>50–360</td>
<td>Lee et al. 2005</td>
</tr>
<tr>
<td>A municipal WWTP</td>
<td>2010–2011</td>
<td>n/d</td>
<td>695 (winter) 1307 (summer)</td>
<td>269 (winter) 87 (summer)</td>
<td>Personal communication³</td>
</tr>
<tr>
<td>A municipal WWTP</td>
<td>2010–2011</td>
<td>n/d</td>
<td>1292 (winter) 2523 (summer)</td>
<td>112 (winter) 70 (summer)</td>
<td>Personal communication³</td>
</tr>
<tr>
<td>British Columbia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A municipal WWTP</td>
<td>2010–2011</td>
<td>n/d</td>
<td>1140 (winter) 1393 (summer)</td>
<td>248 (winter) 131 (summer)</td>
<td>Personal communication³</td>
</tr>
<tr>
<td>A municipal WWTP in the metropolitan area of Vancouver</td>
<td>2006</td>
<td>1 000 000</td>
<td>n/a</td>
<td>192</td>
<td>Personal communication³</td>
</tr>
<tr>
<td>Capital Regional District Victoria outfall</td>
<td></td>
<td>n/a</td>
<td>n/a</td>
<td>2200–4160</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: max, maximum; min, minimum; n/a, not available; n/d, not divulgeable; UV, ultraviolet; WWTP, wastewater treatment plant

1 Environment Canada (2009).

2 Information is available, but cannot be divulged here. Divulging this information could lead to the identification of the WWTP, which was requested to be kept confidential. Certain WWTPs are the same across studies.

3 2011 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced.

4 2008 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced.

### 4.1.2.2 Removal by WWTPs

The fate of triclosan within WWTPs is somewhat complex and has been the subject of several investigations (Bester 2003, 2005; Sabaliunas et al. 2003; Thomas and Foster 2005; Waltman et al. 2006). WWTPs are quite efficient in removing triclosan from wastewater. In Canada, Lishman et al. (2006) reported 74–98% removal of triclosan in WWTPs located along the Thames River in Ontario. Most of these plants included secondary treatment with activated sludge as part of their process. Lee et al. (2003) reported a median removal efficiency of 81% (range: 49–94%) in WWTPs located in southern Ontario. Again, most of these plants employed
at least secondary treatment. These removal efficiencies compare with those measured in other
countries. Indeed, Bester (2003, 2005) reported triclosan removal efficiencies of 87–96% in
WWTPs in Germany, whereas McAvoy et al. (2002) reported removal of 95–96% for plants in
the United States. Singer et al. (2002) and Sabaliunas et al. (2003) reported 94% and 95%
removal in WWTPs in Switzerland and the United Kingdom, respectively. All the plants
investigated in those studies employed secondary treatment. Thomas and Foster (2005) reported
that the majority of triclosan removal occurs during secondary treatment (55–88%) and that a
smaller proportion (10–44%) is removed during primary treatment. Overall, the percent removal
for the WWTPs sampled in that study (located in the United States) was 98–99%. These
numbers show that even though WWTPs are efficient at removing triclosan, this is mainly due to
secondary treatment. It should be mentioned that, based on data from 2004, 26% of the 22
million Canadians serviced by municipal sewer systems were provided only with primary
wastewater treatment or less (Environment Canada 2007).

The removal mechanisms of triclosan from wastewater were investigated in a few studies.
Thomas and Foster (2005) showed that adsorption to particulate matter is a likely removal
mechanism for triclosan. Bester (2003) reported that 96% of triclosan was removed from
wastewater, of which 22–43% was adsorbed to the sludge. This is in line with the moderately
sorptive nature of this compound (log \( K_{oc} \) up to 4.67; see Table 2). Federle et al. (2002)
conducted a continuous activated sludge test aimed at examining the degradation of triclosan and
at studying the effect of a shock loading with pulses of triclosan. In this test, \(^{14}\text{C}\)-labelled
triclosan was used to establish a material balance. The authors reported that, at steady state,
between 1.5% and 4.5% of triclosan was sorbed to solids, whereas 81–92% was mineralized to
carbon dioxide or incorporated into microbial biomass. The \(^{14}\text{C}\) present in the effluent consisted
of extractable (in ethyl acetate) and non-extractable polar intermediates (0.4–7.2% and 2.3–
10.5%, respectively). Overall removal of the parent compound exceeded 98.5%. A second set of
experiments showed that shock loading with triclosan, which is representative of a situation in
which a WWTP receives a consistent low level of triclosan but with periodical pulses of higher
levels, did not change the removal pattern significantly. The same authors also conducted a batch
activated sludge mineralization test. In this test, 31–52% of triclosan had degraded to \(^{14}\text{CO}_2\) 71
days after its addition to the sludge. Following a lag period of 3–10 days, triclosan was spiked
again in the test system, resulting in 79–81% of this second dose being recovered as \(^{14}\text{CO}_2\) after
52 days.

Even though triclosan is removed efficiently by WWTPs, it may also be methylated to methyl-
triclosan during the treatment process, likely during secondary treatment. The contribution of
this reaction to the overall removal of triclosan from wastewater is not known, but it is expected
to be low, since the levels of methyl-triclosan in effluents from WWTPs are very low (Lindström
et al. 2002; McAvoy et al. 2002). In addition, chloramines either used as an alternative
disinfectant in drinking water treatment or formed during the chlorination of non-nitrified
wastewater effluents can react with triclosan, although the reactivity of triclosan in the presence
of chloramines is low. Greyskoch and Vikesland (2006) examined triclosan reactivity in
chloraminated waters over a pH range of 6.5–10.5. The products of these reactions included
three chlorinated forms of triclosan as well as 2,4-DCP and 2,4,6-trichlorophenol.
4.1.2.3 Releases from WWTPs to Surface Water

In Canada
Results of several surveys have indicated that triclosan is released from Canadian WWTPs as part of their effluent (30–4160 ng/L; see Table 14). The wide range of concentrations measured in effluents reflects the differences in the population served by the WWTPs as well as the various treatment levels used by the plants (from no treatment to treatment with activated sludge).

In Other Countries
In a monitoring study conducted in the United States, samples of influent, primary effluent, and final effluent were collected from five WWTPs and analyzed for triclosan and methyl-triclosan (McAvoy et al. 2002). The plants sampled served populations of 2445–398,000 persons. The concentrations of triclosan in final effluents ranged between 240 and 410 ng/L and between 1610 and 2700 ng/L for plants using activated sludge or trickling filter treatments, respectively. The trickling filter treatment involves the use of a bed of crushed rock or synthetic media to support a film of aerobic microorganisms. This method is recognized as being less effective than the activated sludge treatment. Less than 2% of WWTPs in Canada use this process. Methyl-triclosan, a transformation product, was qualitatively detectable in all samples and was estimated to be present in the range of 2–50 ng/L.

Lindström et al. (2002) collected samples of primary and final effluent from WWTPs in Switzerland in 1997 and 2001. All the WWTPs sampled included a biological treatment process (method not specified), and they served populations of 4500–36,000 persons. Both triclosan and methyl-triclosan were analyzed in the samples. Triclosan in the primary effluent was found at concentrations of 600–1300 ng/L, whereas methyl-triclosan was detected in much lower concentrations, from less than 1 to 4 ng/L. The corresponding final effluent concentrations were between 70 and 650 ng/L for triclosan and between less than 2 and 11 ng/L for methyl-triclosan. The higher concentrations of methyl-triclosan in the final effluent compared with the primary effluent point to the formation of this compound during biological treatment.

A monitoring program in Denmark measured triclosan concentrations in the final effluent of a WWTP serving a population of 750,000 inhabitants as well as industries. This plant included biological treatment as part of its wastewater treatment process. The average triclosan concentration measured in the effluent was below the detection limit of 1000 ng/L (Pedersen and Nielsen 2003). In Sweden, the final effluents from the three largest WWTPs in the country were sampled and analyzed for several organic pollutants, including triclosan (Paxéus 1996). In two of the plants, triclosan was measured at a concentration of 500 ng/L; it was not detected in the effluent of the third plant (method detection limit [MDL] not specified).

Based on the above, releases of triclosan to surface water in Canada from WWTP effluents are similar to those measured in other countries. This is confirmed by the data summarized by the
US EPA, with WWTP effluent concentrations ranging from 10 to 2700 ng/L in the United States, from 80 to 269 000 ng/L in Spain and from 10 to 600 ng/L in Germany (US EPA 2008e).

4.1.3 Releases to Soil

Some of the reported uses for triclosan in Canada may lead to this substance reaching landfills as part of solid wastes (e.g., products made of textile or rubber). No data on the quantity of triclosan following this disposal pathway are available.

Another source of release of triclosan to soil is the spreading of biosolids (sludge) from wastewater treatment facilities on agricultural land. Considering this, the levels of this compound in sludge were investigated.

4.1.3.1 Concentrations in Wastewater Treatment Sludge in Canada

Concentrations of triclosan in municipal wastewater sludge sampled in WWTPs across Canada were reported by Lee and Peart (2002). They sampled 25 plants across Canada, from Vancouver to Moncton (Table 15). Most of the samples collected were from digested sludge (i.e., following secondary wastewater treatment). Triclosan was readily detected in all sludge samples, with a concentration range of 0.90–28.2 μg/g dry weight (dw) (median: 12.5 μg/g dw). The authors of this study stated that triclosan is likely to be the most abundant polychlorinated phenol ever found in wastewater sludge, as only 3 out of 35 samples taken contained less than 5 μg/g dw of triclosan. Chu and Metcalfe (2007) measured similar levels of triclosan (0.68–11.55 μg/g dw) in treated biosolids collected in 2006 from four municipal WWTPs in southern Ontario (locations not provided). In a study conducted for the Canadian Council of Ministers of the Environment to document the occurrence of emerging substances of concern in biosolids, samples were collected in 2009 at 11 WWTPs located across Canada (CCME 2010a; Table 15). Overall, triclosan occurred in 97% of the samples collected; the median concentration for all samples was 6.1 μg/g dw (range: < 0.1–46.4 μg/g dw), the highest value among all of the 82 substances analyzed in this study. According to the study, only the aerobic composting processes appeared successful in reducing the input mass of triclosan in the feed sludges. This substance was not well reduced by anaerobic digestion.

Table 15. Concentrations of triclosan in wastewater sludge in Canada (digested sludge unless specified otherwise)

<table>
<thead>
<tr>
<th>WWTP location</th>
<th>Sampling period</th>
<th>Concentration (μg/g dw)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancouver (BC)</td>
<td>1994 and 1999</td>
<td>8.41–24.7</td>
<td>Lee and Peart 2002</td>
</tr>
<tr>
<td>Calgary (Bonny Brook) (AB)</td>
<td>1999</td>
<td>12.8</td>
<td></td>
</tr>
<tr>
<td>Calgary (Fish Creek) (AB)</td>
<td>1999</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>Edmonton (AB)</td>
<td>2000</td>
<td>22.0</td>
<td></td>
</tr>
<tr>
<td>Regina (SK)</td>
<td>2000</td>
<td>18.9</td>
<td></td>
</tr>
<tr>
<td>Saskatoon (SK)</td>
<td>2000</td>
<td>9.9</td>
<td></td>
</tr>
<tr>
<td>Adelaide¹ (ON)</td>
<td>1998</td>
<td>8.9</td>
<td></td>
</tr>
</tbody>
</table>
### Preliminary Assessment: Triclosan (March 2012)

<table>
<thead>
<tr>
<th>WWTP location</th>
<th>Sampling period</th>
<th>Concentration (μg/g dw)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Burlington (ON)</strong></td>
<td>2001</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td><strong>Galt (ON)</strong></td>
<td>1996</td>
<td>7.48</td>
<td></td>
</tr>
<tr>
<td><strong>Guelph (ON)</strong></td>
<td>1999</td>
<td>28.2</td>
<td></td>
</tr>
<tr>
<td><strong>Hamilton (ON)</strong></td>
<td>1997</td>
<td>16.2</td>
<td></td>
</tr>
<tr>
<td><strong>Ingersoll (ON)</strong></td>
<td>1998</td>
<td>11.5</td>
<td></td>
</tr>
<tr>
<td><strong>Kitchener (ON)</strong></td>
<td>1997</td>
<td>16.1</td>
<td></td>
</tr>
<tr>
<td><strong>Ottawa (ON)</strong></td>
<td>2000</td>
<td>18.6</td>
<td></td>
</tr>
<tr>
<td><strong>Waterloo (ON)</strong></td>
<td>1996</td>
<td>11.7</td>
<td></td>
</tr>
<tr>
<td><strong>Windsor (ON)</strong></td>
<td>1997</td>
<td>8.84</td>
<td></td>
</tr>
<tr>
<td><strong>Toronto (Ashbridges Bay) (ON)</strong></td>
<td>2000</td>
<td>20.3</td>
<td></td>
</tr>
<tr>
<td><strong>Toronto (Highland Creek)</strong></td>
<td>2000</td>
<td>16.5</td>
<td></td>
</tr>
<tr>
<td><strong>Toronto (Humber) (ON)</strong></td>
<td>2000</td>
<td>16.6</td>
<td></td>
</tr>
<tr>
<td><strong>Toronto (North) (ON)</strong></td>
<td>2000</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td><strong>Montréal1 (QC)</strong></td>
<td>1999</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td><strong>Granby (QC)</strong></td>
<td>1996</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td><strong>Québec1 (QC)</strong></td>
<td>2000</td>
<td>5.5–9.8</td>
<td></td>
</tr>
<tr>
<td><strong>Moncton (NB)</strong></td>
<td>1997</td>
<td>1.92</td>
<td></td>
</tr>
<tr>
<td><strong>Truro (NS)</strong></td>
<td>1996</td>
<td>7.53</td>
<td></td>
</tr>
<tr>
<td><strong>4 WWTPs in southern Ontario (ON)</strong></td>
<td>2006</td>
<td>0.68–11.55</td>
<td>Chu and Metcalfe 2007</td>
</tr>
<tr>
<td><strong>Salmon Arm (BC)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Red Deer (AB)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Saskatoon (SK)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prince Albert (SK)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Eganville (ON)2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Smiths Falls (ON)2</strong></td>
<td>2009</td>
<td></td>
<td>CCME 2010a</td>
</tr>
<tr>
<td><strong>Gatineau Valley (QC)2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gatineau Valley (QC)3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Saguenay (QC)2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moncton (NB)4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moncton (NB)3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Halifax (NS)5</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gander (NL)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
No monitoring data could be found for concentrations of methyl-triclosan in wastewater sludge from WWTPs in Canada.

### 4.1.3.2 Concentrations in Wastewater Treatment Sludge in Other Countries

McAvoy et al. (2002) measured the concentrations of triclosan and methyl-triclosan in sludge samples taken from WWTPs in the United States. The concentrations of triclosan ranged from 0.5 to 15.6 μg/g dw, whereas those for methyl-triclosan ranged from below the limit of quantification (LOQ) to 1.03 μg/g dw. Concentrations of chlorinated derivatives up to 0.42 μg/g dw were also measured in the samples. The concentrations of triclosan measured in different sludge samples indicated that triclosan is rapidly removed during the aerobic sludge digestion process. However, samples taken at a trickling filter treatment plant showed little or no removal of triclosan during anaerobic sludge digestion. McClellan and Halden (2010) measured an average triclosan concentration of 12.6 μg/g dw and a maximum concentration of 19.7 μg/g dw in archived biosolids collected in 2001 at 94 WWTPs in the United States as part of a national survey. Among the 38 compounds that were detected in the sludge samples, triclosan had the second highest mean concentration after triclocarban, which is another antimicrobial agent.

In Australia, Langdon et al. (2011) sampled biosolids from 13 WWTPs and found triclosan concentrations ranging from 0.22 to 9.89 μg/g dw, with an average of 3.77 μg/g dw. In Sweden, Svensson (2002) sampled sludge from 19 WWTPs in 2001–2002. The concentration of triclosan in the sludge samples ranged from 0.028 to 6.4 μg/g dw. Another investigation of sludge samples from four Swedish WWTPs in 2001 revealed similar triclosan concentrations (2.8–4.4 μg/g dw) in anaerobically digested sludge (Remberger et al. 2002). For one of the plants surveyed, both a primary and an anaerobically digested sludge sample were analyzed. The results of these analyses supported the findings of McAvoy et al. (2002) that little or no removal of triclosan occurs during anaerobic digestion.

The concentrations of triclosan measured in the United States and in Sweden are within the range of those presented in Table 15 for Canada.
4.2 Environmental Fate

4.2.1 Environmental Distribution

When a substance is able to ionize in water at environmentally relevant pH, its neutral and ionic forms will co-exist in the environment (water, sediment and soil). With a $pK_a$ of 8.1 (see Table 2), triclosan will ionize to some extent in most of the natural water bodies in Canada. The ionization of triclosan proceeds as the proton attached to the phenolic group dissociates from the structure forming an anionic molecule. At pH values of 6, 7, 8 or 9, the fraction of ionized triclosan in pure water will be 1%, 7%, 44% or 89%, respectively, using the equation $F_i = 1 - (1/(1+10^{\text{pH} - pK_a})) \times 100\%$, where $F_i$ is the fraction ionized.

Table 16 summarizes the distribution of the neutral and anionic forms of triclosan among environmental compartments based on the Multispecies Model (version 1.0; Cahill 2008). More specifically, the results provide the proportion (fraction of the total mass emitted to the environment) of each form present in each compartment upon a continuous release to water or soil, at an environmental pH of 7. The model was also run at an environmental pH of 8, since this value is also relevant for many aquatic and terrestrial ecosystems in Canada. The proportion modelled is determined with respect to the total quantity released, so the sum of all proportions adds up to 100%. The physical/chemical properties and half-life values presented in Tables 2 and 17, respectively, were used as input for the model. The input values for the physical/chemical properties of the ionized form of triclosan were based on the corresponding values for the neutral form, after applying correction factors, while the input values for half-lives were the same as for the neutral form. The results in Table 16 represent the net effect of chemical partitioning, intermedia transport and loss by both advection (out of the modelled region) and degradation or transformation processes.

Table 16. Distribution of the two forms of triclosan among environmental compartments at pH 7 and 8

<table>
<thead>
<tr>
<th>Triclosan released to:</th>
<th>Form</th>
<th>Air</th>
<th>Water</th>
<th>Soil</th>
<th>Sediment</th>
</tr>
</thead>
<tbody>
<tr>
<td>At pH 7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water (100%)</td>
<td>Neutral</td>
<td>0.0</td>
<td>72.9</td>
<td>0.0</td>
<td>19.8</td>
</tr>
<tr>
<td></td>
<td>Ionized</td>
<td>0.0</td>
<td>5.8</td>
<td>0.0</td>
<td>1.6</td>
</tr>
<tr>
<td>Soil (100%)</td>
<td>Neutral</td>
<td>0.0</td>
<td>0.1</td>
<td>92.6</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Ionized</td>
<td>0.0</td>
<td>0.0</td>
<td>7.3</td>
<td>0.0</td>
</tr>
<tr>
<td>At pH 8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water (100%)</td>
<td>Neutral</td>
<td>0.0</td>
<td>50.6</td>
<td>0.0</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Ionized</td>
<td>0.0</td>
<td>40.1</td>
<td>0.0</td>
<td>4.1</td>
</tr>
<tr>
<td>Soil (100%)</td>
<td>Neutral</td>
<td>0.0</td>
<td>0.2</td>
<td>55.6</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Ionized</td>
<td>0.0</td>
<td>0.1</td>
<td>44.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

In a scenario where triclosan is exclusively released to water through effluents from WWTPs, it is expected to reside in both water (79–91%) and sediment (9–21%) at pH 7 and 8. If released
only to soil through sludge amendment, triclosan remains almost exclusively in this compartment (> 99%) (details on exposure scenarios are presented in Section 4.6.1). At an environmental pH of 7, triclosan will mainly be present in its neutral form in water, sediment and soil. At a pH of 8 in these same compartments, about 55% of triclosan will be in its neutral form and 45% in its ionized (anionic) form. In the Prairie provinces, for instance, where soil is alkaline (pH 9), triclosan would be present primarily in its anionic form.

4.2.2 Fate in Air

There are no experimental data on the half-life of triclosan in air; therefore, this parameter was modelled using the AOPWIN model (AOPWIN 2008). With a half-life less than 2 days (0.66 day) via reactions with hydroxyl radicals, triclosan is not considered persistent in air based on the criterion set out in the Persistence and Bioaccumulation Regulations (Canada 2000). Also, this half-life of less than 2 days in air and the distribution results presented in Table 16 both indicate that triclosan is not likely to be subject to long-range transport.

4.2.3 Fate in Water

4.2.3.1 Abiotic Processes

Laboratory studies have shown that triclosan is hydrolytically stable at pH 4, 7 and 9 (US EPA 2008e). It is also stable against strong acids and bases (Singer et al. 2002). Its low Henry’s Law constant of \(5.05 \times 10^{-4} \text{ Pa} \cdot \text{m}^3/\text{mol}\) (see Table 2) indicates that it should not volatilize from a water surface.

Triclosan is susceptible to phototransformation in surface waters, as shown in many studies (Lindström et al. 2002; Singer et al. 2002; Tixier et al. 2002; Mezcua et al. 2004; Latch et al. 2005; Lores et al. 2005). Tixier et al. (2002) quantified the phototransformation of triclosan under laboratory and field conditions for a small lake in Switzerland. They highlighted the fact that pH, by affecting the speciation of triclosan (pK\(_a\) = 8.1), has an impact on its absorption of sunlight. Indeed, the direct phototransformation rate of triclosan increases with pH, i.e., with the proportion of the ionized form of triclosan present in solution. Indirect phototransformation (e.g., photosensitization by organic matter) was a negligible process. The study authors estimated that, during the summer season, direct phototransformation accounted for 80% of the observed total elimination of triclosan from the study lake. The remaining major sink for triclosan was the loss in the outflow. The authors also predicted triclosan phototransformation rates for a variety of environmental conditions, including time of year and latitude. The resulting primary degradation half-life values spanned from 2 to 2000 days. For latitudes modelled by the authors that are equivalent to southern Canada (~45–50°N) and for a pH of 8.0, the effective annualized phototransformation half-lives obtained for triclosan in water were less than 100 days throughout the year. For water bodies having a lower pH, somewhat longer half-lives would be expected (but still less than 100 days), and the relative importance of other removal processes, such as biodegradation and sedimentation, would increase.
Latch et al. (2005) performed experiments in both natural and deionized water under natural sunlight and showed that triclosan was rapidly degraded by direct photolysis (half-life of 5 hours at pH 8, midsummer sunlight, 45°N latitude).

Lindström et al. (2002) conducted a photolysis experiment in which triclosan was exposed to natural sunlight in lake water at different pH values. While triclosan was stable at pH 5.6, it degraded rapidly at pH 8.0 (half-life of about 20 minutes). Methyl-triclosan, which reaches surface water as part of WWTP effluents, was also tested in this study; it did not photodegrade at either pH.

Different degradation products can be formed by the photolysis of triclosan. For instance, in addition to showing a short half-life for triclosan (41 minutes), a study conducted under laboratory conditions indicated that 2,4-DCP was formed as a major transformation product (up to 97%; US EPA 2008f). This substance has been the subject of a SIDS Initial Assessment Report under the OECD HPV Chemicals Programme. This report indicates that 2,4-DCP is likely not persistent, not bioaccumulative and moderately toxic to aquatic organisms (OECD 2007).

Mezcua et al. (2004) measured 2,7/2,8-DCDD as major phototransformation products of triclosan under natural sunlight. Two phototransformation experiments were conducted at two different pH values (pH 5 and 7). It was shown that triclosan transformed to dioxin at pH 7 only, confirming the results obtained by Tixier et al. (2002) regarding the high transformation rate of the ionized form compared with the un-ionized form. Mezcua et al. (2004) also measured 2,7/2,8-DCDD in the effluent of a WWTP (4–400 ng/L), thereby revealing its input to receiving surface waters. The phototransformation of triclosan to DCDD was confirmed by Lores et al. (2005) and by Sanchez-Prado et al. (2006) using photo-solid-phase microextraction. Latch et al. (2005) also measured 2,8-DCDD as well as 2,4-DCP as transformation products of triclosan in a photolysis experiment. Yields of these products ranged from 3% to 12%. Finally, the phototransformation of triclosan to 2,8-DCDD was also reported in seawater (Aranami and Readman 2007).

Data available on the degradation of 2,7/2,8-DCDD and the aquatic toxicity of 2,8-DCDD indicate that these compounds should be less harmful to the environment than other dioxins, such as their tetrachlorinated congeners (e.g., 2,3,7,8-TCDD). 2,7/2,8-DCDD are not on the list of 17 dioxins and furans that are of the greatest concern based on international toxicity equivalency factors (NATO 1988). The photolability of 2,7/2,8-DCDD is reported in several studies (Mezcua et al. 2004 [half-life < 20 hours]; Latch et al. 2005; Sanchez-Prado et al. 2006; Aranami and Readman 2007), as is the aerobic microbial degradation of both 2,7- and 2,8-DCDD (e.g., 16–33% within 7 days; Field and Sierra-Alvarez 2008) (Parsons and Storms 1989; Parsons 1992). The toxicity of 2,8-DCDD to fish appears to be low, as suggested by the results of a study in which embryos of the Japanese medaka (Oryzias latipes) hatched and survived for 3 days post-hatch (full exposure duration) when exposed to 50 000 ng/L (Wisk and Cooper 1990). The toxicity of 2,7-DCDD is unknown. Given their probable transient state in the environment and low toxicity, these DCDDs are not likely to be of environmental concern.
Buth et al. (2009) showed that chlorinated triclosan derivatives formed during the disinfection of wastewater can further phototransform to PCDDs, as well as to 2,4-DCP, in natural water. These dioxin congeners (1,2,8-TriCDD, 2,3,7-TriCDD and 1,2,3,8-TCDD) were detected in sediments from the Mississippi River at levels that trended with the historical use of triclosan (Buth et al. 2010). These compounds may be more toxic than 2,7/2,8-DCDD due to their increased chlorine substitution. Buth et al. (2010) estimated that the mass contribution of triclosan-derived dioxins could represent up to 30% of the total dioxin pool in the sediment cores that they analyzed.

4.2.3.2 Biotic processes

**WWTP-Related Conditions**

Based on its chemical structure, triclosan is not expected to biodegrade rapidly. Results obtained for the standardized OECD test guideline 301C (modified MITI test (I)) test indicate that triclosan is not readily or inherently biodegradable (0% degradation after 4 weeks at a test concentration of 100 mg/L) (NITE 2002). In this kind of test, which measures ultimate degradation (measured by the formation of carbon dioxide), an aqueous solution of the test substance is inoculated and incubated under aerobic conditions in the dark or in diffuse light. These results are consistent with previous work by Voets et al. (1976), who observed no loss of triclosan in test systems that were inoculated with a soil extract. However, Federle et al. (2002) suggested that the negative results obtained in these tests are unreliable as a consequence of the likely bacterial toxicity of triclosan at the high concentrations used (1–100 mg/L). This statement is supported by the results of a ready biodegradability study in which triclosan was applied at a rate of 0.2 mg/L to a microbial inoculum in sandy loam soil and activated sludge. Triclosan degraded with an average half-life of 5.2 days (US EPA 2008e). Results of aerobic biodegradation tests conducted at various concentrations (10–500 000 µg/L) for various durations (21–91 days) indicated 18–70% degradation for triclosan (NICNAS 2009). More specifically, Stasinakis et al. (2008) conducted a biodegradability test with triclosan (at 10 µg/L) using the OECD test guideline 301F method (manometric respirometry test). In this 28-day test, 52% ultimate degradation was achieved, and the calculated half-life was 1.8 day. Federle et al. (2002) conducted biodegradation tests with activated sludge at triclosan concentrations of 20–200 µg/L. By the end of the tests (71 days), 31–52% of triclosan had mineralized to carbon dioxide. For comparison purposes, concentrations of triclosan in the influent of WWTPs in Canada are in the range of 0.102–3.6 µg/L (Table 14)—that is, much lower than those tested in the biodegradation tests mentioned above.

Voets et al. (1976) conducted tests with triclosan under anaerobic conditions for sludge digestion in WWTPs. Results of two anaerobic biodegradation tests conducted at 200 and 1000–5000 µg/L for 147 and 21 days, respectively, indicated 10% and 50% degradation, respectively.

**Environmental Conditions**

In an aerobic aquatic metabolism study conducted at 20°C, triclosan disappeared rapidly from the water layer in river water–sandy loam sediment and pond water–silty clay loam sediment systems (US EPA 2008e). In the water layer (pH 7.2–7.3), [14C]triclosan declined from an average 88–93% of the applied radioactivity at time 0 to 49–53% at 1 day to less than or equal
to 0.3% at 56–104 days post-treatment. Volatilized carbon dioxide for the whole system was 21–29% of the applied radioactivity by study termination (day 104). [14C]Triclosan dissipation half-lives for the water layer (resulting from degradation and partitioning) were 1.3–1.4 days based on extractable residues only. Half-lives for sediments and total systems were 54–60 days and 40–56 days, respectively. More details are provided in Section 4.2.4.2 below.

Considering the results above for ultimate biodegradation (i.e., mineralization to carbon dioxide) of triclosan under aerobic conditions, there is evidence that this substance is not persistent in water, based on the criterion set out in the Persistence and Bioaccumulation Regulations (half-life in water ≥ 182 days) (Canada 2000). Results from the aerobic aquatic metabolism study also indicate that triclosan is not persistent in this environmental compartment.

Table 17. Data on the persistence of triclosan in different media

<table>
<thead>
<tr>
<th>Medium</th>
<th>Fate process</th>
<th>Data type</th>
<th>Degradation value</th>
<th>Degradation endpoint, units</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>Atmospheric oxidation</td>
<td>Modelled</td>
<td>0.66(^1)</td>
<td>Half-life, days</td>
<td>AOPWIN 2008</td>
</tr>
<tr>
<td></td>
<td>Hydrolysis (pH 4, 7 and 9, 50°C, for 5 days)</td>
<td>Experimental</td>
<td>Stable</td>
<td>NA</td>
<td>Singer et al. 2002</td>
</tr>
<tr>
<td></td>
<td>Hydrolysis (pH 4, 7 and 9, 50°C, for 5 days)</td>
<td>Experimental</td>
<td>Stable</td>
<td>NA</td>
<td>US EPA 2008e</td>
</tr>
<tr>
<td></td>
<td>Photodegradation (field conditions, pH 8.0, year-round, 50°N)</td>
<td>Experimental</td>
<td>&lt; 100</td>
<td>Primary half-life, days</td>
<td>Tixier et al. 2002</td>
</tr>
<tr>
<td></td>
<td>Photodegradation (laboratory conditions, pH 8.0, summer sunlight, 45°N)</td>
<td>Experimental</td>
<td>5</td>
<td>Primary half-life, hours</td>
<td>Latch et al. 2005</td>
</tr>
<tr>
<td>Water</td>
<td>Photodegradation (laboratory conditions, pH 8.0, summer sunlight, 47°N)</td>
<td>Experimental</td>
<td>0.37</td>
<td>Primary half-life, hours</td>
<td>Lindström et al. 2002</td>
</tr>
<tr>
<td></td>
<td>Photodegradation (laboratory conditions, pH 7.0, artificial light)</td>
<td>Experimental</td>
<td>41</td>
<td>Half-life, minutes</td>
<td>US EPA 2008e</td>
</tr>
<tr>
<td></td>
<td>Biodegradation, WWTP-related conditions (aerobic conditions, various test concentrations and durations)</td>
<td>Experimental</td>
<td>18–70</td>
<td>% degradation</td>
<td>NICNAS 2009</td>
</tr>
<tr>
<td></td>
<td>Biodegradation and partitioning, environmental conditions (aerobic conditions, 20°C, in darkness, for 104 days): - river water–sandy</td>
<td>Experimental</td>
<td>Range for both systems (water layer): 1.3–1.4(^1)</td>
<td>Half-life (dissipation), days</td>
<td>US EPA 2008e</td>
</tr>
<tr>
<td>Medium</td>
<td>Fate process</td>
<td>Data type</td>
<td>Degradation value</td>
<td>Degradation endpoint, units</td>
<td>Reference</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>-------------------</td>
<td>----------------------------</td>
<td>---------------------------</td>
</tr>
</tbody>
</table>
| Sediment        | Biodegradation and partitioning (aerobic conditions, 20°C, in darkness, for 104 days):  
- river water–sandy loam sediment system (pH 7.3)  
- pond water–silty clay loam sediment system (pH 7.2) | Experimental    | Ranges for both systems:  
Sediment: 54–60  
Whole system: 40–56 | Half-life (dissipation), days | US EPA 2008e    |
| Soil            | Biodegradation (aerobic conditions, 20°C, in darkness, for 124 days):  
- sandy loam (pH 7.1)  
- clay loam (pH 6.85)  
- loam (pH 7.3) | Experimental    | 2.9  
3.8  
3.7 | Half-life, days | US EPA 2008e |
|                 | (aerobic conditions, loam, pH 7.4, 22°C)                                        |                 | 18 | Primary half-life, days | Ying et al. 2007 |
|                 | (aerobic conditions, room temperature):  
- silty clay (pH 4.7)  
- sandy loam (pH 4.1)            |                 | 58  
32 | Primary half-life, days | Wu et al. 2009 |
|                 | (aerobic conditions, 20°C in darkness, for 68 days)                            |                 |                 | Primary half-life, days | Xu et al. 2009 |
## 4.2.4 Fate in Sediment

### 4.2.4.1 Abiotic Processes

Triclosan is susceptible to rapid oxidation by manganese oxides, which are present in aerobic sediments and soils (Zhang and Huang 2003). Under environmentally relevant pH and manganese dioxide concentrations, the primary degradation half-life of triclosan was calculated to be less than 21 hours. Degradation products were reported to include 2,4-DCP (< 1% of triclosan loss). However, dissolved metal ions and natural organic matter in water and soil would likely increase this value by competitively adsorbing and reacting with manganese dioxide.

Given its moderate log $K_{oc}$ values of 3.34–4.67 (see Table 2), it can be expected that triclosan (especially the un-ionized form) will adsorb to organic matter present in effluents or in receiving surface waters. As the substance is released to aquatic ecosystems through WWTP effluents, a portion could be removed from the water column through sedimentation. Once in aerobic sediments, triclosan could react with manganese oxides to a certain extent. The balance of these two processes—i.e., input to sediment through sedimentation and output through oxidation—would be difficult to quantify.

### 4.2.4.2 Biotic Processes

As noted previously, triclosan degraded rapidly in river water–sandy loam sediment and pond water–silty clay loam sediment systems under aerobic conditions (US EPA 2008e). In the water layer, $[^{14}\text{C}]$triclosan declined from an average 88–93% of the applied radioactivity at time 0 to less than or equal to 0.3% at 56–104 days post-treatment. In the sediment, $[^{14}\text{C}]$triclosan increased from an average 39–40% of the applied radioactivity at time 0 to 69–75% at 7–14 days and was 21–22% at 104 days post-treatment. In the total system, $[^{14}\text{C}]$triclosan decreased steadily from 88–93% of the applied radioactivity at time 0 to 52–68% at 28 days and to 21.5–21.8% at 104 days post-treatment. $[^{14}\text{C}]$Triclosan dissipation half-lives (degradation and

---

<table>
<thead>
<tr>
<th>Medium</th>
<th>Fate process</th>
<th>Data type</th>
<th>Degradation value</th>
<th>Degradation endpoint, units</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium</td>
<td>Fate process</td>
<td>Data type</td>
<td>Degradation value</td>
<td>Degradation endpoint, units</td>
<td>Reference</td>
</tr>
<tr>
<td>45 days):</td>
<td>- loamy sand (pH 7.5)</td>
<td>- silty clay (pH 7.5)</td>
<td>14</td>
<td>Primary half-life, days</td>
<td>Ying et al. 2007</td>
</tr>
<tr>
<td></td>
<td>- sandy loam (pH 7.1)</td>
<td>- silt loam (pH 7.1)</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Experimental (anaerobic conditions, loam, pH 7.4,</td>
<td>&gt;&gt;&gt; 70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22°C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Value used for fugacity modelling with Multispecies Model.
partitioning) were 1.3–1.4 days (water layer) and 54–60 days (sediment) for both water–sediment systems; degradation half-lives were 40–56 days in total systems. Non-extractable residues (not included in half-life calculations) were 32–33% at study termination, and volatilized carbon dioxide was 21–29%. Methyl-triclosan was identified as a minor transformation product, with a maximum mean of 0.1% of the applied radioactivity at 28 days post-treatment in the water and a maximum mean of 3.4–4.8% at 104 days in the sediment and total system.

No experimentally measured half-lives for triclosan in sediments under anaerobic conditions could be found. However, evidence of the persistence of triclosan in buried anaerobic sediments is shown by monitoring data. Singer et al. (2002) analyzed a sediment core taken from a lake in Switzerland that receives effluents from WWTPs. The concentration profile in the core showed that triclosan has been accumulating in sediments, from less than 5 ng/g dw in 1960–1961 to 42 ng/g dw in 1970–1971 to 53 ng/g dw in 1992–1993. This increase was likely due to its continual input into the lake, showing that it accumulates in anaerobic sediments more rapidly than it degrades. The fact that a relatively high amount of triclosan was contained in the approximately 30-year-old sediment layer (1970–1971) points to a slow degradation rate for triclosan. Triclosan was also detected in cored estuarine sediments from Jamaica Bay, New York. Indeed, Miller et al. (2008) measured peak triclosan concentrations of 600–800 ng/g dw in sediments deposited in that bay between the mid-1960s and late 1970s. For the following years, the concentrations declined to less than 50 ng/g dw, probably due to the introduction of an activated sewage treatment process to the Jamaica Bay WWTP. In China, Zhao et al. (2010) measured triclosan concentrations ranging from 56.5 to 739 ng/g dw in sediments sampled from three rivers flowing in a heavily populated area. As a whole, these sediment core data point to the persistence of triclosan in buried anaerobic sediments.

Given that organisms live mostly under aerobic conditions (even endobenthic fauna), a greater weight is attributed to half-lives measured under these conditions. Triclosan that is present in buried anaerobic sediments is considered of less significance in terms of biological exposure. In addition, if triclosan in these sediments were to be resuspended, it would likely become in contact with oxygen as a result of mixing and could then be subject to biodegradation processes. Half-life values for ultimate degradation under aerobic conditions are not available for sediments. The study conducted with two water–sediment systems indicated half-lives of 40–56 days in those systems. These half-lives represent a mix of primary and ultimate degradation processes, since carbon dioxide was 21–29% of the applied radioactivity by study termination. In this study, a portion of triclosan is not available for biodegradation given its partitioning to sediments (i.e., bound to residues). Based on empirical evidence for rapid primary biodegradation in water and soil (half-lives of days to a few weeks; Table 17) and half-lives of approximately 30–70 days for ultimate degradation in water, it is expected that the triclosan half-life in aerobic sediments will be less than 365 days. Therefore, triclosan is not considered persistent in sediment based on the criterion set out in the Persistence and Bioaccumulation Regulations (Canada 2000).
4.2.5 Fate in Soil

4.2.5.1 Abiotic Processes
As mentioned previously, hydrolysis is not an important transformation process for triclosan. Also, its Henry’s Law constant value (see Table 2) indicates that it should not volatilize from moist soil surfaces. Its log $K_{oc}$ values (3.34–4.67) suggest that it should generally not be mobile in soil, especially if the organic carbon content in soil is high. Other abiotic processes, such as phototransformation, have not been documented for triclosan in the soil compartment. Since its main entry route in soil would likely be through spreading of wastewater treatment sludge on agricultural fields followed by ploughing (see Section 4.6.1.3), a portion of triclosan will likely be incorporated in the deeper soil layers and hence would not be exposed to light. If spread on wood lots or in the forest, triclosan in sludge could be exposed to light in the absence of ploughing. Prior to sludge application, some WWTPs may have placed sludge on a sludge pad or open field for further drying, leaving triclosan susceptible to phototransformation and possible production of degradation products that could be released in the environment.

The leaching potential of triclosan was further examined using both the criteria of Cohen et al. (1984) and the groundwater ubiquity score (Gustafson 1989). These two approaches allow for a semiquantitative determination of the leaching potential of a chemical. Table 18 shows how physical/chemical properties and certain fate data for triclosan compare with the values for the criteria of Cohen et al. (1984). This comparison does not allow for a clear indication regarding the leaching potential of triclosan. In the Prairies, where soils tend to be alkaline, the anionic form of triclosan is expected to predominate, thus increasing its potential for leaching.

Table 18. Comparison of the properties of triclosan with the leaching criteria of Cohen et al. (1984)

<table>
<thead>
<tr>
<th>Property</th>
<th>Criteria of Cohen et al. (1984) indicating a potential for leaching</th>
<th>Triclosan value</th>
<th>Meets criterion for leaching</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solubility in water</td>
<td>$&gt; 30$ mg/L</td>
<td>$10$ mg/L</td>
<td>No</td>
</tr>
<tr>
<td>$K_d$</td>
<td>$&lt; 5$ and usually $&lt; 1$ or $2$</td>
<td>$10$–$282$</td>
<td>No</td>
</tr>
<tr>
<td>$K_{oc}$</td>
<td>$&lt; 300$</td>
<td>$2188$–$46$ 774</td>
<td>No</td>
</tr>
<tr>
<td>Henry’s Law constant</td>
<td>$&lt; 10^{-2}$ atm·m$^3$/mol ($&lt; 1013$ Pa·m$^3$/mol)</td>
<td>$4.99 \times 10^{-9}$ atm·m$^3$/mol ($5.05 \times 10^{-4}$ Pa·m$^3$/mol)</td>
<td>Yes</td>
</tr>
<tr>
<td>$pK_a$</td>
<td>Negatively charged (either fully or partially) at ambient pH</td>
<td>8.1</td>
<td>Yes (varies with ambient pH)</td>
</tr>
<tr>
<td>Hydrolysis half-life</td>
<td>$&gt; 20$ weeks ($&gt; 140$ days)</td>
<td>Stable to hydrolysis</td>
<td>Yes</td>
</tr>
<tr>
<td>Soil phototransformation half-life</td>
<td>$&gt; 1$ week ($&gt; 7$ days)</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Half-life in soil</td>
<td>$&gt; 2$–$3$ weeks ($&gt; 14$–$21$ days)</td>
<td>Aerobic: $2.9$–$58$ days Anaerobic: $&gt;&gt; 70$ days</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Abbreviations used: $K_d$, soil/water partition coefficient; $K_{oc}$, soil organic carbon/water partition coefficient; n/a, not available; $pK_a$, dissociation constant
The method of Gustafson (1989) may also be used to estimate the leaching potential of chemicals. Gustafson’s assessment method uses a groundwater ubiquity score (GUS), which is based on the persistence and mobility of the compound and is expressed as:

\[
\text{GUS} = \log_{10}(t_{\frac{1}{2}} \text{soil}) \times (4 - \log_{10}(K_{oc}))
\]

The GUS value indicates the leachability of the compound. The persistence term in the GUS equation, \( t_{\frac{1}{2}} \text{soil} \), is the field dissipation time (DT\(_{50}\)), as determined in field dissipation studies, and is meant to include dissipation by volatilization, phototransformation and biological transformation. Instead of the field dissipation DT\(_{50}\), however, the laboratory aerobic soil DT\(_{50}\) or \( t_{\frac{1}{2}} \) value was used in the GUS equation; this is because the field dissipation DT\(_{50}\) may also include dissipation from leaching and runoff and therefore may underestimate leaching potential when used in the equation. The GUS classification scheme is as shown in Table 19.

<table>
<thead>
<tr>
<th>GUS</th>
<th>Probable attributes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 2.8</td>
<td>Leacher</td>
</tr>
<tr>
<td>&gt; 1.8 and &lt; 2.8</td>
<td>Borderline leacher</td>
</tr>
<tr>
<td>&lt; 1.8</td>
<td>Non-leacher</td>
</tr>
</tbody>
</table>

For triclosan, a half-life value of 58 days in aerobic soil and a \( K_{oc} \) value of 2188 were used to calculate a conservative value of the GUS index. According to the leachability classification presented in Table 19, triclosan is not a leacher (GUS = 1.16).

\[
\text{GUS for triclosan} = \log_{10}(58) \times (4 - 3.34) = 1.16
\]

When present in soil, triclosan is expected to have a low potential to leach based on the mobility classification (\( K_{oc} \): 2188–46 774: immobile to slight mobility, as per McCall et al. 1981) and the GUS score indicating that it is a non-leacher. It should be noted, however, that triclosan has been detected in groundwater at low levels in various monitoring studies, suggesting that other mechanisms, such as facilitated transport (particle facilitated or macropore/fractures), may contribute to its detection in groundwater. Indeed, in a national reconnaissance of contaminants present in groundwater in the United States in 2000, triclosan was detected in 15% of the 47 sites sampled by Barnes et al. (2008). The concentrations were all below the reporting level of 1 µg/L. The sampling sites consisted mainly of wells and of a few springs and sumps. They were located in areas suspected to be susceptible to contamination from either animal or human wastewaters (i.e., down-gradient of a landfill, unsewered residential development or animal feedlot). In China, Chen et al. (2011) measured triclosan in groundwater that served to irrigate agricultural fields; concentrations of 1.2–10.8 ng/L were measured at three different sites. Triclosan was below the LOQ (1.6 µg/kg) in the corresponding irrigated soils.

Triclosan may also enter into the terrestrial environment through the disposal of products in landfills, but leaching is expected to be limited. This is particularly the case for products in which triclosan is embedded into solid material, such as plastics and textiles. Monitoring data
collected under the Government of Canada’s Chemicals Management Plan monitoring program indicate that triclosan concentrations in leachate are less than 20 µg/L (detection limit) in the 26 samples collected (2011 personal communication from Waste Reduction and Management Division, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced). These data are based on two sampling events conducted in 2010 and 2011 at 10 different landfills in Canada, before and after leachate treatment. Given the relatively high detection limit used, no definite conclusion can be made regarding leaching of triclosan from landfills. Its potential leaching would also depend on the presence at the landfill of a liner, a leachate collection system and/or a leachate treatment system (on-site or off-site).

There is also evidence that triclosan can reach surface water through runoff. Following broadcast application of either liquid or dewatered municipal biosolids to soil and simulating a rainfall, Topp et al. (2008) and Sabourin et al. (2009) measured triclosan concentrations in runoff of 258 ng/L and 110 ng/L, respectively, 1 day after biosolids application. In the study by Topp et al. (2008), the concentration of triclosan in runoff was still above the LOQ on day 266 following application. To explain this persistence, the authors suggested that sorptive and diffusive processes in the soil had sequestered a portion of the chemical, reducing its availability for biodegradation. Lapen et al. (2008) and Edwards et al. (2009) measured maximum triclosan concentrations of 3.68 µg/L and 0.24 µg/L in tile drainage following application of liquid and dewatered municipal biosolids, respectively, which points to the potential of triclosan to reach groundwater. These studies on runoff and tile drainage were conducted in Ontario.

4.2.5.2 Biotic Processes
In an aerobic soil metabolism study conducted at 20°C, triclosan degraded rapidly, with half-lives of 2.9 days (sandy loam), 3.8 days (clay loam) and 3.7 days (loam) (US EPA 2008e). [14C]Triclosan declined from an average 92–95% of the applied radioactivity at time 0 to 42–58% at 2–3 days and to 1.1–4.3% at 61–124 days post-treatment. Non-extractable residues (not included in half-life calculations) were 61–76% of the applied radioactivity at study termination, and volatilized carbon dioxide was 11–16%. The major transformation product was methyltriclosan, at maximum averages of 13–24% of the applied dose at 14–28 days post-treatment. Methyltriclosan then decreased by study termination. Dissipation time ($DT_{50}$) values for methyltriclosan in these soils, as provided in NICNAS (2009), ranged from 39 to 153 days. A supplementary experiment was conducted at 10°C with the sandy loam described above. The $DT_{50}$ value obtained for triclosan was 10.7 days versus 2.5 days for the same soil at 20°C, as provided in NICNAS (2009). The former value is still low in terms of persistence of triclosan in soil.

Ying et al. (2007) studied the biological degradation of triclosan in soil under both aerobic and anaerobic conditions in the laboratory. For the aerobic experiments, triclosan was added to a loam soil (at 1 mg/kg), which was then incubated in darkness for 70 days. The anaerobic experiments were conducted the same way but were carried out in an anaerobic incubation chamber filled with nitrogen. At each sampling time during the experiment, soil samples were extracted with acetone, and triclosan present in the extracted fraction was measured by high-performance liquid chromatography. Sterile soil samples were also incubated to assess abiotic
transformation processes; no degradation occurred in these samples. The results obtained showed that triclosan degraded in aerobic soil, with a half-life of 18 days. However, it had not degraded under anaerobic conditions by the end of the study period (i.e., half-life >> 70 days). Additional measurements indicated that triclosan did not have negative effects on soil microbial activity in the aerobic soil samples; similar measurements were not made in the anaerobic soil. This study indicates that triclosan is not persistent in aerobic soil; however, the extent to which it degrades was not characterized by the study authors (e.g., primary vs. ultimate degradation). Indeed, no attempts were made to identify or quantify degradation products in soil, and no traps were used to collect volatile degradation compounds, such as carbon dioxide. In addition, the fraction of triclosan bound to soil residues (i.e., not extracted with acetone) was not quantified; however, the figures provided in the paper indicate that concentrations of extractable triclosan in sterile soil were rather stable over the study duration. The fact that these concentrations remained stable indicates that the bound residues formed in the non-sterile soil were likely transformation products of triclosan and not parent triclosan, since the latter did not bind to the soil under sterile conditions. In a similar study, Wu et al. (2009) incubated under aerobic conditions two types of soil to which triclosan had been added. The incubation period was 60 days. The half-lives obtained were 58 days and 32 days, respectively, for a silty clay and a sandy loam. The authors also measured the biodegradation rate of triclosan in the same soils that had been amended with biosolids; the corresponding half-lives were found to be 41 days and 20 days. Finally, Xu et al. (2009) incubated four types of soil with triclosan under aerobic conditions for 45 days and observed half-lives of 13–16 days.

In a study comparing the transformation of triclosan in soils that had never received biosolids application and in the same soils to which biosolids were applied in the laboratory, Kwon et al. (2010) observed that the presence of biosolids significantly slowed the transformation of triclosan, likely due to physical and chemical interactions such as adsorption. Half-lives in two different soils were 2 days and 13 days without biosolids; half-lives in the same two soils were 50 days and 108 days, respectively, following biosolids application. Because biosolids are likely the main source of triclosan to the terrestrial environment, these longer half-lives can be expected under field conditions.

As for sediments, given that organisms live mostly under aerobic conditions in soil, a greater weight is attributed to half-lives measured under these conditions. Half-life values for ultimate degradation in soil are not available. The only aerobic soil metabolism study in which carbon dioxide was trapped and measured indicates triclosan half-lives of 2.9–3.8 days and a production of 11–16% carbon dioxide after 124 days. These half-lives represent a mix of primary and ultimate degradation processes. Generally, carbon dioxide is not expected to reach high levels, because a large proportion of triclosan partitions to soil residues and hence is not available for degradation. Based on the evidence for rapid primary biodegradation in the various aerobic soil studies described above (half-lives of 2.9–58 days), triclosan is not considered persistent in soils, based on the criterion set out in the *Persistence and Bioaccumulation Regulations* (half-life in soil ≥ 182 days) (Canada 2000).
4.3 Bioaccumulation

4.3.1 Aquatic Organisms

Although no information could be found on the levels of triclosan in wild organisms in Canada, experimental data on the presence or bioaccumulation of triclosan in organisms were available in the literature for other countries. Adolfsson-Erici et al. (2002) reported accumulation of triclosan in the bile of fish exposed in different ways to effluents from WWTPs (Table 20). Some fish were exposed to effluents in the laboratory for 3–4 weeks, whereas others were caged for 3 weeks downstream from a WWTP. Wild fish were also caught, for which the exposure period is uncertain. When taken together, the concentrations measured in the bile of fish for all exposure types ranged from 0.24 to 120 mg/kg wet weight (ww). Although no bioaccumulation factor (BAF) can be calculated from this study, the results show that triclosan is bioavailable when released in water. The data also highlight the potential for excretion of unmetabolized triclosan by fish. Results reported by Valters et al. (2005) show that triclosan is present to a much lesser extent in the plasma of fish (0.750–10 ng/g ww). Boehmer et al. (2004) measured triclosan concentrations up to 3.4 ng/g ww in the muscle of fish sampled in two rivers in Germany. Corresponding concentrations of methyl-triclosan in the same samples were up to about 90 times higher than the triclosan concentrations. Fair et al. (2009) collected blood plasma from wild bottlenose dolphins in South Carolina and Florida. Triclosan concentrations in plasma ranged from 0.025 to 0.27 ng/g ww, with up to 31% of the sampled individuals having detectable triclosan. In humans and other mammals, triclosan is extensively metabolized via glucuronide and sulfate conjugation (NICNAS 2009). There is no evidence of bioaccumulation in mammals, although there may be retention of triclosan and/or its metabolites in the liver. No information is available on the metabolism of triclosan in other organisms.
### Table 20. Experimental data on the presence or bioaccumulation of triclosan and methyl-triclosan in biota

<table>
<thead>
<tr>
<th>Test organism</th>
<th>Endpoint</th>
<th>Value (based on wet weight)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Triclosan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rainbow trout (<em>Oncorhynchus mykiss</em>)</td>
<td>Concentration in bile</td>
<td>34–120 mg/kg¹</td>
<td>Adolfsson-Erici et al. 2002</td>
</tr>
<tr>
<td>Rainbow trout (<em>Oncorhynchus mykiss</em>)</td>
<td></td>
<td>17–47 mg/kg²</td>
<td></td>
</tr>
<tr>
<td>Roach (<em>Rutilus rutilus</em>)</td>
<td>Concentration in bile</td>
<td>4.4 mg/kg³</td>
<td></td>
</tr>
<tr>
<td>Eelpout (<em>Zoarces viviparus</em>)</td>
<td></td>
<td>0.24–0.90 mg/kg³</td>
<td></td>
</tr>
<tr>
<td>Perch (<em>Perca fluviatilis</em>)</td>
<td>Concentration in bile</td>
<td>0.44 mg/kg³</td>
<td></td>
</tr>
<tr>
<td>13 fish species collected in the Detroit River (near Windsor, Ontario)</td>
<td>Concentration in blood plasma</td>
<td>0.750–10 ng/g</td>
<td>Valters et al. 2005</td>
</tr>
<tr>
<td>Bottlenose dolphins (<em>Tursiops truncatus</em>)</td>
<td>Concentration in blood plasma</td>
<td>0.025–0.27 ng/g</td>
<td>Fair et al. 2009</td>
</tr>
<tr>
<td>Bream (<em>Abramis brama</em>)</td>
<td>Concentration in muscle</td>
<td>&lt; 0.25–3.4 ng/g</td>
<td>Boehmer et al. 2004</td>
</tr>
<tr>
<td>Zebrafish (<em>Danio rerio</em>)</td>
<td>BCF</td>
<td>2532–4157</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td>Zebrafish (<em>Brachydanio rerio</em>)</td>
<td>BCF</td>
<td>3700–8700</td>
<td>Schettgen et al. 1999</td>
</tr>
<tr>
<td>Common carp (<em>Cyprinus carpio</em>)</td>
<td>BCF</td>
<td>16–90</td>
<td>NITE 2006</td>
</tr>
<tr>
<td>Algae (field samples, various species)</td>
<td>BAF</td>
<td>900–2100</td>
<td>Coogan et al. 2007</td>
</tr>
<tr>
<td>Snail (<em>Helisoma trivolvis</em>)</td>
<td>BAF</td>
<td>500</td>
<td>Coogan and La Point 2008</td>
</tr>
<tr>
<td>Macrophytes (<em>Sesbania herbacea</em> and <em>Bidens frondosa</em>)</td>
<td>BCF</td>
<td>0.4–101</td>
<td>Stevens et al. 2009</td>
</tr>
<tr>
<td>Earthworms (species not identified)</td>
<td>BAF</td>
<td>10–27</td>
<td>Kinney et al. 2008</td>
</tr>
<tr>
<td>Soybean (<em>Glycine max</em>)</td>
<td>BCF</td>
<td>2.5–5.9</td>
<td>Wu et al. 2010a</td>
</tr>
<tr>
<td><strong>Methyl-triclosan</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topmouth gudgeon (<em>Pseudorasbora parva</em>)</td>
<td>Concentration in whole body</td>
<td>1–38 µg/kg</td>
<td>Miyazaki et al. 1984</td>
</tr>
<tr>
<td>Goby (<em>Acanthogobius flavimanus</em>)</td>
<td></td>
<td>&lt; 1–2 µg/kg</td>
<td></td>
</tr>
<tr>
<td>Short-necked clam (<em>Tapes philippinarum</em>)</td>
<td></td>
<td>3 µg/kg</td>
<td></td>
</tr>
<tr>
<td>Thin-shelled surf clam (<em>Mactra veneriformis</em>)</td>
<td></td>
<td>5 µg/kg</td>
<td></td>
</tr>
</tbody>
</table>
### Preliminary Assessment: Triclosan (March 2012)

<table>
<thead>
<tr>
<th>Test organism</th>
<th>Endpoint</th>
<th>Value (based on wet weight)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oyster (Crassostrea gigas)</td>
<td></td>
<td>13 µg/kg</td>
<td></td>
</tr>
<tr>
<td>Blue mussel (Mytilus edulis)</td>
<td></td>
<td>20 µg/kg</td>
<td></td>
</tr>
<tr>
<td>White fish (Coregonus sp.)</td>
<td>Concentration in whole body</td>
<td>4–211 µg/kg</td>
<td>Balmer et al. 2004</td>
</tr>
<tr>
<td>Roach (Rutilus rutilus)</td>
<td>Concentration in plasma</td>
<td>&lt; 2&lt;sup&gt;5&lt;/sup&gt;–365 µg/kg</td>
<td></td>
</tr>
<tr>
<td>Lake trout (Salmo trutta)</td>
<td></td>
<td>&lt; 1 µg/kg&lt;sup&gt;4,5&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>13 fish species collected in the Detroit River (near Windsor, Ontario)</td>
<td>Concentration in plasma</td>
<td>&lt; 0.000 01 µg/kg</td>
<td>Valters et al. 2005</td>
</tr>
<tr>
<td>Bream (Abramis brama)</td>
<td>Concentration in muscle</td>
<td>3.8–26.1 ng/g</td>
<td>Boehmer et al. 2004</td>
</tr>
<tr>
<td>White fish (Coregonus sp.) and roach (Rutilus rutilus)</td>
<td>BAF</td>
<td>2000–5200</td>
<td>Balmer et al. 2004</td>
</tr>
<tr>
<td>Algae (field samples, various species)</td>
<td>BAF</td>
<td>700–1500</td>
<td>Coogan et al. 2007</td>
</tr>
<tr>
<td>Snail (Helisoma trivolvis)</td>
<td>BAF</td>
<td>1200</td>
<td>Coogan and La Point 2008</td>
</tr>
</tbody>
</table>

1. Fish exposed to effluents from WWTPs in tanks in laboratory.
2. Fish caged downstream from a WWTP.
3. Wild fish caught downstream from WWTPs. Levels in fish from reference site were < 0.01 mg/kg.
4. Values on a lipid basis.
5. The value of < 2 µg/kg is for reference lakes.

Orvos et al. (2002) conducted a bioconcentration test with zebrafish (Danio rerio) in a flow-through test system based on methods modified from OECD test guideline 305C. Fish were exposed to either 3 or 30 µg/L of triclosan in the test water. Uptake and depuration periods were 5 and 2 weeks, respectively. [¹⁴C]Triclosan was used for the experiment, and results were based on total radioactivity measured in water and fish tissues. The pH at which the experiment was conducted was not mentioned; given the pKₐ of 8.1 for triclosan, the study pH can have an important influence on its bioaccumulation potential. Steady state did not appear to be reached during the 5-week uptake period, as bioconcentration factor (BCF) values fluctuated during this period at both exposure concentrations. The maximum BCF values were reached at week 3, but then decreased until week 5. This could be due to a decrease in the test compound concentrations during that time; however, measured concentrations were not reported. The average BCFs over the 5-week uptake period were calculated to be 4157 at 3 µg/L and 2532 at 30 µg/L; maximum BCF values were 5337 and 3408, respectively. Because such measurements based on total radioactivity cannot distinguish between the parent compound and possible metabolites, these BCF values are likely overestimates. Depuration rate constants (k<sub>2</sub>) at 3 µg/L and 30 µg/L were 0.142/day and 0.141/day, respectively. Given the deficiencies of this study, mainly the lack of equilibrium during the uptake phase, its results are uncertain and thus have low reliability. As such, this study is attributed a low weight in the weight of evidence approach used to determine
the potential of triclosan to meet the bioaccumulation criterion as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Schettgen et al. (1999) conducted a bioconcentration study with triclosan at different pH values (6–9) based on OECD test guideline 305E. Zebrafish (*Brachydanio rerio*) were exposed to either 35 or 50 µg/L of triclosan for about 150 hours before being transferred to clean water for an additional 100 hours for the depuration phase. Concentrations of triclosan in fish and water were analyzed by gas chromatography–electron capture detection, and rate constants for uptake ($k_1$) and clearance ($k_2$) were calculated. Based on the uptake and elimination curve obtained, equilibrium seems to have been reached during the experiment. The exposure period for the uptake phase (150 hours) exceeded the time to reach 80% of steady state (80% time to steady state = 1.6/$k_2$ = 1.6/(0.0347/hour) = 46 hours), which is an additional indication that steady state was reached. The BCF values (± standard deviation) were determined as the ratio of the rate constants and were as follows: 8700 (±2632), 8150 (±1417), 6350 (±963) and 3700 (±1232) at pH 6, 7, 8 and 9, respectively. These values show the expected decrease in uptake rate with increasing ionization of triclosan from pH 6 to 9; the clearance rate constant had similar values for all pH values tested, ranging from 0.0347/hour to 0.0413/hour. The uptake rate constants decreased from 356/hour to 129/hour with increasing pH values. It should be noted that the exposure concentrations used in this test are 6–9% of the 96-hour median lethal concentration ($LC_{50}$) for zebrafish (540 µg/L; unreviewed study cited in NICNAS 2009). OECD test guideline 305 recommends that the highest concentration be set at 1% of the acute asymptotic $LC_{50}$ to avoid toxic effects that could affect fish metabolism. In this experiment, the uptake and depuration processes, and hence the BCF values, may have been slightly affected by the concentrations of triclosan used. In spite of the latter deficiency, the results of this study are considered reliable to determine the bioaccumulation potential for triclosan. They are attributed a higher weight in the weight of evidence approach than the results obtained by Orvos et al. (2002) for *Danio rerio*.

The Japanese National Institute of Technology and Evaluation (NITE) conducted a bioconcentration study with carp (*Cyprinus carpio*) in which fish were exposed to either 3 or 30 µg/L of triclosan for 8 weeks under flow-through conditions (NITE 2006). The protocol followed the NITE test guideline for bioaccumulation in carp, which corresponds to OECD test guideline 305C. Measured concentrations of triclosan in test water over the study duration fluctuated from 22.4 to 26.0 µg/L and from 2.00 to 2.46 µg/L for the 30 µg/L and 3 µg/L exposure concentrations, respectively. The study report did not mention whether a depuration phase occurred during the experiment. Also, the pH of the test water was not reported. As in the study by Orvos et al. (2002), BCF values fluctuated during the NITE study, making it difficult to determine whether steady state was reached. Average BCF values at the 3 µg/L exposure concentration were 55, 69, 56, 39 and 80 at 1, 2, 4, 6 and 8 weeks, respectively. At the 30 µg/L exposure concentration, average BCF values were 36, 36, 30, 36 and 18 at 1, 2, 4, 6 and 8 weeks, respectively. The minimum and maximum BCF values were 16 and 90, respectively, when considering both exposure concentrations. Since the measured concentrations in water were relatively stable, fluctuations in BCF values could be due to fluctuations in fish tissue concentrations; however, these data were not available. No values were reported for the uptake...
rate constant \( (k_1) \). Given these data gaps and deficiencies (e.g., steady state uncertain, no mention of depuration phase), this study is attributed a low weight in the weight of evidence approach to assess the bioaccumulation potential for triclosan.

The large differences observed between the fish BCF values reported by Orvos et al. (2002), Schettgen et al. (1999) and NITE (2006) could be due to interspecies variation, different size of fish used, different lipid contents, etc., in addition to the study deficiencies mentioned.

Coogan et al. (2007) calculated a BAF ranging from 900 to 2100 for algae collected in a creek receiving the effluent from a WWTP, while a BAF of 500 was calculated for snails that had been caged in the same creek for 2 weeks (Coogan and La Point 2008). It is unknown but likely that a steady state in triclosan concentration in snails was reached by the end of the exposure period.

Finally, the bioconcentration of triclosan in two species of wetland macrophytes was measured by Stevens et al. (2009). They exposed the organisms to 10, 100 and 1000 µg/L in flow-through systems for 28 days. They measured BCF values ranging from 0.4 to 2.8 and from 1.4 to 101 in plant shoots and roots, respectively.

There are no BAF values available for fish; however, the \( K_{oc} \) and \( K_{ow} \) of triclosan suggest that the BCF is a very relevant metric for this chemical. Indeed, at a log \( K_{oc} \) of 4.7, the predicted bioavailable fraction of triclosan in the water column according to mass balance fish models is approximately 99\%, which means that practically all of the total water concentration of triclosan will be in the dissolved phase. This suggests that uptake from water via the gills is a very relevant exposure for this substance. This also suggests that the contribution of the diet to the total body burden of triclosan in aquatic organisms is likely quite low. In fact, the calculated BAF using the Arnot-Gobas mass balance (version 1.11) (Arnot and Gobas 2003) is only 3\% greater than the BCF. In addition, steric effects are not expected to mitigate the uptake rate of triclosan via the gills, as the maximum diameter of 1.3 nm and effective diameter of 0.81 nm suggest that triclosan will be passively diffused through the lipid bilayer without restriction. Information regarding molecular size and cross-sectional diameters is useful to consider and is commonly used by international jurisdictions such as the EU (ECHA 2008) as weight of evidence for bioaccumulation potential. Recent investigations relating fish BCF data and molecular size parameters (Dimitrov et al., 2002, 2005) suggest that the probability of a molecule crossing cell membranes as a result of passive diffusion declines significantly with increasing maximum diameter. The probability of passive diffusion decreases appreciably when the maximum diameter is greater than about 1.5 nm and much more so for molecules having a maximum diameter greater than 1.7 nm. Sakuratani et al. (2008) also investigated the effect of cross-sectional diameter on passive diffusion in a BCF test set of about 1200 new and existing chemicals. They observed that substances that do not have a very high bioconcentration potential (BCF < 5000) often have a maximum diameter of greater than 2.0 nm and an effective diameter of greater than 1.1 nm.

Based on the data presented above for triclosan in aquatic organisms, especially the study conducted with *Brachydanio rerio*, and given that the BCF is a relevant metric to assess the
bioaccumulation potential of this chemical, it is concluded that triclosan meets the bioaccumulation criterion (BCF or BAF ≥ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000). It is, however, recognized that the wide range of BCF values, especially in fish (from 2.7 to 8700), raises some uncertainty regarding the actual bioaccumulation potential of triclosan. Additional studies could be conducted to help address this uncertainty.

### 4.3.2 Terrestrial Organisms

Kinney et al. (2008) sampled earthworms from agricultural soils that had been amended with biosolids from municipal WWTPs. Based on the ratio of triclosan concentrations measured in earthworm tissues and in soil, BAF values of 10 and 27 were calculated at 31 and 156 days following soil amendment, respectively. It is unknown but likely that steady state in triclosan body concentrations was reached by 156 days, even though data are available for only two sampling times. Under field conditions similar to those in this case, the exposure is dynamic rather than static, given the pulses created by biosolids application followed by dissipation of triclosan through various processes. Wu et al. (2010a) grew soybean plants in a sandy soil that had been either amended with biosolids or irrigated with wastewater containing triclosan. The BCF values (root/soil) measured after 60 and 110 days of growth in the soil amended with biosolids were about 2.5 and 5.9, respectively. No BCF values could be calculated for plants grown in the soil irrigated with wastewater, as triclosan was not detected in the soil; however, triclosan did accumulate in plant tissues (root, stem, leaf and bean; 24.2–80.1 ng/g after 110 days). Again, it is unknown whether steady state was reached in this experiment.

Potential for secondary poisoning by triclosan in terrestrial food chains was assessed using the model BASL4 (BASL4 2008; see Section 4.6.1.3 for more details). In this model, the exposure of earthworms to triclosan present in soil following the application of wastewater sludge to fields is estimated based on factors such as soil ingestion, metabolism and growth dilution. The bioaccumulation of triclosan in shrews consuming these earthworms is then estimated based on similar factors. Two sludge application scenarios were run (a lower end and an upper end; see Section 4.6.1.3). In both scenarios, peak concentrations in soils (149 µg/kg and 254 µg/kg for lower-end and upper-end scenarios, respectively) occur right after sludge application, but then decrease to <1 µg/kg about 36 and 80 days later, respectively. Based on the highest modelled concentrations in soil, earthworms (~155 000 µg/kg and ~260 000 µg/kg for lower-end and upper-end scenarios, respectively) and shrews (~4500 µg/kg and ~7000 µg/kg for lower-end and upper-end scenarios, respectively), the modelled BAF values for earthworms (i.e., concentration in earthworms divided by concentration in soil) are approximately 1000, while the modelled BAF values for shrews (i.e., concentration in shrews divided by concentration in soil) are approximately 30. The modelled biomagnification factor values (i.e., concentration in shrews divided by concentration in earthworms) are less than 1. The model results indicate that triclosan concentrations will increase from soil to earthworms, but will then decrease from earthworms to shrews. This result is in line with the fact that triclosan is extensively metabolized in mammals. Field data cited above indicate BAFs of 10–27 for earthworms sampled in sludge-amended fields (Kinney et al. 2008).
4.3.3 Methyl-triclosan

Methyl-triclosan has often been detected in aquatic organisms in waters contaminated with triclosan (NICNAS 2009). Miyazaki et al. (1984) were the first to report accumulation of methyl-triclosan in aquatic biota. They detected various levels of this compound in species of fish and shellfish sampled in the Tama River and Tokyo Bay in Japan. The concentrations ranged from 1 to 38 \( \mu g/kg \) and from 3 to 20 \( \mu g/kg \) in fish and shellfish, respectively (Table 20). The authors attributed the presence of this compound to biological methylation of triclosan in the environment.

Balmer et al. (2004) measured methyl-triclosan in white fish, roach and lake trout from lakes in Switzerland that receive effluents from WWTPs, as well as in reference lakes not influenced by WWTPs. They also sampled water using semipermeable membrane devices in order to derive a concentration for dissolved methyl-triclosan. The concentrations of methyl-triclosan in fish were up to 35 \( \mu g/kg \) on a wet weight basis and up to 365 \( \mu g/kg \) on a lipid basis. No methyl-triclosan was detected in fish from the reference lakes. The concentrations of methyl-triclosan in fish correlated well \( (r^2 = 0.85) \) with the ratio of the human population in the watershed to the water flow of the lakes, which is considered to be a measure of the domestic burden from WWTPs to a lake. A BAF was estimated for methyl-triclosan using the concentrations in fish as well as the water concentrations derived from the semipermeable membrane devices; the resulting BAF was in the order of 100 000–260 000 (lipid basis). Assuming an average fat content in fish of 2\%, the study authors estimated the BAF for methyl-triclosan to be 2000–5200 (log BAF of 3.3–3.7) on a wet weight basis.

BAF values of 700–1500 were reported for methyl-triclosan for algae collected in a creek receiving the effluent from a WWTP (Coogan et al. 2007), while a BAF of 1200 was calculated for snails that had been caged in the same creek for 2 weeks (Coogan and La Point 2008). It is unknown but likely that steady state was reached in this experiment, given the length of the exposure period.

4.4 Environmental Concentrations

4.4.1 Concentrations in Air

No monitoring data for concentrations of triclosan and methyl-triclosan in air could be found for Canada or other countries. This is line with the fact that 1) no releases of these substances are expected to air and 2) the physical/chemical properties of both substances do not suggest that they would partition to air. Therefore, this environmental compartment is not expected to contribute significantly to exposure.
4.4.2 Concentrations in Water

4.4.2.1 Measured Concentrations

Canada
Table 21 presents the range of triclosan concentrations measured in surface water in Canada. Data were available for four provinces from 2002 to 2010. Levels reported spanned almost four orders of magnitude, from below the lowest MDL (0.10 ng/L) to 691 ng/L; mean concentrations for each site ranged from below the MDL to 168 ng/L. This range is expected to be representative of inland waters in Canada during the sampling years, since surface waters from both heavily and lightly populated areas were sampled.

Table 21. Concentrations of triclosan in surface water in Canada

<table>
<thead>
<tr>
<th>Water body</th>
<th>Sampling period</th>
<th>Number of samples</th>
<th>Concentration (ng/L)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detroit River, 600 m downstream of Little River WWTP (City of Windsor)</td>
<td>2003</td>
<td>3</td>
<td>n/a</td>
<td>Hua et al. 2005</td>
</tr>
<tr>
<td>Mouth of Niagara River</td>
<td>2004–2005</td>
<td>10</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Head of Niagara River</td>
<td>2004–2005</td>
<td>11</td>
<td>0.10</td>
<td>Personal communication²</td>
</tr>
<tr>
<td>St. Lawrence River (south channel) at outlet of Lake Ontario</td>
<td>2004–2005</td>
<td>11</td>
<td>&lt; MDL</td>
<td>0.17</td>
</tr>
<tr>
<td>Thames River</td>
<td>2002</td>
<td>86</td>
<td>&lt; MDL</td>
<td>44</td>
</tr>
<tr>
<td>Hamilton Harbour</td>
<td>2003–2004</td>
<td>59</td>
<td>&lt; MDL</td>
<td>52</td>
</tr>
<tr>
<td>Grand River</td>
<td>2003–2004</td>
<td>71</td>
<td>&lt; MDL</td>
<td>23</td>
</tr>
<tr>
<td>Andrews Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Blyth Brook</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Egbert Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Indian Creek</td>
<td>2005</td>
<td>4</td>
<td>&lt; MDL</td>
<td>165</td>
</tr>
<tr>
<td>Kerrys Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Laurel Creek</td>
<td>2005</td>
<td>5</td>
<td>&lt; MDL</td>
<td>29</td>
</tr>
<tr>
<td>Little Ausable River</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Middle Maitland River</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Mill Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Nineteen Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>Nissouri Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>North Maitland River</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td></td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Water body</th>
<th>Sampling period</th>
<th>Number of samples</th>
<th>Concentration (ng/L)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Min</td>
<td>Mean</td>
</tr>
<tr>
<td>Nottawasaga River</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td>20</td>
</tr>
<tr>
<td>Spring Creek</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td>32</td>
</tr>
<tr>
<td>Stokes River</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td>24</td>
</tr>
<tr>
<td>Twenty Mile Creek</td>
<td>2005</td>
<td>15</td>
<td>&lt; MDL</td>
<td>62</td>
</tr>
<tr>
<td>Vineland Creek</td>
<td>2005</td>
<td>5</td>
<td>&lt; MDL</td>
<td>36</td>
</tr>
<tr>
<td>West Don River</td>
<td>2005</td>
<td>6</td>
<td>&lt; MDL</td>
<td>31</td>
</tr>
</tbody>
</table>

### Quebec

<table>
<thead>
<tr>
<th>Water body</th>
<th>Sampling period</th>
<th>Number of samples</th>
<th>Concentration (ng/L)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Min</td>
<td>Mean</td>
</tr>
<tr>
<td>Ottawa River (downstream of Carillon dam)</td>
<td>2006–2008</td>
<td>10</td>
<td>&lt; MDL</td>
<td>6.4</td>
</tr>
<tr>
<td>Saint Maurice River</td>
<td>2007–2008</td>
<td>4</td>
<td>&lt; MDL</td>
<td></td>
</tr>
<tr>
<td>St. Lawrence River (at Lavaltrie, downstream of Montréal)</td>
<td>2006-2009</td>
<td>11</td>
<td>&lt; MDL</td>
<td>16</td>
</tr>
<tr>
<td>St. Lawrence River (at Bécancour)</td>
<td>2007–2009</td>
<td>10</td>
<td>&lt; MDL</td>
<td>9.2</td>
</tr>
<tr>
<td>Richelieu River (at Sorel)</td>
<td>2006–2009</td>
<td>11</td>
<td>&lt; MDL</td>
<td>6.7</td>
</tr>
<tr>
<td>St. Lawrence River (at Lévis)</td>
<td>2007–2009</td>
<td>11</td>
<td>&lt; MDL</td>
<td>10</td>
</tr>
</tbody>
</table>

### British Columbia<sup>5</sup>

<table>
<thead>
<tr>
<th>Water body</th>
<th>Sampling period</th>
<th>Number of samples</th>
<th>Concentration (ng/L)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Min</td>
<td>Mean</td>
</tr>
<tr>
<td>Columbia River (at Waneta)</td>
<td>2009</td>
<td>1</td>
<td>&lt; 147</td>
<td></td>
</tr>
<tr>
<td>Fishtrap Creek</td>
<td>2008–2009</td>
<td>2</td>
<td>&lt; 69</td>
<td></td>
</tr>
<tr>
<td>Fraser River</td>
<td>2008</td>
<td>2</td>
<td>&lt; 240</td>
<td></td>
</tr>
<tr>
<td>Mill Creek (Kelowna)</td>
<td>2008–2010</td>
<td>18</td>
<td>&lt; 63 – &lt; 249</td>
<td></td>
</tr>
<tr>
<td>Okanagan River (at Oliver and Penticton)</td>
<td>2008–2010</td>
<td>17</td>
<td>&lt; 62 – &lt; 248</td>
<td></td>
</tr>
<tr>
<td>Still Creek (Burnaby)</td>
<td>2008, 2010</td>
<td>3</td>
<td>&lt; 64 – &lt; 241</td>
<td></td>
</tr>
<tr>
<td>Sumas River</td>
<td>2008–2010</td>
<td>4</td>
<td>&lt; 64 – &lt; 245</td>
<td></td>
</tr>
<tr>
<td>BX Creek (Vernon)</td>
<td>2009–2010</td>
<td>3</td>
<td>&lt; 70 – &lt; 120</td>
<td></td>
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<tr>
<td>Ellis Creek (Penticton)</td>
<td>2009–2010</td>
<td>4</td>
<td>&lt; 64 – &lt; 131</td>
<td></td>
</tr>
<tr>
<td>Hastings Creek (North Vancouver)</td>
<td>2010</td>
<td>1</td>
<td>&lt; 63</td>
<td></td>
</tr>
<tr>
<td>Osoyoos Lake</td>
<td>2009–2010</td>
<td>2</td>
<td>&lt; 67 – &lt; 111</td>
<td></td>
</tr>
</tbody>
</table>

### Saskatchewan

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<sup>1</sup> Concentration units are nanograms per liter (ng/L). MDL: Method Detection Limit.
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<table>
<thead>
<tr>
<th>Water body</th>
<th>Sampling period</th>
<th>Number of samples</th>
<th>Concentration (ng/L)(^1)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wascana Creek (downstream of Regina)</td>
<td>2002–2003</td>
<td>23</td>
<td>12</td>
<td>168</td>
</tr>
<tr>
<td>Wascana Creek (upstream to downstream of Regina)</td>
<td>2006</td>
<td>5</td>
<td>&lt; MDL</td>
<td>118</td>
</tr>
<tr>
<td>Qu’Appelle River (upstream to downstream of Wascana Creek)</td>
<td>2006–2007</td>
<td>10</td>
<td>&lt; MDL</td>
<td>43</td>
</tr>
<tr>
<td>Pasqua Lake</td>
<td>2006</td>
<td>1</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: max, maximum; MDL, method detection limit; min, minimum; MQL, method quantification limit; n/a, not available; SDL, sample detection limit

1 Ontario: MDL = 0.10 ng/L for mouth and head of Niagara River and St. Lawrence River; MDL = 5 ng/L for Grand River and Hamilton Harbour; MDL = 20 ng/L for all other rivers.

Quebec: MDL = 6 ng/L.

Saskatchewan: MDL = 25 ng/L (Waiser et al. 2011) and 5 ng/L (2011 personal communication from Water Quality Monitoring and Surveillance Division, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced).

MQL = 4 ng/L for Detroit River.

2 2006 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced.

3 2007 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced.

4 2010 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced.

5 Values are presented as < SDL. The SDL varies by sample and can be lower or higher than the MDL depending on the sample’s cleanness (i.e., presence or absence of interfering constituents).

6 2011 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced.

Regarding methyl-triclosan, Andresen et al. (2007) reported approximately 1 ng/L and 0.1 ng/L of this compound in water samples from Hamilton Harbour and Lake Ontario, respectively. In Saskatchewan, Waiser et al. (2011) measured concentrations ranging from 3 to 17 ng/L in Wascana Creek downstream of Regina’s WWTP.

### Other Countries

Levels of triclosan have been monitored in the United States. In a national reconnaissance survey of 139 streams across 30 states during 1999 and 2000, Kolpin et al. (2002) measured a maximum triclosan concentration of 2300 ng/L, about 3 times the maximum value reported for surface waters in Canada. In Texas, Coogan et al. (2007) measured triclosan and methyl-triclosan concentrations of 60–120 ng/L and 50–80 ng/L, respectively, in a creek receiving an effluent from a WWTP.
Okumura and Nishikawa (1996) measured triclosan at concentrations of 50–150 ng/L in a river in Japan. In Switzerland, concentrations of triclosan in rivers and lakes ranged from 1.4 to 74 ng/L, as reported by Lindström et al. (2002). Still in Switzerland, Singer et al. (2002) measured a methyl-triclosan concentration of about 0.5 ng/L (between the method quantification limit [MQL] and MDL) in water sampled in both the epilimnion and hypolimnion of a lake.

Brausch and Rand (2011) reviewed all studies conducted on triclosan that were published before April 2010 and calculated that this compound has been detected in 56.8% of the surface water samples analyzed \(n = 710\), with a median concentration of 48 ng/L (range: < 0.1–2300 ng/L). Their review included data for surface water in the United States, Romania, the United Kingdom, the Republic of Korea and Switzerland, to name a few.

4.4.2.2 Speciation in Aqueous Solution
As mentioned previously, triclosan is a phenolic compound that ionizes at environmentally relevant pH (pK\(_a\) of 8.1; see Table 2). The speciation, or ionization state, of a weak organic acid like triclosan will influence its fate in the environment and its bioavailability. For instance, the ionized form of triclosan has a different light absorption spectrum than the neutral form. Also, organisms may more readily take up the neutral form; this was highlighted by Orvos et al. (2002), who showed that, for the same species, the toxicity of triclosan decreased with increasing pH. More generally, the results obtained by Erickson et al. (2006a,b) suggest that the ionized form of weak organic acids is also available for uptake through a variety of mechanisms. Hence, ionized triclosan could also accumulate in organisms.

In natural waters, triclosan may form complexes with dissolved organic matter, which could influence the concentrations of freely dissolved triclosan. As such, only a fraction of total triclosan present in the water column could actually be bioavailable (i.e., present in the freely dissolved form), assuming that dissolved organic matter–triclosan complexes cannot cross a cell membrane. No studies quantifying the effect of dissolved organic matter on the bioaccumulation of triclosan in aquatic organisms could be found in the literature. However, according to a mass balance fish model, the predicted bioavailable fraction of triclosan in the water column is approximately 99%, based on its log \(K_{oc}\) of 4.7 (see Section 4.3.1).

4.4.3 Concentrations in Sediments
The only monitoring data available for triclosan in sediments are for Switzerland, Sweden, the United States and China. Singer et al. (2002) analyzed a sediment core taken from a lake in Switzerland that receives effluents from WWTPs. The profile in the core showed triclosan concentrations ranging from less than 5 ng/g dw in 1960–1961 to 53 ng/g dw in 1992–1993. In Sweden, Remberger et al. (2002) reported triclosan concentrations of 8–17 ng/g dw in sea sediments sampled in an industrial area. Triclosan was also detected by Miller et al. (2008) in cored estuarine sediments from Jamaica Bay, New York. The peak concentrations were 600–800 ng/g dw in sediments deposited between the mid-1960s and late 1970s; they then declined to less than 50 ng/g in the following years. Zhao et al. (2010) measured triclosan concentrations ranging from 56.5 to 739 ng/g dw in sediments sampled from three rivers flowing in a heavily populated
area of China. No monitoring data for concentrations of methyl-triclosan in sediments were found for Canada or other countries.

4.4.4 Concentrations in Soils

No monitoring data for concentrations of triclosan or methyl-triclosan in soil were found for Canada. In Sweden, Remberger et al. (2002) measured triclosan concentrations in two contaminated (industrial) areas and in one pristine forest area. Triclosan concentrations in the contaminated sites ranged from less than 3 to 15 μg/kg dw, while they were less than 3 μg/kg dw (detection limit) in the forest soil. In the United States, Wu et al. (2010b) measured triclosan in soils that had been amended with biosolids. The concentrations of triclosan in biosolids ranged from 0.76 to 1.3 μg/g dw, and those in amended soils ranged from 1.6 to 11 μg/kg dw.

4.5 Ecological Effects

4.5.1 Mode of Action

Triclosan has numerous intracellular and cytoplasmic target sites and may influence the transcription of genes involved in amino acid, carbohydrate and lipid metabolism as well as signalling pathways, as shown in the bacteria *Staphylococcus aureus* (Jang et al. 2008). Several authors have shown that triclosan blocks lipid biosynthesis in bacteria by specifically inhibiting the enzyme enoyl–acyl carrier protein reductase, which is involved in type II bacterial fatty acid synthesis (McMurry et al. 1998; Heath et al. 1999; Hoang and Schweizer 1999; Levy et al. 1999). Plants share similar fatty acid synthesis pathways with bacteria. Experiments conducted with *Arabidopsis* in the family Brassicaceae have shown that enoyl–acyl carrier protein reductase is a possible target of triclosan (Serrano et al. 2007). In the mouse, activation of PPARα is the primary MOA for triclosan-induced hepatocarcinogenesis (see Section 3.1.8).

In addition, the molecular structure of triclosan resembles that of several non-steroidal estrogens, such as diethylstilbestrol and bisphenol A, in that it contains two phenol functional groups. This suggests the potential to act as an endocrine-disrupting agent (Ishibashi et al. 2004; see Section 4.5.2.1). The Profiler function of the OECD QSAR (quantitative structure–activity relationship) Toolbox was used to determine which structural alerts are associated with triclosan regarding its possible mechanisms of action (QSAR 2008). To do this, the Profiler compares the chemical structure of the compound entered in the Toolbox with the structure of chemicals present in its database for which toxicity information is available. Alerts for high-toxicity classification were found for triclosan: estrogen receptor binding (strong binder), acute aquatic toxicity by OASIS (phenols and anilines) and high hazard class according to Cramer rules. These alerts suggest that triclosan exerts toxicity beyond a baseline narcotic MOA.

4.5.2 Ecotoxicity

Several toxicity data for triclosan were retrieved from the literature, including data from chronic studies. The determination of whether an endpoint is acute or chronic was based on the lifespan
of each species considered. The key toxicity studies for the environmental media of concern—namely, water, sediments and soil—are presented below. For aquatic toxicity tests, the pH of the test solutions was noted when available, given its possible impact on toxicity due to the triclosan pKₐ of 8.1.

4.5.2.1 Aquatic Organisms

**Algae, Macrophytes and Bacterial Communities**

Single-species toxicity tests as well as community-level studies have been conducted with bacteria, algae and macrophytes exposed to triclosan. Orvos et al. (2002) tested five algal species as well as the macrophyte *Lemna gibba*. The blue-green alga *Anabaena flos-aquae* was the most sensitive species, with an effective concentration for a 10% response (EC₁₀ value) of 0.97 μg/L (Table 22). It is worth noting that the only marine species tested (the diatom *Skeletonema costatum*) was the least sensitive among the five algal species tested, which could suggest that the salinity of the test water may have had an impact on triclosan speciation and bioavailability (i.e., higher proportion of the ionized form). However, DeLorenzo and Fleming (2008) measured a 96-hour EC₅₀ of 3.55 μg/L for a marine phytoplankton species, which is comparable with the toxicity measured by Orvos et al. (2002) for certain freshwater algae. Yang et al. (2008) measured a 72-hour EC₅₀ of 0.53 μg/L for *Pseudokirchneriella subcapitata*, which is much lower than the one reported by Orvos et al. (2002) for the same species (96-hour EC₅₀ of 4.46 μg/L).

The effect of triclosan on seed germination and seedling development of three wetland plants was studied by Stevens et al. (2009). While germination and shoot weight were not affected at the highest concentration tested (1000 μg/L), root length was affected at 0.6 μg/L for two of the species tested (Table 22).

### Table 22. Chronic toxicity of triclosan to aquatic organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Endpoint, duration</th>
<th>Effect</th>
<th>Concentration (µg/L)</th>
<th>Used in SSD?</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protozoa and metazoa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotifera sp.</td>
<td>LOEC, 14 d</td>
<td>Growth</td>
<td>0.5</td>
<td>Yes</td>
<td>Lawrence et al. 2009</td>
</tr>
<tr>
<td>Algae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Scenedesmus subspicatus</em></td>
<td>MATC, 72 h</td>
<td>Biomass and growth</td>
<td>0.77</td>
<td>Yes</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td></td>
<td>EC₅₀, 72 h</td>
<td>Growth</td>
<td>2.8</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td><em>Anabaena flos-aquae</em></td>
<td>EC₁₀, 96 h</td>
<td>Biomass</td>
<td>0.97</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>EC₂₅, 96 h</td>
<td>Growth</td>
<td>0.67</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td><em>Pseudokirchneriella subcapitata</em></td>
<td>EC₂₅, 96 h</td>
<td>Growth</td>
<td>2.44</td>
<td>Yes</td>
<td>Tatarazako et al. 2004</td>
</tr>
<tr>
<td></td>
<td>EC₂₅, 72 h</td>
<td></td>
<td>3.4</td>
<td>No</td>
<td>Yang et al. 2008</td>
</tr>
<tr>
<td></td>
<td>EC₅₀, 72 h</td>
<td></td>
<td>0.53</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Algal and bacterial community</td>
<td>LOEC, 8 weeks</td>
<td>Community shift, reduction in algal</td>
<td>10</td>
<td>Yes</td>
<td>Lawrence et al. 2009</td>
</tr>
<tr>
<td>Organism</td>
<td>Endpoint, duration</td>
<td>Effect</td>
<td>Concentration (µg/L)</td>
<td>Used in SSD?</td>
<td>Reference</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------------------</td>
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</tr>
<tr>
<td><em>Navicula pelliculosa</em></td>
<td>EC$_{25}$, 96 h</td>
<td>Growth</td>
<td>10.7</td>
<td>Yes</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td><em>Skeletonema costatum</em></td>
<td>EC$_{25}$, 96 h</td>
<td>Growth</td>
<td>&gt; 66.0</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td><em>Dunaliella tertiolecta</em></td>
<td>EC$_{50}$, 96 h</td>
<td>Growth</td>
<td>3.55</td>
<td>No</td>
<td>DeLorenzo and Fleming 2008</td>
</tr>
<tr>
<td><em>Sesbania herbacea</em></td>
<td>LOEC, 28 d</td>
<td>Root length</td>
<td>0.6</td>
<td>Yes</td>
<td>Stevens et al. 2009</td>
</tr>
<tr>
<td><em>Bidens frondosa</em></td>
<td>LOEC, 28 d</td>
<td>Root length</td>
<td>0.6</td>
<td>Yes</td>
<td></td>
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<tr>
<td><em>Eclipta prostrata</em></td>
<td>MATC, 28 d</td>
<td>Root length</td>
<td>2.2</td>
<td>Yes</td>
<td>Borgmann et al. 2007</td>
</tr>
<tr>
<td></td>
<td>NOEC, 28 d</td>
<td></td>
<td>0.6</td>
<td>No</td>
<td>Dussault et al. 2008</td>
</tr>
<tr>
<td></td>
<td>LOEC, 28 d</td>
<td></td>
<td>7.8</td>
<td>No</td>
<td></td>
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<tr>
<td><em>Lemna gibba</em></td>
<td>EC$_{25}$, 7 d</td>
<td>Growth</td>
<td>&gt; 62.5</td>
<td>Yes</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td><strong>Macrophytes</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><em>Dunaliella tertiolecta</em></td>
<td>LOEC, 28 d</td>
<td>Reproduction</td>
<td>170</td>
<td>No</td>
<td>Tatarazako et al. 2004</td>
</tr>
<tr>
<td><em>Ceriodaphnia dubia</em></td>
<td>NOEC, 7 d</td>
<td>Reproduction</td>
<td>6</td>
<td>No</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td></td>
<td>NOEC, 7 d</td>
<td>Survival</td>
<td>50</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IC$_{25}$, 7 d</td>
<td>Survival and reproduction</td>
<td>170</td>
<td>Yes</td>
<td></td>
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<tr>
<td><em>Hyalella azteca</em></td>
<td>NOEC, 3 generations</td>
<td>Survival, mating, body size, reproduction</td>
<td>&gt; 0.127$^1$</td>
<td>No</td>
<td>Borgmann et al. 2007</td>
</tr>
<tr>
<td></td>
<td>LC$_{10}$, 10 d</td>
<td>Survival</td>
<td>5</td>
<td>No</td>
<td>Dussault et al. 2008</td>
</tr>
<tr>
<td></td>
<td>EC$_{10}$, 10 d</td>
<td>Growth</td>
<td>50</td>
<td>Yes</td>
<td></td>
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<tr>
<td><em>Ceriodaphnia dubia</em></td>
<td>NOEC, 7 d</td>
<td>Reproduction</td>
<td>6</td>
<td>No</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td></td>
<td>NOEC, 7 d</td>
<td>Survival</td>
<td>50</td>
<td>No</td>
<td></td>
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<tr>
<td></td>
<td>IC$_{25}$, 7 d</td>
<td>Survival and reproduction</td>
<td>170</td>
<td>Yes</td>
<td>Tatarazako et al. 2004</td>
</tr>
<tr>
<td><em>Daphnia magna</em></td>
<td>NOEC, 21 d</td>
<td>Survival of parental generation</td>
<td>200$^1$</td>
<td>No</td>
<td>Orvos et al. 2002</td>
</tr>
<tr>
<td></td>
<td>NOEC, 21 d</td>
<td>Reproduction</td>
<td>40$^1$</td>
<td>No</td>
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<tr>
<td></td>
<td>LOEC, 21 d</td>
<td>Reproduction</td>
<td>200</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MATC, 21 d</td>
<td>Reproduction</td>
<td>89</td>
<td>Yes</td>
<td></td>
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<tr>
<td></td>
<td>LOEC, 30 d</td>
<td>Sex ratio</td>
<td>10$^1$</td>
<td>No</td>
<td>Flaherty and Dodson 2005</td>
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<td><strong>Insects</strong></td>
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<td></td>
<td></td>
</tr>
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<td><em>Chironomus tentans</em></td>
<td>LC$_{10}$, 10 d</td>
<td>Survival</td>
<td>20$^1$</td>
<td>No</td>
<td>Dussault et al. 2008</td>
</tr>
<tr>
<td></td>
<td>EC$_{10}$, 10 d</td>
<td>Growth</td>
<td>80$^1$</td>
<td>Yes</td>
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<td><strong>Molluscs</strong></td>
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<td><em>Dreissena polymorpha</em></td>
<td>LOEC, 96 h</td>
<td>Genetic biomarkers</td>
<td>0.29–0.87</td>
<td>No</td>
<td>Binelli et al. 2009</td>
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<td><strong>Amphibians</strong></td>
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<td></td>
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<tr>
<td><em>African clawed frog</em></td>
<td>LOEC, 24 h</td>
<td>Gene expression (in cell lines)</td>
<td>0.030</td>
<td>No</td>
<td>Veldhoen et al. 2006</td>
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<tr>
<td><em>Xenopus laevis</em></td>
<td>MATC, 32 d</td>
<td>Growth</td>
<td>2.8</td>
<td>Yes</td>
<td>Study Submissions 2009; Fort et</td>
</tr>
</tbody>
</table>
### Preliminary Assessment: Triclosan (March 2012)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Endpoint, duration</th>
<th>Effect</th>
<th>Concentration (µg/L)</th>
<th>Used in SSD?</th>
<th>Reference</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>al. 2011</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Northern leopard frog</td>
<td>NOEC, 14 d</td>
<td>Vitellogenin synthesis</td>
<td>&gt; 200</td>
<td>Matsumura et al. 2005</td>
<td></td>
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<td>Rana pипiens</td>
<td>LOEC, 24 d</td>
<td>Activity level (decrease)</td>
<td>0.23</td>
<td>No</td>
<td></td>
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<td>American toad</td>
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<td>Activity level (increase)</td>
<td>0.23¹</td>
<td>No</td>
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<td>Bufo americanus</td>
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<td>Gene expression</td>
<td>0.30</td>
<td>Veldhoen et al. 2006</td>
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<td>Bullfrog Rana catesbeiana</td>
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<td>Fish</td>
<td></td>
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<td></td>
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<td>Rainbow trout</td>
<td>NOEC, 61 d</td>
<td>Fry survival</td>
<td>34.1¹</td>
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<td></td>
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<td>Oncorhynchus mykiss</td>
<td>LOEC, 61 d</td>
<td>Fry survival</td>
<td>71.3¹</td>
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<tr>
<td></td>
<td>MATC, 61 d</td>
<td>Fry survival</td>
<td>49.3¹</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Mosquitofish Gambusia affinis</td>
<td>MATC, 35 d</td>
<td>Sperm count</td>
<td>76.6</td>
<td>Raut and Angus 2010</td>
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<tr>
<td>Zebrafish Danio rerio</td>
<td>IC₂₅, 9 d</td>
<td>Hatchability</td>
<td>160</td>
<td>Yes</td>
<td></td>
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<td></td>
<td>LOEC, 4 d</td>
<td>Embryotoxicological effects</td>
<td>500</td>
<td>No</td>
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<td>Japanese medaka</td>
<td>NOEC, 14 d</td>
<td>Hatchability</td>
<td>156</td>
<td>No</td>
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<tr>
<td>Oryzias latipes</td>
<td>NOEC, 21 d</td>
<td>Fecundity, fertility</td>
<td>≥ 200</td>
<td>No</td>
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<td></td>
<td>IC₂₅, 14 d</td>
<td>Hatchability</td>
<td>290</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations used: ECₓ, the concentration of a substance that is estimated to cause some effect on x% of the test organisms; ICₓ, the inhibitory concentration for a specified percent effect; a point estimate of the concentration of a test substance that causes x% reduction in quantitative biological measurements such as growth rate; LCₓ, the concentration of a substance that is estimated to be lethal to x% of the test organisms; LOEC, lowest-observed-effect concentration; MATC, maximum allowable toxicant concentration, generally presented as the range between NOEC and LOEC or as the geometric mean of the two measures; NOEC, no-observed-effect concentration; SSD, species sensitivity distribution

¹ Tests conducted at a pH between 8 and 9 (most often between pH 8.1 and 8.5). The other tests (when information was available) were conducted at a pH between 6.5 and 8.0. Most of the algae tests are usually initiated at about pH 7.5 and end at about pH 8.5 due to carbon dioxide consumption.

Wilson et al. (2003) reported an algal community structure shift at triclosan levels as low as 0.015 µg/L. This study used natural algal assemblages as well as natural water, making the outcome of the bioassays more environmentally realistic. However, because insufficient data were reported, such as measurements of exposure concentrations, there is uncertainty about the actual threshold of effects. Hence, the results of this study were not used for the derivation of a chronic toxicity threshold for triclosan, but they are still considered as a line of evidence in this assessment. Lawrence et al. (2009) investigated the effects of triclosan on the structure and function of river biofilm communities, which are a key component of whole ecosystem function. Using South Saskatchewan River water as a source of inoculum and nutrients, they employed a
variety of techniques, including microscale analyses, molecular probes and physiological
determinations, to determine the effects of a continuous exposure to triclosan at 10 μg/L.
Analyses of the biofilm communities indicated shifts in the algal and bacterial composition, as
well as a significant reduction in algal biomass, in test systems containing triclosan as compared
with controls (Table 22). The general shift observed was towards a more heterotrophic
community, which may have significant ecological implications for carbon and energy flow.
This kind of shift can also result in changes in both the nutrient processing capacity and the
natural food web structure of river communities. Using pure cultures of protozoa, Lawrence et al.
(2009) found no detectable effects of triclosan at 50 μg/L for *Euplotes* sp., *Dileptus* sp.,
*Blepharisma* sp., *Stentor* sp., *Spirostomum* sp., *Euglena* sp. and *Paramecium* sp., but showed
effects at 0.5 μg/L for unspecified members of *Rotifera* (Table 22). Miyoshi et al. (2003)
reported deleterious effects of triclosan on two *Paramecium* species at concentrations of 1564
and 400 μg/L after 5 days. However, lack of experimental information, notably regarding
exposure concentrations, makes the reliability of this study questionable; hence, the results were
not further considered.

**Invertebrates**

Regarding freshwater crustaceans, Orvos et al. (2002) measured acute and chronic toxic effects
for daphnids at 390 μg/L and 89 μg/L, respectively. The same authors estimated a no-observed-
effect concentration for the reproduction of *Ceriodaphnia dubia* at triclosan concentrations of 6
μg/L (Table 22), while Tatarazako et al. (2004) observed inhibition of reproduction for the same
species at 170 μg/L of triclosan. Flaherty and Dodson (2005) observed that *Daphnia* exposed to
10 μg/L of triclosan on a chronic basis produced twice as many male individuals as their control
counterparts. However, when *Daphnia* was exposed to triclosan in a mixture of pharmaceuticals,
there was a decrease in sex ratio, with 20% fewer male offspring.

Borgmann et al. (2007) tested the effects of a mixture of pharmaceuticals, including triclosan, on
the freshwater amphipod *Hyalella azteca*. Survival, mating, body size and reproduction were
monitored over three generations. No effects were observed on any of the endpoints measured.
The mean measured concentration of triclosan over the experiment was 127 ng/L. Dussault et al.
(2008) conducted a chronic toxicity test with this amphipod and obtained LC_{10} and EC_{10} values
of 5 μg/L and 50 μg/L for survival and growth, respectively. The same authors also tested larvae
of the aquatic dipteran *Chironomus tentans* and obtained similar LC_{10} and EC_{10} values (20 and
80 μg/L). Even though *Hyalella* and *Chironomus* are benthic organisms, the tests mentioned
above were conducted using spiked water only (and not spiked sediments).

Triclosan was found to have genotoxic and cytotoxic effects *in vivo* in hemocytes of the
freshwater zebra mussel (*Dreissena polymorpha*). Several biomarkers were assessed over a 96-
hour exposure period. Significant increases in all genetic biomarkers (e.g., micronucleus test,
apoptotic frequency) as well as a clear destabilization of lysosomal membranes were observed
following exposure to triclosan at 290–870 ng/L (Binelli et al. 2009).

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Fish
Orvos et al. (2002) determined acute toxicity (96-hour LC$_{50}$) values of 260 µg/L and 370 µg/L of triclosan for the fathead minnow and bluegill sunfish, respectively. For chronic toxicity, they measured a no-observed-effect concentration (NOEC) and lowest-observed-effect concentration (LOEC) of 34.1 µg/L and 71.3 µg/L, respectively, for the rainbow trout in an early life cycle test. A study performed by Oliveira et al. (2009) concluded that triclosan had deleterious effects on adult and early life stages of zebrafish (*Danio rerio*). Effects included embryotoxicity and hatching delay. The authors attributed the high embryo mortality to the incorporation of triclosan into the eggs. The 96-hour LC$_{50}$ value for embryo survival was 420 µg/L. Embryotoxicological effects, such as spine malformation and reduced size, were observed after 4 days of exposure to 500 µg/L of triclosan. Tatarazako et al. (2004) also observed adverse effects on hatchability for larvae of the same species after 9 days of exposure (Table 22).

Ishibashi et al. (2004) studied the effects of triclosan on the early life stages and reproduction of Japanese medaka (*Oryzias latipes*) (Table 22). Among other findings, they observed that gonadosomatic and hepatosomatic indices were significantly higher in adults exposed to concentrations of 20 µg/L and higher. Also, concentrations of hepatic vitellogenin were increased significantly in males exposed to 20 and 100 µg/L. Investigations by Foran et al. (2000) of possible estrogenic properties of triclosan on the same species indicated that this substance does not display estrogenic activity at levels ranging from 1 to 100 µg/L. However, based on the evaluation of changes in secondary sexual characteristics, these authors suggested that triclosan is potentially weakly androgenic. It should also be noted that the species *Oryzias latipes* is not found in the Canadian environment, and no surrogate species exist.

In a study conducted on male western mosquitofish (*Gambusia affinis*), Raut and Angus (2010) observed a significant increase in normally female-limited vitellogenin mRNA expression at a triclosan treatment of 101 µg/L. In this study, which suggested that triclosan has the potential to act as an endocrine disruptor in male mosquitofish, it was also found that triclosan both decreased sperm counts and increased the mean hepatosomatic index at 101 µg/L. Other concentrations tested were 29 and 58 µg/L. Decreased sperm counts could have an impact at the population level; hence, it is considered an ecologically relevant endpoint. However, it should be noted that the concentrations tested in this study are 2–3 orders of magnitude higher than those measured in aquatic ecosystems in Canada.

Amphibians
Fraker and Smith (2004) observed a decreased activity in *Rana pipiens* tadpoles exposed to triclosan for 24 days. They determined a LOEC of 230 ng/L, indicating a high sensitivity of amphibians to triclosan. In contrast, Smith and Burgett (2005) observed an increased activity in *Bufo americanus* tadpoles exposed to triclosan at 230 ng/L for 14 days. They did not observe any effect on growth or survival at this concentration.

Based on acute LC$_{50}$ values, Palenske et al. (2010) concluded that amphibian larvae were most sensitive to triclosan during their early developmental stages. The study was conducted on one larval stage of three North American species, *Acris crepitans blanchardii*, *Bufo woodhousii*...
woodhousii and Rana sphenocephala, and on four larval stages of the African clawed frog, Xenopus laevis. The 96-hour LC50 values for these species were 367, 152, 562 and 259–664 µg/L (for four stages of X. laevis), respectively. There was a significant difference between the LC50 values for the North American species, and there was a significant difference between the LC50 values for the earlier versus later larval stages of X. laevis. Metabolic rate and heart rate in amphibian larvae were also monitored and seemed to be affected at various triclosan concentrations, but not in a clear dose-dependent manner.

Matsumura et al. (2005) showed no significant difference in the level of plasma vitellogenin synthesis in male adult clawed frogs exposed to 20–200 µg/L of triclosan in a 14-day waterborne exposure test.

Studies have also been conducted to assess the influence of triclosan on thyroid hormone–mediated metamorphosis in frogs. Veldhoen et al. (2006) studied the effects of triclosan on precocious metamorphosis in bullfrog (Rana catesbeiana) tadpoles. Premetamorphic tadpoles were injected with T3 to induce metamorphosis and exposed to measured triclosan concentrations of 0.12–11.2 µg/L for 18 days. A reduction in body weight was observed for the frogs exposed to 0.12 µg/L, but not in the frogs exposed to higher concentrations. Snout-vent and tail length were not significantly affected in any of the triclosan treatment exposures. However, the development of tadpoles, based on differences in developmental stages as defined by Nieuwkoop and Faber (1994), was advanced in all triclosan exposures. Although R. catesbeiana is not the species used in standardized protocols for testing amphibian metamorphosis, this species is native to eastern Canada. Using a X. laevis cell line, the same authors reported that exposure to low levels of triclosan (30–300 ng/L) resulted in altered (i.e., increased) TRα and TRβ mRNA expression. An increase in TRβ transcript levels may be indicative of advanced metamorphosis.

In contrast, Fort et al. (2010, 2011) concluded that triclosan does not alter the normal course of metamorphosis of X. laevis. In a 21-day test where prometamorphic tadpoles (NF stage 51) were exposed to triclosan concentrations of 0.6, 1.5, 7.2 and 32.2 µg/L, Fort et al. (2010) observed that larval growth (i.e., whole body length and weight, snout-vent and hind limb length) was reduced at 1.5 µg/L, but not at the other treatment levels. Based on developmental stages, the postembryonic development of X. laevis was advanced, although not in a dose-related manner. Indeed, a significant induction in TRβ mRNA expression occurred in the 1.5 and 7.2 µg/L treatments only. Such a lack of a dose–response relationship is not unusual. For instance, in recent studies conducted with chemicals that are known to alter endocrine function (reviewed in Welshons et al. 2003), the effects observed were not necessarily manifested following a linear dose–response relationship and, in several instances, were found to follow a non-monotonic response curve. In a similar 32-day test, NF stage 47 X. laevis (prometamorphic) tadpoles were exposed to triclosan concentrations of 0.3, 1.3, 5.9 and 29.6 µg/L (Study Submissions 2009; Fort et al. 2011). Effects on growth endpoints such as a significant increase in mean whole body length and weight as well as snout-vent length were observed at concentrations of 0.3 µg/L and 1.3 µg/L, respectively. Contrary to the 21-day study, the postembryonic development of X. laevis was delayed in the treatment groups when compared with the control, but no statistical
significance was detected. Although minimal, occurrences of thyroid gland hypertrophy and congestion were noted in all treatment levels, with the number of cases increasing with exposure concentration. Thyroid histology (e.g., follicle count, follicle size, colloid content/follicle) was not significantly different from that of control; however, the variability among individuals was high in the highest treatment levels for some parameters. Finally, TRβ mRNA expression was not significantly affected at any of the concentrations tested in this 32-day test. The authors of these two studies concluded that triclosan seems capable of increasing tadpole growth during their development, but not advancing thyroid-mediated metamorphosis (Fort et al., 2011). The authors suggested that increased growth was due to non-thyroidal mechanisms, such as reduced bacterial stressors in culture.

Overall, these studies do not demonstrate a consistent effect of triclosan on thyroid-mediated amphibian metamorphosis. However, they demonstrated effects on developmental stage and TRβ mRNA induction. These effects suggest that triclosan may interfere with the action of natural thyroid hormone in amphibians.

**Species Sensitivity Distribution**

Given the abundance of aquatic toxicity data available, and for the purpose of identifying a critical toxicity value (CTV), a species sensitivity distribution (SSD) was developed for triclosan. Toxicity data for chronic endpoints only were chosen to derive the SSD, given that chronic exposure to triclosan is expected in receiving ecosystems. The SSD comprises endpoints for three fish, one amphibian, four invertebrate, four macrophyte, four algal and one metazoan species, as well as on an algal/bacterial community; the resulting distribution is shown in Figure 3. When more than one value for a chronic endpoint was available for a single species, the preferred endpoint, according to guidance provided by the Canadian Council of Ministers of the Environment (CCME 2007), was chosen. If multiple preferred endpoints were available, the lowest value was chosen. Robust study summaries were completed for all the endpoints that were included in the SSD to ensure that they came from reliable studies.

Several of the data mentioned above were not used in the derivation of the SSD for reasons other than not being the preferred endpoint. The toxicity values for the alga *Skeletonema costatum* and *Dunaliella tertiolecta* were not considered for the SSD because they are marine species and the exposure data available are for fresh water. The toxicity value for *Hyalella azteca* from Borgmann et al. (2007) was not used, as this test was conducted with a mixture of substances. Toxicity to Japanese medaka was also excluded from the SSD, as this species is not relevant to the Canadian environment. The toxicity value for the algal community from Wilson et al. (2003) and the values for *Paramecium* species from Miyoshi et al. (2003) were not used, since these studies did not meet the reliability standards of the robust study summary, as insufficient information on the data was reported. No amphibian or mollusc data were used in the SSD, exclusive of the toxicity value for *Xenopus laevis* growth (Study Submissions 2009), because the endpoints measured in these tests differ from those measured for other taxonomic groups and are difficult to translate in terms of impacts on population dynamics. Thus, these results were left out

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1 Available upon request from Environment Canada.
of the SSD, but are still used as a separate line of evidence to characterize the potential ecological effects of triclosan.

The software SSD Master version 2.0 (Rodney et al. 2008) was used to plot the SSD. Several cumulative distribution functions (normal, logistic, Gompertz and Fisher-Tippett) were fit to the data using regression methods. Model fit was assessed using statistical and graphical techniques. The best model was selected based on consideration of goodness of fit and model feasibility. Model assumptions were verified graphically and with statistical tests. The normal model provided the best fit of the models tested (Anderson-Darling Statistic \( A^2 \) = 0.698), and the 5th percentile (HC5, i.e., hazardous concentration to 5% of species) of the SSD plot is 115 ng/L, with lower and upper confidence limits of 67 and 198 ng/L, respectively (Figure 3). The species potentially affected at this concentration are expected to be algae and metazoa. The HC5 of 115 ng/L calculated from the SSD is selected as the CTV for toxicity to freshwater organisms.

![SSD for triclosan](image)

**Figure 3.** Species sensitivity distribution (SSD) for triclosan based on selected chronic toxicity data for freshwater aquatic organisms. The normal model fit to the data is shown on the graph along with the 95% confidence intervals. The data used in the SSD are identified in Table 22.

### 4.5.2.2 Benthic Organisms

The toxicity of triclosan to benthic organisms was assessed by conducting a test with chironomids (*Chironomus riparius*) using spiked sediments, in accordance with OECD test guideline 218. After 28 days, no adverse effects were observed on the emergence ratio or development rate at any of the concentrations tested (Study Submissions 2009). Based on these results, the NOEC for triclosan is greater than or equal to 100 mg/kg dw, the highest
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concentration tested. The concentrations of triclosan in sediments were measured in the control, middle and highest treatment levels and were constant throughout the test. The concentrations of triclosan residues in the overlying water column were very low throughout the test period (< 1% of applied radiolabelled triclosan). Similarly, very low amounts of radioactivity were measured in the pore water samples (0.1% of applied radioactivity). This indicates that triclosan was mainly bound to the sediment, but most of this fraction was extractable. The latter contrasts with results from the aerobic aquatic metabolism study mentioned in Section 4.2.4.2, which indicates that about one third of the triclosan that was bound to sediment by study termination (104 days) was not extractable. The difference between this fate study and the chironomid toxicity study may be due to different study durations or different types of sediments. The sediments used in the toxicity study were mainly composed of sand silica, a substrate that has a low adsorption capacity.

4.5.2.3 Terrestrial organisms

A summary of toxicity data available for triclosan for terrestrial organisms is presented in Table 23.

Table 23. Toxicity of triclosan to terrestrial organisms

<table>
<thead>
<tr>
<th>Organism</th>
<th>Endpoint, duration</th>
<th>Effect</th>
<th>Concentration (mg/kg dw or mg/kg bw per day)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corn Zea mays</td>
<td>LOEC, 21 d</td>
<td>No effect observed</td>
<td>&gt; 0.610</td>
<td></td>
</tr>
<tr>
<td>Tomato Solanum lycopersicon</td>
<td>NOEC, 21 d</td>
<td>Root and shoot weight</td>
<td>0.162</td>
<td></td>
</tr>
<tr>
<td>Ryegrass Lolium perenne</td>
<td>NOEC, 21 d</td>
<td>Root weight</td>
<td>0.162</td>
<td></td>
</tr>
<tr>
<td>Wheat Triticum aestivalum</td>
<td>NOEC, 21 d</td>
<td>Shoot weight</td>
<td>0.162</td>
<td></td>
</tr>
<tr>
<td>Soybean Glycine max</td>
<td>LOEC, 21 d</td>
<td>No effect observed</td>
<td>&gt; 0.610</td>
<td></td>
</tr>
<tr>
<td>Cucumber Cucumis sativus</td>
<td>NOEC, 21 d</td>
<td>Shoot length</td>
<td>0.065</td>
<td>Liu et al. 2009²</td>
</tr>
<tr>
<td></td>
<td>NOEC, 28 d</td>
<td>No effect observed</td>
<td>&gt; 0.446</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NOEC, 20 d</td>
<td>Shoot and root length</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LOEC, 20 d</td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Rice Oryza sativa</td>
<td>NOEC, 20 d</td>
<td>Root length</td>
<td>1</td>
<td>Amorim et al. 2010</td>
</tr>
<tr>
<td></td>
<td>LOEC, 20 d</td>
<td></td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Wheat Triticum aestivalum</td>
<td>EC₂₀, 14 d</td>
<td>Shoot weight</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Invertebrates</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eisenia foetida</td>
<td>NOEC, 14 d</td>
<td>Survival</td>
<td>1026</td>
<td>Reiss et al. 2009</td>
</tr>
<tr>
<td>Eisenia andrei</td>
<td>LC₅₀, 14 d</td>
<td>Adult survival</td>
<td>866</td>
<td>Amorim et al. 2010</td>
</tr>
<tr>
<td></td>
<td>EC₁₀, 56 d</td>
<td>Reproduction</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Birds</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Organism</th>
<th>Endpoint, duration</th>
<th>Effect</th>
<th>Concentration (mg/kg dw or mg/kg bw per day)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mallard duck <em>Anas platyrhynchos</em></td>
<td>LD₅₀, 14 d (acute oral)</td>
<td>Survival</td>
<td>≥ 2150</td>
<td>US EPA 2008f</td>
</tr>
<tr>
<td>Bobwhite quail <em>Colinus virginianus</em></td>
<td>LD₅₀, 14 d (acute oral)</td>
<td>Survival</td>
<td>825</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LC₅₀, 8 d (dietary)</td>
<td>≥ 5000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Mammals

<table>
<thead>
<tr>
<th></th>
<th>Endpoint, duration</th>
<th>Effect</th>
<th>Concentration (mg/kg dw or mg/kg bw per day)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>LD₅₀ (acute oral)</td>
<td>Survival</td>
<td>&gt; 5000</td>
<td>US EPA 2008b</td>
</tr>
<tr>
<td></td>
<td>NOAEL, 90 d</td>
<td>Histopathological changes in the liver</td>
<td>65 (males) 82 (females)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LOAEL, 90 d</td>
<td></td>
<td>203 (males) 259 (females)</td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>NOAEL, 90 d</td>
<td>Increased liver weights and liver pathology, decrease in hematology parameters (red blood cells, hemoglobin and hematocrit) and cholesterol</td>
<td>25</td>
<td>Health Canada (see Section 3.1)</td>
</tr>
<tr>
<td></td>
<td>LOAEL, 90 d</td>
<td></td>
<td>75</td>
<td></td>
</tr>
</tbody>
</table>

#### Soil microorganisms

|                           | NOEC, 1 h to 28 d  | Respiration, nitrification, phosphatase, glucosidase, chitinase | 1 | Waller and Kookana 2009 |

Abbreviations used: ECₓ, the concentration of a substance that is estimated to cause some effect on x% of the test organisms; LCₓ, the concentration of a substance that is estimated to be lethal to x% of the test organisms; LDₓ, the dose of a substance that is estimated to be lethal to x% of the test organisms; LOEC, lowest-observed-effect concentration; NOAEL, no-observed-adverse-effect level; NOEC, no-observed-effect concentration; LOAEL, lowest-observed-adverse-effect level

1 Based on time-weighted mean measured concentrations.
2 Based on nominal concentrations.

**Invertebrates**

The acute toxicity of triclosan to earthworms (*Eisenia fetida*) was reported by Reiss et al. (2009). The nominal concentrations tested ranged from 64 to 1026 mg/kg dw soil. No mortality had occurred in any of the test concentrations by the end of the 14-day study period. Lin et al. (2010) exposed the same species of earthworms to soil spiked with triclosan. They observed inhibitory effects on certain enzymes, such as catalase and glutathione S-transferase. A comet assay also demonstrated DNA damage induced by triclosan. However, all these sublethal...
Effects were observed at levels of triclosan unlikely to be reached in soils (≥ 50 mg/kg). Amorim et al. (2010) measured a 56-day EC\textsubscript{10} of 0.6 mg/kg for the effect of triclosan on the reproduction of *Eisenia andrei*. These authors also tested the worm *Enchytraeus albidus* and the collembolan *Folsomia candida*. No clear dose–response curve was obtained for these species; however, a visual inspection of the curve indicates that juveniles of both species seemed significantly affected at the highest concentration tested of 320 mg/kg dw soil.

**Plants**

Five studies were conducted to assess the effect of triclosan on terrestrial plants. In the first study, six plant species (corn, ryegrass, wheat, cucumber, soybean and tomato) were exposed to triclosan in a sandy soil at nominal concentrations of 10–1000 μg/kg dw for 21 days. Cucumber proved to be the most sensitive species, with a measured time-weighted average NOEC of 65 μg/kg dw soil for shoot length (Study Submissions 2009). In the second study, the seed germination and seedling growth of cucumber exposed to triclosan in a sandy loam at nominal concentrations of 10–1000 μg/kg dw were studied over 28 days. No adverse effects were observed at the highest concentration tested, resulting in a time-weighted average NOEC of 446 μg/kg dw based on measured concentrations (Study Submissions 2009). In the third study, 10 plant species (corn, ryegrass, wheat, cucumber, soybean, tomato, lettuce, radish, vetch and pea) were exposed for 14 days (post–median control emergence) to triclosan in a sandy loam at nominal concentrations ranging from 0.2 to 1000 mg/kg, following OECD test guideline 208 (Büche et al. 2009). The most sensitive species was lettuce, with NOEC and LOEC values for shoot weights of 50 and 75 mg/kg, respectively, based on nominal concentrations. The NOEC for shoot weight for all other species tested was 1000 mg/kg. The fourth study indicated that rice seedlings were more sensitive to triclosan than cucumber, with NOEC and LOEC values for root elongation of 1 mg/kg and 10 mg/kg, respectively (Liu et al. 2009). In that study, root length was more sensitive than shoot length as a test endpoint. The growth test lasted 20 days and was conducted in a paddy soil. Finally, the fifth study was conducted by Amorim et al. (2010) with wheat and field mustard. The emergence, growth and biomass of these plants were recorded after 14 days of exposure to a soil spiked with triclosan. For both species, a dose–response curve was obtained, and EC\textsubscript{10}, EC\textsubscript{20} and EC\textsubscript{50} values with 95% confidence intervals were calculated. However, for field mustard, none of the EC\textsubscript{10}, EC\textsubscript{20} and EC\textsubscript{50} values obtained fell within the corresponding confidence intervals, which make the values questionable. For wheat, the most sensitive growth parameter was shoot fresh weight, with EC\textsubscript{10}, EC\textsubscript{20} and EC\textsubscript{50} values of 44 mg/kg, 98 mg/kg and 378 mg/kg, respectively.

**Birds and Mammals**

Based on a limited data set, triclosan seems not toxic to slightly toxic to birds (median lethal dose [LD\textsubscript{50}] ≥ 2150 mg/kg bw and 825 mg/kg bw for mallard duck and bobwhite quail, respectively) and not toxic to mammals (rat, LD\textsubscript{50} > 5000 mg/kg bw) on an acute oral basis. Subchronic oral toxicity data indicate a NOAEL of 25 mg/kg bw per day based on treatment-related effects observed in mice (see Section 3.1.3). Oral toxicity studies were also conducted with dogs and baboons, but the results of these studies were not considered in this assessment due to a number of factors (see Section 3.2.3). There were no indications of adverse effects on thyroid function in mammals (see Section 3.1.10).
Microorganisms
The effect of triclosan on microbial activity was studied by Waller and Kookana (2009) in two types of soils (sandy loam and clay). Substrate-induced respiration and nitrification were decreased at a concentration of 50 mg/kg and 5 mg/kg, respectively. The activities of four enzymes—namely, the acid and alkali phosphatase, β-glucosidase and chitinase—were also measured, but did not seem affected by triclosan, except for the β-glucosidase in the sandy soil. No adverse effects were noted on any of the microbial processes at the lowest concentration tested of 1 mg/kg. In a study by Liu et al. (2009), soil respiration in a paddy soil was inhibited after 22 days of incubation at triclosan concentrations of 10 mg/kg and above. The phosphatase activity seemed to decrease with increasing triclosan concentrations in soil; however, the differences were not significant.

4.5.3 Methyl-triclosan
A study conducted to assess the toxicity of methyl-triclosan to *Daphnia magna* indicates that the 48-hour NOEC for immobilization is greater than or equal to 180 µg/L. In another study, the 72-hour EC50 values for biomass and growth rate for the alga *Scenedesmus subspicatus* were 120 µg/L and 170 µg/L, respectively. The corresponding EC10 values were 55 µg/L and 76 µg/L, respectively (Study Submissions 2009). These results suggest that methyl-triclosan is less toxic to aquatic organisms than triclosan, but is nonetheless of high toxicity.

4.6 Potential to Cause Ecological Harm

4.6.1 Calculation of Risk Quotients
A risk quotient is the ratio of a predicted environmental concentration (PEC) to a toxicity endpoint (predicted no-effects concentration [PNEC]) determined for each medium of concern and exposure scenario. The risk quotient is an important line of evidence in characterizing the potential of a substance to cause harm to ecosystems.

As described in Section 4.1.2, the main release of triclosan to the environment is to aquatic ecosystems via effluents from WWTPs. Once in the water column, results from the Multispecies Model indicate that triclosan either will remain in water (60%) or will partition to sediment (40%). As well, another important release of triclosan is to agricultural soils via the spreading of wastewater treatment sludge. Therefore, the risk should be assessed for each of these three compartments.

4.6.1.1 Water

*Site-Specific Scenario Based on Monitoring Data*
Because monitoring data are available for receiving waters in densely populated areas of Canada, and because these data account for all fate processes, a realistic PEC was selected based on these data. Table 21 indicates that the highest triclosan concentration measured in surface
water is 691 ng/L. This value was measured in 2002 in the Thames River, downstream from the WWTP that serves the municipality of Ingersoll, Ontario. For comparison purposes, the mean concentration measured upstream from this WWTP was 153 ng/L. It can be noted that other WWTPs are located along the Thames River, both upstream and downstream from Ingersoll. Based on uncertain trends regarding the use of triclosan in products used in Canada between 2002 and the present, there is uncertainty as to whether the concentrations of triclosan measured in surface water have generally decreased or increased since the early 2000s. The value of 691 ng/L was chosen as a realistic PEC for the risk quotient analysis. Even though this value represents only one site in Canada, it is not necessarily the highest that exists, so it was deemed not overly conservative to select it for the risk quotient analysis.

For the above scenario, the PNEC was selected as the HC₅ of 115 ng/L calculated from the SSD of chronic effects to aquatic organisms (see Section 4.5.2.1). Since this value is based on a chronic SSD that covers multiple taxa, an assessment factor was not used to derive the PNEC.

The risk quotient obtained for water is 6 (= 691 ng/L / 115 ng/L), indicating that triclosan would pose a risk for aquatic ecosystems, specifically in water bodies receiving WWTP effluents like the Thames River in Ontario. Generally, a risk quotient greater than 1 indicates a potential for adverse ecological effects.

Several of the monitoring data included in Table 21 are higher than the levels of triclosan (30–300 ng/L) that are sufficient to disrupt thyroid hormone–associated gene expression and to alter thyroid hormone–mediated postembryonic development in tadpoles (Fraker and Smith 2004; Veldhoen et al. 2006). These effects point to the potential toxicity of triclosan to amphibians, which is not fully reflected in the risk quotient analysis above, since most of the amphibian endpoints were not included in the SSD.

**Nationwide Scenario Extrapolated Based on Monitoring Data**

In order to assess the risk to aquatic ecosystems on a national scale, exposure calculations were done using the spreadsheet tool Mega Flush (version 3.1.1; Environment Canada 2009). This tool combined information on triclosan loadings to WWTPs and on removal efficiency for different wastewater treatment types (e.g., primary, secondary) with locations of WWTPs across Canada as well as receiving water bodies to estimate the potential risk posed by triclosan to the aquatic environment. More specifically, the combined information allowed for the generation of a PEC value for each wastewater treatment facility discharging to a receiving water body. Each PEC was then compared with the PNEC, which resulted in each discharge site having its own specific risk quotient. The proportion of discharge points across Canada having a risk quotient greater than 1, indicating a potential for adverse ecological effects, was then calculated, which provided an overview of the potential extent of risk on a national basis.

To calculate triclosan loadings to WWTPs, concentrations of triclosan measured in the influent of WWTPs located across the country (see Table 14) were multiplied by the influent flow for each corresponding WWTP. Loadings were then divided by the population served by each WWTP in order to generate a daily mass of triclosan released per capita. This was done for the
26 WWTPs listed in Table 14. Whenever data were available for a single WWTP for two different sampling years, data for the most recent year were used. WWTPs for which the influent flow and/or the population served were unknown could not be included in the calculations. The median value obtained for the daily mass of triclosan released per capita for the 26 WWTPs is 0.82 mg/person per day (25th and 75th percentiles of 0.60 and 1.1, respectively). For comparison purposes, values of 0.63–2.74 mg/person per day were estimated for the United Kingdom (Price et al. 2010). The value of 0.82 was used as a representative value for the whole country, since it is based on numerous WWTPs that serve populations of various sizes. The use pattern of products containing triclosan is not expected to vary a lot spatially within populated areas of Canada. The daily mass of triclosan released per capita is based on the assumption that there is a high correlation between triclosan loadings to WWTPs and population served. A regression analysis based on these two parameters showed a linear relationship with an $r^2$ of 0.93 after plotting data for the 26 WWTPs considered. This relationship does not consider, however, the influence of industrial releases to WWTPs in terms of triclosan loadings. The importance of the latter is unknown.

The median daily mass of triclosan released per capita (0.82 mg/person per day) was entered in the Mega Flush spreadsheet tool and, by combining it with relevant information available for approximately 1000 WWTPs located across the country (e.g., population served, influent and effluent flows, removal efficiency, flow of the receiving water body) (Environment Canada 2009), a PEC was estimated for each discharge point. Except for those WWTPs that have no or only preliminary treatment, the removal efficiencies used in Mega Flush were estimated based on measured concentrations of triclosan in influent and effluent for a series of WWTPs in Canada (Lee et al. 2003, 2005; Lishman et al. 2006; 2011 personal communication from Water Science and Technology Directorate, Environment Canada, to Science and Risk Assessment Directorate, Environment Canada; unreferenced) and were as follows: 0% for no or preliminary treatment (assumption), 10% for primary treatment (based on one WWTP), 85% for secondary treatment (based on 24 WWTPs) and 95% for lagoons (based on two lagoons). It should be noted that the data available for the two lagoons actually indicated 99% removal efficiency. However, for modelling purposes, the maximum value used was set at 95%, since data were not available for all different types of lagoons, which may have different removal efficiencies. The study in which 99% removal was obtained for lagoons used wastewater samples that were sampled between October and December, so likely the effect of low temperatures would be taken into account, but only to a certain extent. The higher removal efficiency in lagoons as compared with secondary treatment could be due to the fact that photodegradation can occur in the former (Lishman et al. 2006).

Assuming an instantaneous dilution of the effluent, a PEC was calculated at each discharge point using either the 10th percentile of the annual distribution of the receiving water body flow or a maximum dilution factor of 10, whichever provided the lowest dilution. In those cases where the receiving environment is a lake rather than a watercourse, a dilution factor of 10 was also used.

The worst-case assumption was made that triclosan will not degrade further once in the water column. Experimental studies have shown that triclosan can photodegrade within hours under
laboratory conditions. However, given that effluents from WWTPs can have elevated concentrations of suspended matter, the photodegradation of triclosan could be mitigated to a certain extent. Monitoring data provide evidence that triclosan is present at various concentrations in watercourses, although this is most probably due to its continual release from WWTPs.

The median PEC value obtained with Mega Flush is 20 ng/L in receiving water bodies, which is comparable to the mean values measured for some creeks in Canada for which monitoring data are available (Table 21). To compare with other modelled values, Price et al. (2010) conducted higher-tier exposure assessment for triclosan using the LF2000-WQX water quality model. The mean PEC values that they calculated under low-flow conditions (percentile not specified) were 124–149 ng/L for two rivers flowing in densely populated areas in England. Their PEC values represented the concentration immediately downstream of WWTPs after the effluent was considered to have fully mixed in the channel. These authors also calculated \( C_{river} \) values, which are concentrations that take into account releases from the WWTPs in the upstream catchment as well as in-stream degradation, among other things. The \( C_{river} \) values that they obtained under low-flow conditions were 73–74 ng/L for the two rivers.

Comparing the resulting PEC for each water body with the PNEC calculated from the SSD (115 ng/L) indicates that 12% of the discharge points across Canada that receive wastewater are potentially at risk with respect to triclosan. The inner 90% of risk quotients range from 0.036 (5th percentile) to 1.76 (95th percentile), with a 50th percentile value of 0.18. The highest risk quotient is 14. The sites at risk are mainly those with either no or preliminary treatment of wastewater, followed by those with secondary treatment. Sites for which the receiving water body has a low dilution capacity are also more at risk. Overall, these results support the ones obtained based on measured concentrations in surface water indicating that triclosan may cause harm to aquatic organisms.

The potential risk posed by methyl-triclosan to aquatic ecosystems was also assessed, since this substance is released from WWTPs and there is evidence of its presence in certain water bodies in Canada. For this substance, the worst-case scenario would be equivalent to assuming 100% transformation of triclosan to methyl-triclosan. Although it was not quantified, the portion of triclosan actually biotransformed to methyl-triclosan is expected to be much lower than this, as suggested by the results of the studies conducted on the fate of triclosan in WWTPs. A more realistic scenario would be to take into account all the fate pathways—that is, to base the PEC on monitoring data for water. Monitoring data for methyl-triclosan in Canada were available only for Hamilton Harbour, Lake Ontario and Wascana Creek (Saskatchewan); the highest value was 17 ng/L for Wascana Creek. Therefore, the PEC for methyl-triclosan in water was chosen to be 17 ng/L.

The results of only two aquatic toxicity studies are available for methyl-triclosan (acute tests with daphnids and algae). The lowest endpoint from these studies was selected as the CTV—that is, a 72-hour EC_{10} value of 55 µg/L for biomass of the alga *Scenedesmus subspicatus* (Study Submissions 2009).
An assessment factor of 100 was chosen to derive a PNEC from this value, given the very limited data set from which it was taken. Dividing the PEC of 17 ng/L by the PNEC of 550 ng/L results in a risk quotient of 0.03, indicating that methyl-triclosan would be unlikely to represent a risk to aquatic organisms.

4.6.1.2 Sediment
The only toxicity data available for benthic organisms are for chironomids. They indicate that the NOEC for triclosan is $\geq 100$ mg/kg dw (Study Submissions 2009). Even though no measured data for concentrations of triclosan in sediments were available for Canada, data from other countries showed levels of $< 1$ mg/kg (see Section 4.2.4.2). It is therefore unlikely that the concentrations would be higher than the NOEC obtained for chironomids. However, other benthic organisms could be more sensitive than chironomids to triclosan.

As for triclosan, a PEC for methyl-triclosan in sediment was not derived, because toxicity data on benthic organisms with which to derive a PNEC and risk quotient for this compartment are lacking.

4.6.1.3 Soil
The main release of triclosan to soils is via the spreading of sludge from WWTPs. In Canada, about 40% of this type of sludge is applied to various types of land (i.e., agricultural, forest or dedicated land) (Apedaile 2001). A PEC based on monitoring data (i.e., triclosan concentrations in soil) cannot be determined, as such data were not found for Canada. However, numerous monitoring data were available for triclosan in wastewater sludge; these data can be used to derive a PEC for soil. As presented in Section 4.1.3.1, the concentration of triclosan in wastewater sludge from various WWTPs across the country ranges from less than 1 to 46.4 μg/g dw. In Canada, the worst-case conditions for wastewater sludge application to an agricultural soil are a maximum application rate of 8300 kg dw/ha per year (based on the highest existing provincial regulatory limit) with a mixing depth of 0.2 m (plough depth) and a soil density of 0.0017 kg/cm$^3$ (Environment Canada 2006). The following equation was used for deriving a soil PEC:

$$ PEC = \frac{[\text{triclosan}]_{\text{sludge}} \cdot \text{application rate}}{\text{depth} \cdot \text{density}} $$

Taking the highest triclosan concentration found in sludge (46.4 μg/g dw, Gatineau Valley; Table 15) and the maximum application rate described above for sludge spreading, a PEC of 113 μg/kg dw is obtained. Assuming a yearly application of sludge over 10 years, the cumulative triclosan concentration in soil would be 1246 μg/kg dw. This PEC value is based on the highly conservative assumption that triclosan will not degrade further once mixed into soil and that it will not leach or run off. In order to estimate more realistic PEC values, the Biosolids-Amended Soil Level 4 (BASL4) model was used (BASL4 2008). This model is a fugacity-based model and uses equilibrium partitioning principles to deduce the overall fate of a chemical in the soil. In
this model, a chemical can be removed from the soil by volatilization, degradation, leaching, runoff and erosion processes.

Two scenarios were modelled in BASL4 to simulate the lower and upper ends of a range of possible PECs in soil based on two triclosan half-lives, two wastewater sludge application rates and the highest triclosan concentration found in sludge (46.4 μg/g dw). In the first scenario (lower end), a half-life of 18 days was used based on results from laboratory experiments (Table 17), and an application rate of 5000 kg dw/ha per year was used based on average existing provincial regulatory limits. In the second scenario (upper end), a half-life of 200 days was arbitrarily chosen as an estimate of a field biodegradation half-life; Lozano et al. (2010) reported a dissipation half-life of 107 days for a field that had received one application of biosolids. Since the latter number would include contributions from processes such as leaching and volatilization, in addition to biodegradation, the value of 200 days was conservatively chosen to account for biodegradation only. Still in that second scenario, an application rate of 8300 kg dw/ha per year was used based on the highest existing provincial regulatory limit. A 10-year period was simulated; however, BASL4 can handle only three sludge application events. A yearly application during the first 3 years of the 10-year period was modelled.

The results obtained for the lower-end scenario show that the highest triclosan concentrations in soil would be reached at the time of sludge applications—i.e., at time 1 day, 366 days and 731 days (average of 149 μg/kg). These numbers are higher than the value of 113 μg/kg obtained above assuming no dissipation, probably because the equation used to calculate the latter assumes instantaneous mixing in the soil layer. The three peak modelled concentrations in soil drop below 1 μg/kg less than 36 days following each sludge application. There is no buildup in concentrations due to cumulative applications. The results for the upper-end scenario show that the highest concentrations in soil would again be reached at the time of sludge applications (average of 254 μg/kg). These peak concentrations would drop by a factor of 2 about 40 days following each sludge application and would drop below 1 μg/kg about 80 days following each application. Hence, the concentration in soil would also be less than 1 μg/kg after 10 years.

For comparison purposes, Fuchsman et al. (2010) conducted a terrestrial risk assessment for triclosan and modelled concentrations in soil using two half-lives (2 weeks, based on laboratory studies, and 16 weeks, based on soil dissipation studies) and two application frequencies (1 and 3 times a year; average application rate of 19 000 kg/ha per year). Their modelling exercise showed that there is no buildup of triclosan in soil, except for one of the four scenarios tested (one application and half-life of 16 weeks), in which the concentration of triclosan stabilizes over the years at approximately 110% of the initial soil concentration.

Measurements of triclosan in soils that were amended with biosolids are available from the literature. Wu et al. (2010b) measured triclosan in soils that had been amended with biosolids in Ohio. The soil for which the highest concentration of triclosan was measured (11 μg/kg dw in November 2008) is a clay that had historically received two biosolids applications (0.76 μg/g dw in biosolids), one in December 2006 and the other in November 2008. For comparison with the numbers provided above for Canada, the application rates for these two dates were 11 600 and
9900 kg dw/ha, respectively. In another study conducted in Virginia, Lozano et al. (2010) measured triclosan concentrations in soils that had been amended once with biosolids (average of 15.6 μg/g dw in biosolids) to vary between 4.1 and 4.5 μg/kg dw and between 24 and 67 μg/kg dw, 16 months and less than a year after application, respectively. In fields where there had been multiple applications of triclosan, there was a slight buildup in concentrations observed over the years, but these were much lower than the predictions made by the authors using an equation similar to the one above. In the Midwestern United States, Kinney et al. (2008) found triclosan concentrations of 160 and 96 μg/kg dw in soil samples that were collected 31 and 156 days following biosolids application, respectively. The sludge was applied once at a rate of 18 000 kg dw/ha, and its triclosan concentration was 10.5 μg/g dw. Finally, Sánchez-Brunete et al. (2010) measured triclosan concentrations of 4.7 and 1.7 μg/kg dw in agricultural soil sampled 1 day and 6 months following biosolids application (12 000 kg dw/ha; triclosan concentration in sludge not mentioned), respectively. The same authors measured methyl-triclosan concentrations of 1.7 and 3.8 μg/kg dw in the same soil samples. Overall, when compared with results from soil biodegradation studies, these data suggest that the persistence of triclosan in soil is greater when it is applied in biosolids, likely because it is present as bound residues. As such, its bioavailability to soil organisms is probably lower as compared with laboratory conditions.

Use of wastewater to irrigate agricultural fields, as well as other types of field (e.g., golf courses), can also contribute to the introduction of triclosan in the terrestrial environment. This practice is used worldwide, including in Canada (Hogg et al. 2007). However, no data are available to quantify the relative importance of this source as compared with biosolids application.

The calculation of a PNEC for the soil compartment is based on the most sensitive endpoint identified for terrestrial organisms (shoot length for cucumber, NOEC = 65 μg/kg; see Table 23). Because this value is a no-effect endpoint and because it was measured in a sandy soil, which is expected to have low adsorption capacity and therefore maximize the bioavailability of triclosan, an assessment factor was not used. The resulting PNEC for soil is therefore 65 μg/kg. The risk quotients based on the average peak soil concentrations obtained for the lower-end and upper-end scenarios modelled in BASL4 are 149 μg/kg / 65 μg/kg = 2.3 and 254 μg/kg / 65 μg/kg = 3.9, respectively. Because the PNEC used for the risk quotients is based on a no-effect value, the risk quotients are actually expected to be less than 2.3 and less than 3.9.

The potential risk of exposure of terrestrial wildlife to triclosan was not quantitatively assessed, since results from repeated oral dose toxicity studies in mammals show relatively low effects (e.g., NOAEL of 25 mg/kg bw per day in mice; Table 23). In addition, the low BAF values in terrestrial organisms, such as earthworms and shrews (modelled BAFs of ~1000 and ~30 based on BASL4; see Section 4.3.2), coupled with some metabolism of triclosan that would occur following prey ingestion, would both mitigate exposure levels in top predators.

4.6.2 Characterization of Ecological Risk
An ecological risk assessment integrates the environmental exposure and ecotoxicology data to estimate the potential for adverse ecological effects. The approach taken in this ecological screening assessment is to examine various technical information and develop conclusions based on a weight of evidence approach and applying precaution as required under CEPA 1999. One important line of evidence is the risk quotient analysis. As well, consideration is also given to chemical transformation, persistence, bioaccumulation, potential for toxicity, nature of potential effects, nature and extent of sources and fate in the environment for both triclosan and, to a lesser extent, its transformation products.

In Canada, triclosan is used in many consumer products that will end up in wastewater. A portion of triclosan will be removed from wastewater before being released to surface water as an effluent. During the wastewater treatment process, a fraction of triclosan partitions to sludge; the sludge may eventually be spread on land, hence potentially releasing triclosan to the terrestrial environment. A portion may also be methylated during wastewater treatment to form methyl-triclosan.

When in surface water, triclosan is either ionized or protonated (neutral form), depending on the ambient pH. The ionized form is rapidly photodegraded (within hours) if exposed to sunlight. Potential transformation products include 2,4-DCP and 2,7/2,8-DCDD. Triclosan’s half-life in aquatic aerobic water–sediment systems was 40–56 days (total system). Thus, triclosan is not anticipated to persist in water. However, its continual input to surface water through WWTP effluents is likely to result in its continuous presence in receiving aquatic ecosystems. There are empirical test data indicating that triclosan is bioaccumulative and highly toxic to aquatic organisms.

Even though monitoring data were available mainly for Ontario, the widespread use of triclosan across the country strongly suggests that this compound is currently ubiquitous in water bodies located near populated areas and can reach concentrations in water that exceed chronic toxicity thresholds for aquatic organisms, particularly macrophytes and algae. For example, the risk quotients calculated for an extensive nationwide exposure scenario indicate that 12% of the discharge points across Canada that receive wastewater are potentially at risk with respect to triclosan. The highest risk quotient calculated for these sites was 14, while the 95th percentile of all risk quotients was 1.76. The risk quotient obtained for the worst site monitored so far in Canada, a site located on the Thames River in Ontario, was 6. Even though some of the most sensitive organisms (macrophytes and algae) can recover quickly from a decrease in growth, such a recovery can be compromised if exposure to triclosan is continuous. Triclosan has been shown to have endocrine disruption effects in amphibians at environmentally realistic concentrations. Such types of effects are not captured in the risk quotient analysis. Endocrine disruption effects were also noted in fish and mammals at very high concentrations that may not be environmentally relevant. In addition, shifts in algal community structure were observed at triclosan concentrations in the order of 15 ng/L (Wilson et al. 2003)—i.e., below the concentrations measured in many water bodies in Canada (Table 21).
The results of the Multispecies Model indicate that triclosan will partition to sediments when released to the water compartment. Although triclosan may degrade slowly in buried anaerobic sediment, its estimated aerobic degradation half-life values of less than 365 days in sediment indicate that triclosan should not persist in sediments. The only toxicity data available for benthic organisms indicate that triclosan has a low toxicity (NOEC \( \geq 100 \text{ mg/kg dw} \) for chironomids).

The main route of entry of triclosan into soil is through the spreading of wastewater sludge. Experimental evidence shows that triclosan is not persistent in aerobic soil (half-life < 182 days). The input of triclosan to soil will in some cases be indirectly limited through existing provincial regulations on sludge application. Triclosan does not seem to bioaccumulate to a great extent in terrestrial organisms based on BCF/BAF values of 2.5–27 measured for earthworms and soybean plants. BAF values modelled for earthworms and shrews using BASL4 were approximately 1000 and approximately 30, respectively. The model results indicated that triclosan concentrations would increase from soil to earthworms, but would then decrease from earthworms to shrews. Risk quotients of less than 2.2 and less than 3.9 were calculated for terrestrial organisms based on existing regulated application rates for biosolids in Canada, on concentrations of triclosan in biosolids in Canada, on measured half-lives in soil under laboratory conditions or on estimated half-lives under field conditions, as well as on effects data for the most sensitive organism (cucumber) for which experimental data are available.

In order to characterize the land area potentially affected by triclosan, the number of tonnes of biosolids generated per year in Canada (388 700 dry tonnes) was multiplied by the estimated proportion of sludge applied to land (43%), based on data from the end of the 1990s (Apedaile 2001). Considering the maximum application rate allowed in Canada for application of biosolids to land (8.3 dry tonnes/ha per year; Environment Canada 2006), the resulting area is 201 km\(^2\). Only the fraction of this area that would be amended with highly contaminated sludge (triclosan concentration close to or higher than 46 \( \mu \text{g/g dw sludge} \)) could be at risk shortly after sludge application. Although a greater area could receive sludge amendment if maximal application rates were not reached, this would translate into lower PEC values and, therefore, lower risks. However, it should be noted that some provinces do not have restrictions on the application rate and/or frequency of land application of biosolids. Also, there are existing guidelines and standards for the concentration in biosolids of certain metals and organic chemicals, but not for triclosan (CCME 2010b).

Triclosan reaching small water bodies through runoff following broadcast application of biosolids to soil could, however, be of concern. Indeed, as mentioned previously in this report, triclosan concentrations up to 258 ng/L have been measured in runoff 1 day after biosolids application. Given the aquatic PNEC of 115 ng/L for triclosan, organisms living in water bodies that have a low dilution capacity (e.g., below 2) could be at risk.

Triclosan is a precursor of 2,7/2,8-DCDD. PCDDs have been found to be both persistent and bioaccumulative and to be harmful to the environment and human health as defined under paragraphs 11(a) and 11(c) of CEPA 1988 (Canada 1990). However, given their probable
transient state in aerobic environments and their low toxicity, 2,7/2,8-DCDD are not likely to be of environmental concern. Other PCDDs that are present in sediments as a result of triclosan transformation (e.g., 1,2,8-TriCDD, 2,3,7-TriCDD and 1,2,3,8-TCDD; Buth et al. 2010) could be of concern, depending on their toxicity.

Another transformation product is methyl-triclosan. This substance is likely present in surface waters over wide areas associated with triclosan, since it is formed in WWTPs and since it is a transformation product of triclosan in water–sediment systems. In field studies where both triclosan and methyl-triclosan were measured, environmental levels were sometimes in the same range. For instance, concentrations of triclosan and methyl-triclosan ranged from less than the MDL to 178 ng/L and from 3 to 17 ng/L, respectively, in Wascana Creek in Saskatchewan (Waiser et al. 2011). Similarly, concentrations were 60–120 ng/L and 50–80 ng/L, respectively, in a creek in Texas (Coogan et al. 2007). Methyl-triclosan is bioaccumulative in aquatic organisms, with a reported BAF greater than 5000 in fish (Balmer et al. 2004). Also, in a field study in which both triclosan and methyl-triclosan were measured in fish muscles, the latter was found at concentrations 90 times higher than triclosan (Boehmer et al. 2004). Methyl-triclosan has a high toxicity to aquatic organisms, based on data available for two species. The risk quotient analysis presented in Section 4.6.1.1 suggests that methyl-triclosan in aquatic ecosystems does not reach levels that would be harmful to organisms. Methyl-triclosan seems to be persistent in wastewater sludge, likely as bound residues due to the high organic carbon content in sludge, and it also seems persistent in anaerobic sediments. Methyl-triclosan can reach soil through the application of wastewater treatment sludge to land. It appeared as a major transformation product in an aerobic soil biotransformation study. A risk quotient analysis could not be done for terrestrial ecosystems due to a lack of data on the toxicity of methyl-triclosan to terrestrial organisms.

Based on the available evidence, including continued release and presence in receiving water bodies, potential bioaccumulation in aquatic organisms, high inherent toxicity and possible endocrine disruption effects in aquatic organisms, potential risks identified for certain water bodies receiving WWTP effluents and land receiving WWTP sludge, and transformation into certain chemicals, triclosan is likely to cause ecological harm, particularly in aquatic ecosystems.

4.7 Uncertainties in the Evaluation of Ecological Risk

The risk assessment for triclosan in aquatic ecosystems was based on numerous measured concentrations in water as well as on several experimental chronic toxicity data, which provided sufficient confidence to identify potential risk to the aquatic environment. Measured environmental concentrations integrate simultaneous fate processes occurring in surface water and are thereby realistic. However, they often provide only a snapshot of concentrations in time and space. For instance, Price et al. (2010) showed that triclosan concentrations measured over a single month at one site in a river in England varied from 21 to 195 ng/L. This was mainly due to variations in river discharges.
Regarding risk to aquatic ecosystems, it is expected to be higher following overflow events. These events occur commonly when an influent cannot be processed through a WWTP because the volume of water exceeds the capacity of the plant (e.g., after a rainstorm). In such cases, the overflow (i.e., bulk influent) is directly released to the receiving watercourse. It is not possible to tell whether the monitoring data included in this assessment were taken from sites that received untreated or partially treated wastewater. In addition, this assessment of triclosan in the aquatic environment does not take into account the fact that effluents from WWTPs are complex mixtures of many substances. Chemical interactions between substances released to surface water may produce synergistic or antagonistic effects.

Two of the three available bioconcentration studies conducted with triclosan in fish had serious deficiencies and were attributed a low weight when concluding on the bioaccumulation potential of triclosan. The range of BCF values obtained for all three studies (2.7–8700) raises some uncertainty, though, regarding this parameter. Additional reliable studies could help address this uncertainty.

There is uncertainty regarding the risk of triclosan to benthic organisms, as only one study was available to assess its effects (chronic toxicity study with chironomids).

Compared with the aquatic portion of the risk assessment, the terrestrial portion of this assessment contains much more uncertainty. First, no environmental concentrations of triclosan in Canadian soils were available. The PEC for triclosan in soil was estimated based on the application of wastewater sludge on agricultural fields using assumptions with varying levels of conservatism regarding, among other factors, the application rate and the biodegradation half-life for triclosan under field conditions. In addition, there was limited information on chronic effects of triclosan on terrestrial organisms. The data available for the presumably most sensitive species, cucumber, were somewhat contradictory, with a study showing a no-effect value in the order of parts per billion of triclosan in soil, while other studies showed no effects at the parts per million level.

Due to a lack of data, there is uncertainty about the degradation products of triclosan. Methyltriclosan is formed in WWTPs and released from WWTPs to the receiving ecosystems. Except for three data points for concentrations in water, there has not been any report of levels of methyl-triclosan in the Canadian environment. There is experimental evidence that methyl-triclosan can bioaccumulate in aquatic organisms. Methyl-triclosan seems to have a high toxicity to aquatic organisms, although this is based on only two studies. Methyl-triclosan is a major transformation product in aerobic soil as a result of the degradation of triclosan. No toxicity data are available for this compound for terrestrial organisms. Given its potential widespread presence in the environment (i.e., water bodies receiving WWTP effluent and soil amended with biosolids), additional information on this compound would be required to better assess its potential impact on ecosystems.
4.8 Toxic Substances Management Policy Considerations

The TSMP\(^2\) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy: i.e., toxic as defined by CEPA 1999, present in the environment primarily as a result of human activity, persistent in air, soil, water and/or sediment, and bioaccumulative). Corresponding criteria for persistence and bioaccumulation are also set out in the Persistence and Bioaccumulation Regulations under CEPA 1999 (Canada 2000). During the review process, triclosan and its transformation products were assessed and evaluated against these criteria (see Appendix 4).

Based on existing information, the Government of Canada has concluded the following:

- The environmental release of triclosan and its transformation products is primarily a result of human activity.
- Triclosan is inherently toxic and, as such, it meets the criteria for toxicity equivalence as defined by CEPA 1999. It also meets the bioaccumulation criteria, but does not meet the persistence criteria; thus, it is not considered a Track 1 substance.
- Methyl-triclosan is inherently toxic and, as such, it meets the criteria for toxicity equivalence as defined by CEPA 1999. It also meets the bioaccumulation criteria; however, preliminary assessment indicates that the persistence criteria in soil and air are not met. Data were not available to calculate half-lives in aquatic systems.
  - Methyl-triclosan, a major environmental transformation product, is produced by the addition of a methyl group to triclosan in soil and aquatic systems as well as during wastewater treatment.
  - Cleavage of the methyl group releases triclosan back into the environment. Methyl-triclosan is a transformation product, but should not be considered a degradation product of triclosan.
  - The aerobic soil biotransformation study indicates that the estimated soil half-lives for triclosan and methyl-triclosan are below the criterion cut-off value for persistence. There is some evidence, however, that the application of biosolids increases the persistence of these substances.
  - Half-lives in aquatic systems could not be estimated. The fate of methyl-triclosan was not assessed in the aquatic aerobic biotransformation study conducted with triclosan. Since methyl-triclosan is widely distributed in the environment and municipal effluents behave as continuous sources, estimating aquatic half-lives for methyl-triclosan from field data may not be possible.
  - There is evidence of the bioaccumulation of methyl-triclosan in aquatic organisms. A field monitoring study in fish showed residues 90 times higher than those for triclosan. A second field monitoring study reported fish BAFs greater than 5000.

\(^2\) The federal TSMP is available through Environment Canada’s website at [www.ec.gc.ca/toxiques-toxics/default.asp?lang=En\&n=2A55771E-1]
Methyl-triclosan is considered inherently toxic to the environment despite showing lower acute toxicity to daphnia and algae because of the following:

- There is a potential for long-term exposure due to the continuous environmental loading from municipal effluent.
- There is no information with which to evaluate chronic toxicity.
- Bioaccumulation has been observed under field conditions.
- Biologically active triclosan is released back into the environment when the methyl group is cleaved from the methyl-triclosan molecule.

- 2,7/2,8-DCDD are lower chlorinated dioxins produced when triclosan is exposed to sunlight in water. They are not likely to be of environmental concern, since they are transient (not persistent) and are less harmful to the environment than other dioxins, such as the tetrachlorinated congeners (e.g., 2,3,7,8-TCDD).
5. Proposed Conclusions

5.1 Proposed Conclusions under CEPA 1999

Based upon the adequacy of the MOEs between estimates of aggregated exposure to triclosan and critical effect levels, it is proposed that triclosan is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

Based on the information presented in this preliminary assessment, it is proposed that triclosan is entering or may enter the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity. Therefore, it is proposed that triclosan meets the criterion as set out under paragraph 64(a) of CEPA 1999. It is also proposed that triclosan meets the criterion for bioaccumulation but not the criteria for persistence as set out in the Persistence and Bioaccumulation Regulations (Canada 2000).

5.2 Proposed Conclusions under PCPA

Based on the preliminary risk assessment, PMRA proposes to conclude that the use of pest control products containing triclosan in Canada does not pose an unacceptable risk to human health. While use of these products may contribute to environmental exposure to triclosan, given the registered uses and the life cycle of triclosan-treated products (e.g., treated plastics, textiles, leather, paper and rubber), pest control products are not expected to contribute significantly to the risks to aquatic organisms identified in the preliminary assessment. Therefore, PMRA proposes to conclude that the use of pest control products containing triclosan does not pose an unacceptable risk to the environment. No further risk mitigation measures will be required at this time, as the current registrant of triclosan has chosen not to maintain its Canadian registration. Should a registrant seek to re-enter the Canadian market, further data may be required to supplement the current risk assessment.
References


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Preliminary Assessment: Triclosan (March 2012)


List of Abbreviations

ACGIH  American Conference of Governmental Industrial Hygienists
ADI   acceptable daily intake
a.i.   active ingredient
AUC   area under the plasma concentration versus time curve
BAF   bioaccumulation factor
BASL4 Biosolids-Amended Soil Level 4
BCF   bioconcentration factor
BMDL lower 95% confidence limit on the benchmark dose
bw    body weight
CAF   composite assessment factor
CAR   constitutive androstane receptor
CAS   Chemical Abstracts Service
CEPA  Canadian Environmental Protection Act
CMA   Chemical Manufacturers’ Association
C\(_{\text{max}}\) maximum concentration in plasma
CTV   critical toxicity value
CYP   cytochrome P450
DCDD dichlorodibenzo-p-dioxin
DCP   dichlorophenol
DNA   deoxyribonucleic acid
DNT   developmental neurotoxicity
DSL   Domestic Substances List
DT\(_{50}\) median dissipation time
dw    dry weight
EC    effective concentration
EU    European Union
FIFRA Federal Insecticide, Fungicide, and Rodenticide Act
GUS   groundwater ubiquity score
HC\(_{5}\) hazardous concentration to 5% of species
HPV   high production volume
IC    inhibitory concentration
IUPAC International Union of Pure and Applied Chemistry
\(K_d\) soil/water partition coefficient
\(K_{oa}\) octanol/air partition coefficient
\(K_{oc}\) organic carbon partition coefficient
\(K_{ow}\) \(n\)-octanol/water partition coefficient
LC\(_{50}\) median lethal concentration
LD\(_{50}\) median lethal dose
LOAEL lowest-observed-adverse-effect level
LOD   limit of detection
LOEC  lowest-observed-effect concentration
LOEL  lowest-observed-effect level
LOQ   limit of quantification
MATC  maximum allowable toxicant concentration
MDL   method detection limit
MITI  Ministry of International Trade and Industry (Japan)
MOA   mode of action
MOE   margin of exposure
MQL   method quantification limit
NHANES National Health and Nutrition Examination Survey (United States)
NICNAS National Industrial Chemicals Notification and Assessment Scheme (Australia)
NITE  National Institute of Technology and Evaluation (Japan)
NOAEL no-observed-adverse-effect level
NOEC  no-observed-effect concentration
NOEL  no-observed-effect level
OECD  Organisation for Economic Co-operation and Development
OSHA  Occupational Safety and Health Administration (United States)
P4    Plastic and Personal-Care Product Use in Pregnancy
PCDD polychlorinated dibenzodioxin
PCDF polychlorinated dibenzofuran
PCPA  *Pest Control Products Act*
PEC   predicted environmental concentration
PEL   permissible exposure level
pK<sub>a</sub> −log<sub>10</sub> acid dissociation constant
PMRA  Pest Management Regulatory Agency
PND   postnatal day
PNEC  predicted no-effects concentration
PPAR  peroxisome proliferator-activated receptor
ppb   parts per billion
ppm   parts per million
PXR   pregnane X receptor
QSAR  quantitative structure–activity relationship
RED   Reregistration Eligibility Decision
RN    registry number
RNA   ribonucleic acid
SCCP  Scientific Committee on Consumer Products
SCCS  Scientific Committee on Consumer Safety
SIDS  Screening Information Data Set
SCENIHR Scientific Committee on Emerging and Newly Identified Health Risks
SSD   species sensitivity distribution
<sub>½</sub>  half-life
T<sub>3</sub>  triiodothyronine
T<sub>4</sub>  thyroxine
TCDD  tetrachlorodibenzo-<i>p</i>-dioxin
TLV   threshold limit value
TR    thyroid receptor
TriCDD  trichlorodibenzo-<i>p</i>-dioxin
Appendix 1: Triclosan Products Registered under the Pest Control Products Act

<table>
<thead>
<tr>
<th>Registration number</th>
<th>Marketing class</th>
<th>Registrant</th>
<th>Product name</th>
<th>Formulation type</th>
<th>Guarantee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12895</td>
<td>Commercial</td>
<td>Thomson Research Associates</td>
<td>Ultra-Fresh 300DD Non-ionic Liquid Germistat</td>
<td>Emulsifiable concentrate</td>
<td>1.6</td>
</tr>
<tr>
<td>13615</td>
<td>Commercial</td>
<td>Sanitized Inc.</td>
<td>Sanitized Brand Bacteriostat S-2 Liquid</td>
<td>Emulsifiable concentrate</td>
<td>2</td>
</tr>
<tr>
<td>13981</td>
<td>Commercial</td>
<td>Sanitized Inc.</td>
<td>Sanitized Brand Bacteriostat T 96-21 Liquid</td>
<td>Emulsifiable concentrate</td>
<td>10</td>
</tr>
<tr>
<td>14234</td>
<td>Commercial</td>
<td>Sanitized Inc.</td>
<td>Sanitized Brand Bacteriostat SN Liquid</td>
<td>Emulsifiable concentrate</td>
<td>25</td>
</tr>
<tr>
<td>14278</td>
<td>Commercial</td>
<td>Thomson Research Associates</td>
<td>Ultra-fresh NM Germistat</td>
<td>Emulsifiable concentrate</td>
<td>3</td>
</tr>
<tr>
<td>28553</td>
<td>Technical</td>
<td>Ciba Canada Inc.</td>
<td>Irgasan DP-300R Technical</td>
<td>Powder</td>
<td>99</td>
</tr>
</tbody>
</table>
## Appendix 2: Toxicological Endpoints for Triclosan Health Risk Assessments

<table>
<thead>
<tr>
<th>Exposure scenario</th>
<th>Dose (mg/kg bw per day)</th>
<th>Study</th>
<th>Toxicological effects</th>
<th>Database UF</th>
<th>PCPA factor</th>
<th>CAF or target MOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADI / aggregate All populations</td>
<td>NOAEL = 25 ADI = 0.08</td>
<td>90-day toxicity study in mice</td>
<td>Increased liver weights and liver pathology, decrease in hematology parameters (red blood cells, hemoglobin and hematocrit) and cholesterol at 75 mg/kg bw per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-term incidental oral (direct exposure of children)</td>
<td>NOAEL = 25</td>
<td>As per ADI (above)</td>
<td>As above</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal (all durations)</td>
<td>NOAEL = 40</td>
<td>90-day dermal toxicity study in rats</td>
<td>Based on increased incidence of occult blood in the urine, minor decrease in hematology parameters (red blood cells, hemoglobin, hematocrit), decrease in triglyceride (males) and cholesterol levels (males and females) and a slight focal degeneration of cortical tubules in males at 80 mg/kg bw per day</td>
<td></td>
<td></td>
<td>3 (lack of DNT study)</td>
</tr>
<tr>
<td>Acute, short-term, intermediate-term and long-term inhalation</td>
<td>NOAEL = 3.21</td>
<td>21-day inhalation toxicity study in rats</td>
<td>Based on decreased thrombocytes and total serum proteins, increased alkaline phosphatase in male rats at 3.21 mg/kg bw per day</td>
<td></td>
<td></td>
<td>1 300^1</td>
</tr>
</tbody>
</table>

Abbreviations used: ADI, acceptable daily intake; CAF, composite assessment factor; DNT, developmental neurotoxicity; NOAEL, no-observed-adverse-effect level; PCPA, Pest Control Products Act; target MOE, target margin of exposure for occupational and residential assessments; UF, uncertainty factor

^1 CAF/target MOE of 300 based on the application of a 10-fold uncertainty factor to account for interspecies extrapolation and a 10-fold uncertainty factor for intraspecies variation, as well as a 3-fold database deficiency factor (for lack of a DNT study). The PCPA factor was reduced to 1-fold, since uncertainties...
with respect to the completeness of the data were accounted for through application of the database deficiency factor, and there was a low level of concern for prenatal and postnatal toxicity given the endpoints and uncertainty factors selected for risk assessment.
Appendix 3: Infant Urine Volumes

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Sample size</th>
<th>Value reported in reference</th>
<th>Mean 24 h urine volume (mL/day)</th>
<th>Mean 24 h urine volume per body weight (mL/kg bw per day)¹</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants less than 1 week old</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Not specified</td>
<td>17 mL/day</td>
<td>17</td>
<td>5.1</td>
<td>Ingelfinger 1991</td>
</tr>
<tr>
<td>1</td>
<td>Not specified</td>
<td>15–60 mL/24 h</td>
<td>15–60</td>
<td>4.5–17.9</td>
<td>Walker 2011</td>
</tr>
<tr>
<td>1</td>
<td>Not specified</td>
<td>20 mL/kg bw per day</td>
<td>67</td>
<td>20</td>
<td>Aggarwal et al. [date not specified]</td>
</tr>
<tr>
<td>1</td>
<td>Not specified</td>
<td>17 mL/day</td>
<td>17</td>
<td>5.1</td>
<td>Aas 1961</td>
</tr>
<tr>
<td>0–2</td>
<td>Not specified</td>
<td>20 mL/day</td>
<td>20</td>
<td>6</td>
<td>Water UK 2006</td>
</tr>
<tr>
<td>1–2</td>
<td>Not specified</td>
<td>30–60 mL/day</td>
<td>30–60</td>
<td>9.0–17.9</td>
<td>Wu 2006</td>
</tr>
<tr>
<td>7</td>
<td>Not specified</td>
<td>34 mL/day</td>
<td>34</td>
<td>10.1</td>
<td>Ingelfinger 1991</td>
</tr>
<tr>
<td>7</td>
<td>Not specified</td>
<td>34 mL/day</td>
<td>34</td>
<td>10.1</td>
<td>Aas 1961</td>
</tr>
<tr>
<td>Range of values</td>
<td></td>
<td>15–60 mL/day</td>
<td>4.5–20 mL/kg bw per day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infants 2–12 weeks old</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>Not specified</td>
<td>200 mL/day</td>
<td>200</td>
<td>33.8</td>
<td>Water UK 2006</td>
</tr>
<tr>
<td>2 weeks</td>
<td>Not specified</td>
<td>250–400 mL/24 h</td>
<td>250–400</td>
<td>42.0–67.2</td>
<td>Walker 2011</td>
</tr>
<tr>
<td>6 weeks, breastfed</td>
<td>10</td>
<td>0.45–0.61 L/day</td>
<td>530</td>
<td>89.1</td>
<td>Prentice 1987</td>
</tr>
<tr>
<td>6 weeks, formula fed</td>
<td>10</td>
<td>0.37–0.83 L/day</td>
<td>550</td>
<td>92.4</td>
<td>Prentice 1987</td>
</tr>
<tr>
<td>10–60 days</td>
<td>Not specified</td>
<td>250–450 mL/day</td>
<td>250–450</td>
<td>42–75.6</td>
<td>Wu 2006</td>
</tr>
<tr>
<td>8 weeks</td>
<td>Not specified</td>
<td>250–400 mL/24 h</td>
<td>250–400</td>
<td>42.0–67.2</td>
<td>Walker 2011</td>
</tr>
<tr>
<td>12 weeks, breastfed</td>
<td>12</td>
<td>0.42–0.70 L/day</td>
<td>530</td>
<td>89.1</td>
<td>Prentice 1987</td>
</tr>
<tr>
<td>12 weeks,</td>
<td>12</td>
<td>0.38–0.81 L/day</td>
<td>580</td>
<td>97.5</td>
<td>Prentice 1987</td>
</tr>
<tr>
<td>Age (days)</td>
<td>Sample size</td>
<td>Value reported in reference</td>
<td>Mean 24 h urine volume (mL/day)</td>
<td>Mean 24 h urine volume per body weight (mL/kg bw per day)(^1)</td>
<td>Reference</td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>-----------------------------</td>
<td>-------------------------------</td>
<td>------------------------------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>formula fed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>Not specified</td>
<td>300 mL/day</td>
<td>300</td>
<td>50.4</td>
<td>Water UK 2006</td>
</tr>
<tr>
<td></td>
<td>Range of values</td>
<td>200–580 mL/day</td>
<td>33.8–97.5 mL/kg bw per day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Assumed body weights of 3.35 kg for infants 1–7 days old and 5.95 kg for infants 2–12 weeks old (Kuczmarski et al. 2002) to convert the mL/day values to mL/kg bw per day.
### Appendix 4: Toxic Substances Management Policy Considerations for Pest Control Products—Comparison with TSMP Track 1 Criteria

<table>
<thead>
<tr>
<th>TSMP Track 1 criteria</th>
<th>TSMP Track 1 criterion value</th>
<th>Triclosan</th>
<th>Methyl-triclosan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistence¹</td>
<td></td>
<td>2.9–3.8 days(^{2,3}) (20°C) 10.7 days (10°C) 13–58 days</td>
<td>39–159 days(^{2,7}) (20°C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>There is some uncertainty given that the system was dosed with triclosan (not methyl-triclosan) and there was a significant amount of uncharacterized bound residues (61–70%).</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Formation was observed in aquatic biotransformation study, in other laboratory studies in the published literature and under field conditions. No half-life estimates are available.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Field information indicates that in some areas, concentrations appear to be increasing over time. No half-life estimates are available.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not expected to be volatile Long-range atmospheric transport is unlikely</td>
<td>Not expected to be volatile Long-range atmospheric transport is unlikely</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18–70% degradation over 21–91 days(^5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other values were not deemed to be relevant due to the high concentrations tested. These were much higher than environmentally relevant concentrations and caused bacterial toxicity.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Concentrations of methyl-triclosan were much higher than those of triclosan at the same sample sites. Concentrations appear to be increasing over time.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>900–2100 (algae) 16–90 (carp) (\text{2532–8700}) (zebrafish)</td>
<td>No information</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 (snail)</td>
<td>400–1500 (algae) 1200 (snail)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4–101 (aquatic plants)</td>
<td></td>
</tr>
</tbody>
</table>

\(\text{Log } K_{\text{ow}} \geq 5\) 4.76 4.8–5.2

\(\text{BCF} \geq 5000\) 16–90 (carp) \(\text{2532–8700}\) (zebrafish) No information

\(\text{BAF} \geq 5000\) 500 (snail) | 400–1500 (algae) 1200 (snail)
**Preliminary Assessment: Triclosan (March 2012)**

<table>
<thead>
<tr>
<th>TSMP Track 1 criteria</th>
<th>TSMP Track 1 criterion value</th>
<th>Triclosan</th>
<th>Methyl-triclosan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No BAFs reported for fish</td>
<td>2000–5200 (fish)</td>
</tr>
<tr>
<td>Additional field information</td>
<td>Triclosan was observed in bile, blood plasma and muscle of fish under field conditions. No analysis of whole fish and/or lipid concentrations reported.</td>
<td>Fish muscle analyzed from lakes receiving WWTP effluent had 90 times higher residues of methyl-triclosan than triclosan (Boehmer et al. 2004).</td>
<td>Accumulation of methyl-triclosan in aquatic species including fish under field conditions observed (Miyazaki et al. 1984; Balmer et al. 2004; Leiker et al. 2009)</td>
</tr>
<tr>
<td>Terrestrial bioaccumulation</td>
<td>Mammals</td>
<td>Triclosan is extensively metabolized via glucuronide and sulfate conjugation. No evidence of bioaccumulation potential, although there may be retention of triclosan and/or its metabolites in the liver.</td>
<td>No information</td>
</tr>
<tr>
<td>Plants</td>
<td>BAF: 2.5–5.9</td>
<td>No information</td>
<td></td>
</tr>
<tr>
<td>Toxic or toxic equivalent as defined by CEPA 1999⁴</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Predominantly anthropogenic⁵</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Is the chemical a TSMP Track 1 substance (all four criteria must be met)?</td>
<td>Meets the bioaccumulation criterion based on a BCF exceeding 5000. Does not meet the persistence criteria.</td>
<td>Meets the TSMP Track 1 criteria for bioaccumulation based on a field BAF exceeding 5000. A preliminary assessment indicates that it does not meet the persistence criteria.</td>
<td></td>
</tr>
</tbody>
</table>

1 Assumption made under the PCPA: If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one medium (soil, water, sediment or air), then the criterion for persistence is considered to be met.
2 Radiolabelled study.
3 Standard protocol.
4 All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (i.e., all other TSMP criteria are met).
5 The policy considers a substance “predominantly anthropogenic” if, based on expert judgement, its concentration in a specific environmental medium is largely due to human activity, rather than to natural sources or releases.
6 Field data (e.g., BAFs) are preferred over laboratory data (e.g., BCFs), which, in turn, are preferred over chemical properties (e.g., log $K_{ow}$).

Bolded values indicate criteria are met or exceeded.