

**TAB 12 FDA Reviewer's Literature Summary Regarding Potential
Environmental Hazards of Biocides**



CONSUMER ANTISEPTIC DRUG PRODUCTS REVIEW

Office of Nonprescription Products (HFD-560)
Center for Drug Evaluation and Research • Food and Drug Administration

REVIEW DATE: August 22, 2005

FDA DOCKET NO.: 75N-0183H

PHARMACOLOGIC CATEGORY: Consumer Antiseptic Drug Products

REVIEWER: Colleen Kane Rogers, Ph.D.

I. Purpose

This review provides a general overview of the literature relating to potential environmental hazards of the active ingredients used in consumer antiseptics. A PubMed literature search was performed using combinations of the following search terms: “benzalkonium,” “benzethonium,” “chloroxylenol OR PCMX,” “trichlorocarbanilide,” “triclocarban,” or “triclosan,” with “algae,” “environment,” “fish,” “soil,” or “water.” Pertinent references from the bibliographies of key articles also were included. The following overview is limited to articles written in English and published prior to July 2005, with an emphasis on articles published since 2000. Furthermore, please note that only a subset of environmental journals is represented in the PubMed database.

II. Overview and Summary

Previously unrecognized environmental pollutants are now being discovered due to more vigilant monitoring and improved analytical detection techniques. Pharmaceuticals and personal care products (PPCPs) comprise one broad class of these environmental pollutants. PPCPs include a wide range of chemicals from products such as prescription and nonprescription drugs, fragrances, sunscreens, detergents, and toothpastes. One reason for concern is that these chemicals are not completely removed during wastewater treatment. As a result, humans may be exposed to minute quantities of these chemicals via alternate routes of exposure, with unknown consequences. Other potential concerns from the environmental presence of these compounds include abnormal physiology or reproductive impairment in

aquatic organisms, increased incidence of cancer, the development of antibiotic-resistant bacteria, and the potential increased toxicity of chemical mixtures.⁷

While FDA does not monitor or regulate biocides in the environment, we felt it was important to consider this issue as a potential hazard resulting from the use of consumer antiseptics. FDA is required under the National Environmental Policy Act of 1969 (NEPA) to consider the environmental impacts of approving new drug and biologics applications as an integral part of its regulatory process. For these environmental assessments, FDA considers harm to the environment to include not only toxicity to environmental organisms but also environmental effects other than toxicity, such as lasting effects on ecological community dynamics. In contrast, environmental assessments are not usually considered as part of the over-the-counter drug review.

Most antiseptic products are disposed of down residential drains, where they undergo treatment by local wastewater treatment plants (WWTPs). During wastewater treatment, many of the chemicals, including biocides, are removed, but some chemicals still reach surface waters (e.g., rivers and lakes). The efficiency with which WWTPs remove contaminants depends upon the particular chemical and also on the technology used (e.g., physical, biologic). However, no municipal sewage treatment plants are engineered to remove PPCPs.⁷

By far the most information we found pertained to the occurrence and fate of triclosan in the environment. Much of the information about the presence of triclosan in surface waters comes from Europe, although recent studies have examined rivers and streams in the US. Overall, these studies suggest that many organic contaminants, including triclosan, survive wastewater treatment and biodegradation, and can be detected at low levels in the environment, particularly in surface waters and sediment.

Despite continual introduction of triclosan into water sources, researchers have identified a number of mechanisms for its removal. Some of the triclosan leaves surface waters and WWTP influent via sedimentation. In addition, several investigators have shown that triclosan in surface waters can be degraded in the presence of sunlight. However, this photodegradation can result in harmful products, such as dioxin. The calculated half-life of triclosan exposed to sunlight ranged from less than an hour to 2000 days, depending on the latitude and time of year. On the other hand, triclosan does not have to have a long half-life to persist in the environment; constant introduction into surface waters would have the same effect as persistence. Triclosan can also undergo other transformation processes, such as methylation. But, the fate and effect of these environmental transformation products is largely unknown.

Finally, triclosan has some adverse effects on aquatic organisms. Triclosan appears to inhibit the growth of algae and reduce algal species diversity. This is notable because the biocide is affecting organisms at the bottom of the food chain, with unknown consequences on organisms higher up the chain. In higher organisms, triclosan appears to be toxic to early life-stages of fish, but does not appear to have an adverse effect on their reproductive

capabilities. However, triclosan induced behavioral changes in both tadpoles and fish that may affect their ability to evade predators or feed properly.

III. Literature Summary

A. Presence of Biocides in the Environment

Household, industrial, and commercial liquid waste is carried via sewers to a common treatment facility, known as a WWTP. Wastewater treatment frequently involves several steps to make the effluent fit to be received in the environment, including physical, chemical, or biological methods. Triclosan has been detected in WWTP influents at concentrations ranging from 62 to 21,900 ng/L.^{16, 17, 21, 22} The amount of triclosan, or other chemicals, that is removed from this influent depends upon the wastewater treatment method employed. Studies from both the US and Europe have shown that approximately 95% of the triclosan in wastewater is eliminated via the activated sludge mechanism of treatment.^{4, 24, 26} However, WWTPs that use other treatment mechanisms, for example trickling filter, are not as efficient at removing triclosan from wastewater (from 58 to 97%).^{4, 26} As a result of incomplete removal, a percentage of the triclosan entering WWTPs leaves through plant effluent and is introduced into the environment via receiving waters.

Triclosan has been measured in WWTP effluents and, perhaps not surprisingly, concentrations were higher in these effluents than in surface waters. Triclosan was detected at 160 to 480 ng/L in WWTP effluents in Norway.²⁸ Similarly, triclosan was detected at 10 to 600 ng/L in Germany,⁴ and at 42 to 213 ng/L in WWTP effluents in Switzerland.²⁴ In the US, triclosan concentrations in WWTP effluents ranged from 200 to 2700 ng/L.¹⁷ In contrast, a study conducted in Louisiana found triclosan in WWTP effluent at concentrations of only 10 to 21 ng/L.⁶ Furthermore, triclosan was not detected in Mississippi River water or in drinking water purification plant samples from Louisiana or Ontario, Canada.

PPCPs in WWTP effluents are diluted once the effluent mixes with surface waters. Despite this, PPCPs can still be detected from a variety of water sources. Triclosan has been detected in various bodies of water throughout Europe. Samples from Germany demonstrated a maximum triclosan concentration of 10 ng/L in Ruhr River water, which receives WWTP effluent and also serves as a source for drinking water purification plants.⁴ Swiss rivers receiving WWTP effluent were found to have between 11 and 98 ng/L triclosan²⁴, and triclosan was detected in concentrations up to 74 ng/L in several lakes and a river in another Swiss study.¹⁶ In contrast, triclosan was below the limit of detection (<0.4 ng/L) in a remote mountain lake that received no WWTP effluent.¹⁶

In Louisiana, investigators detected triclosan at a maximum of 3.1 ng/L in the Mississippi River and up to 14.9 ng/L in Lake Pontchartrain.⁵ In New Orleans, stormwater is diverted through drainage canals and discharged into the Mississippi River and Lake Pontchartrain. Interestingly, up to 29 ng/L triclosan was detected in these stormwater canals, which do not receive WWTP effluent. Detection of PPCPs was greater during rainfall, which was attributed to contamination of the canals with sewage from the aging sewer system.

Kolpin and colleagues from the US Geological Survey recently conducted the first nationwide reconnaissance of the occurrence of a broad range of organic wastewater contaminants in US water resources.¹³ Water samples from 139 streams in 30 states were sampled for the presence of 95 organic contaminants, including triclosan. The investigators chose streams that were considered susceptible to contamination from various wastewater sources, so the results are not representative of all streams. Of the 95 compounds analyzed, triclosan was the sixth-most-common chemical detected. Furthermore, triclosan was detected in nearly 60% of the samples analyzed, at a maximum concentration of 2300 ng/L.

Triclocarban (TCC), like triclosan, is a common antimicrobial ingredient in personal care products; however, the environmental fate of TCC is largely unknown. Halden and Paull developed methods to detect TCC in aquatic environments at the ng/L level.⁹ TCC was found in river water and wastewater at concentrations of up to 5600 and 6750 ng/L, respectively. Conversely, TCC was not detected in drinking water. In a subsequent study, both triclosan and TCC were detected in six urban streams in the greater Baltimore area.¹⁰ The results of this study suggest that TCC likely ranks in the top 10 in occurrence rate and in the top 20 in maximum concentration among the organic pollutants considered by Kolpin and colleagues.¹³ The authors note that contamination was not solely due to incomplete removal during wastewater treatment; the biocides may have been introduced into the streams due to sewage spills and leakage. The authors also note that the TCC concentrations found in this study (6750 ng/L) are markedly higher than the maximum TCC concentrations (≤ 240 ng/L) used by the EPA for evaluating the ecological and human health risks of this chemical.¹⁰

B. Breakdown/Removal of Biocides in the Environment

Despite continual introduction of triclosan into surface waters, some of the biocide is removed by mechanisms other than flushing or dilution. Triclosan may be removed from surface waters through absorption or adsorption (i.e., sorption) and transport into sediments, chemical or biological degradation, or photolysis.¹⁶

Several investigators have examined the role of pH and irradiation on the fate of triclosan. Lindström and colleagues exposed triclosan to natural sunlight in lake water at different pH values in the laboratory.¹⁶ Triclosan was rapidly degraded at pH 8.0, but not at pH 5.6; the half-life of triclosan was calculated to be less than 1 hour in August at 47° latitude. The authors conclude that triclosan is degraded by direct photolysis, and this reaction is pH-dependent. Furthermore, a dynamic lake model predicted a marked seasonal variation in triclosan concentration near the lake surface as a consequence of seasonally varying sunlight intensity.¹⁶

Tixier and others also demonstrated pH-dependent photolysis of triclosan in the laboratory.²⁷ Furthermore, based on computer modeling, these investigators found that direct phototransformation accounted for 80% of the total elimination of triclosan from a Swiss lake over a 3-month summer period. Daily average triclosan half-lives varied from 2 to 2000 days, depending on latitude and time of year. Furthermore, the presence of dissolved organic matter in the lake water led to approximately a 20% decrease in the phototransformation rate of triclosan due to light absorption from the organic matter.

Latch and colleagues also found that triclosan was rapidly degraded by direct photolysis at pH 8 in noon summer sunlight (45°N latitude), with a half-life of 5 hours.¹⁵ In addition, these investigators analyzed the photolysis products of triclosan. When Mississippi River water was spiked with triclosan and irradiated, triclosan was photodegraded to 2,8-dichlorodibenzo-*p*-dioxin (2,8-DCDD) and 2,4-dichlorophenol (2,4-DCP).^{14, 15} The dioxin yield (1-12%) varied based on pH and irradiation wavelength. Production of these photoproducts is a concern because chlorinated dioxins are known to be toxic and 2,4-DCP is an EPA priority pollutant. However, both 2,8-DCDD and 2,4-DCP were shown to be intermediate products and were further photodegraded.¹⁵ The authors conclude that triclosan likely is converted to dioxin in surface waters exposed to sunlight.

Rule and others found that triclosan readily reacts with free chlorine to form several deleterious products under pH conditions that are typically encountered in drinking water.²¹ Both chloroform and 2,4-DCP were produced, as well as several chlorinated triclosan intermediates. The authors also performed an experiment where they added plain or triclosan-containing dish soap (1.4 mg triclosan/g soap) to chlorinated water at a concentration of 0.25 g/L. Chloroform was detected at 15,000 ng/L after 5 minutes and 49,000 ng/L within 120 minutes from the triclosan-containing soap.²¹ In contrast, the plain soap had barely detectable chloroform levels. The authors conclude that the potential exists for substantial chloroform production to occur via daily household use of triclosan-containing products.

In addition to photolysis and biodegradation, triclosan can be removed from surface waters by sorption to organic particles and sedimentation.¹⁸ Triclosan was found to couple to dissolved organic matter in the presence of sunlight.¹⁵ Furthermore, an analysis of lake sediment revealed triclosan in increasing concentrations starting from the early 1970s.²⁴ The high amount of triclosan detected in the sediment suggests that it is degraded very slowly. Similarly, TCC may be sedimented and degrade slowly; TCC has a predicted half-life of 540 days in sediment.¹⁰

C. Presence of Biocides in Animals

Several investigators looked for triclosan accumulation in fish. A group from the Netherlands identified both triclosan (14-80 µg/mL) and chloroxylenol (PCMX; 0.1 µg/mL) in a screen of fish bile for estrogenic compounds.¹¹ In a series of laboratory studies, triclosan accumulated to a significantly lesser extent in fish than the organic pollutant chlordane.¹⁹ Lethal body burdens of triclosan ranged from 0.7 to 3.4 mM/kg in fish. The authors concluded that because the neutral form of triclosan was associated with the observed toxicity, ionization and sorption may mitigate some of these effects.

A Swedish study found that fish caged outside a WWTP for 3 weeks had 47 mg/kg triclosan in their bile, compared to 17 mg/kg for fish caged 2 km downstream from the plant.¹ Wild-living fish had as much as 4.4 mg/kg triclosan in their bile. Fish exposed to sewage water had a bile concentration as high as 120 mg/kg, which was reduced to 94 mg/kg when exposed to filtrated sewer water. In contrast, control fish has less than 0.08 mg/kg triclosan in their bile.

Finally, Balmer and colleagues found methyl triclosan, an environmental transformation product of triclosan, in fish from various lakes in Switzerland that receive input from WWTPs.³ Unlike triclosan, methyl triclosan is not photolyzed or is photolyzed very slowly, resulting in a higher bioaccumulation potential.¹⁶ Methyl triclosan was detected in fish up to 365 ng/g on a lipid basis, which results in a bioconcentration factor in the range of other persistent organic pollutants.³ Furthermore, the authors suggest that the main process responsible for the presence of methyl triclosan in the fish is direct uptake from the water through exposed surfaces (bioconcentration), rather than uptake through consumption (biomagnification).

Although investigators have looked for the presence of triclosan in fish, almost nothing is known about its presence in humans or other organisms. One study examined the levels of triclosan in human breast milk samples. High levels were found in three of five samples tested (60-300 µg/kg lipid weight).¹

D. Effects of Biocides on Aquatic Organisms

Given the widespread distribution of PCPPs in aquatic systems, there is a possibility that these chemicals may affect organisms that reside in this habitat. Several investigators have examined the effects of triclosan on algae, crustaceans, fish, and other aquatic organisms.

Effects on Algae

Algae are sensitive indicators of changes in the environment. Therefore, adverse effects on these organisms may be an early warning of future environmental problems.²³ Triclosan appears to inhibit algal growth and reduce species diversity. Since algae comprise the first step of the food chain, an effect on the algae may have a 'ripple effect' on organisms higher up the chain.

Orvos and colleagues studied the acute and chronic toxicity of triclosan against bacteria, algae, invertebrates, and fish in a series of laboratory studies.¹⁹ Unicellular algae, particularly green algae and a cyanobacterium, were the most triclosan-sensitive of all the organisms tested. Algal growth was inhibited when exposed to 3.4-13 µg/L triclosan for 4 days. However, when these organisms were moved to lower concentrations of triclosan, they resumed growth, suggesting that triclosan causes algal population stasis rather than death. Similarly, Tatarazako and others found that a species of green alga was 30- to 80-fold more sensitive to triclosan than the other species tested (bacteria and fish).²⁵ The median inhibitory concentration (IC₅₀) of triclosan for the algae was 4.7 µg/L. Likewise, a risk assessment model suggested that some very sensitive algal species could be affected by triclosan discharge into bodies of water with small dilution factors during low flow conditions.²⁰

Finally, bioassays performed by Wilson and colleagues suggest that triclosan may influence the structure and function of algal communities in water receiving WWTP effluents.²⁹ They found a significant reduction of two algal species at triclosan concentrations of 0.15-1.5 µg/L. Even triclosan concentrations as low as 0.015 µg/L reduced the genus richness. The authors conclude, "The loss of algal taxa even at low toxicant concentrations reaffirms

concerns expressed in the literature that subtle effects due to chronic, low level exposures to bioactive PPCPs could lead to cumulative, adverse impacts that might be incorrectly attributed to processes of natural change or ecological succession.²⁹

Effects on Fish and Other Organisms

Various organizations (e.g., ASTM, EPA, and International Organization for Standardization) have developed standard test methods for studying the adverse effects of chemicals on both freshwater and saltwater fishes. One of these methods is the early life-stage toxicity test.² The early life-stage toxicity test using zebrafish and medaka is considered to be a sensitive biosensor for mammalian teratogenicity.²⁵

An early life-stage toxicity study of triclosan in rainbow trout showed a lowest-observed-effect level of 71.3 µg/L.¹⁹ At this concentration, there was a significant decrease in the percentage of fry that survived at 35 or 61 days after hatching compared to controls. In contrast, there was no difference in fish length or weight. However, the triclosan-exposed fish showed loss of equilibrium, locking of the jaw, erratic swimming, spinal curvature, and quiescence. These effects could negatively affect fish survival and feeding behaviors. Furthermore, the median lethal concentration (LC₅₀) of triclosan for fathead minnows and bluegill sunfish was in the range of 260 to 440 µg/L.¹⁹

Ishibashi and coworkers investigated the effect of triclosan on the early life-stages and reproductive capability of fish (medaka).¹² The LC₅₀ for 24-hour-old larvae was 602 µg/L. Hatching was delayed for fertilized eggs that had been exposed to triclosan for 14 days, and hatchability was decreased. The authors conclude, “Embryonic development, hatching, and time to hatching for medaka eggs is affected by triclosan treatment.”

Another group found that a bacterium, crustacean, and two species of fish (medaka and zebrafish) had similar sensitivities to triclosan.²⁵ The medaka was the least sensitive of the tested organisms with a triclosan IC₅₀ of 400 µg/L. The IC₅₀ for both zebrafish and a crustacean (*Ceriodaphnia*) was 220 µg/L. The authors conclude that triclosan is highly toxic to aquatic animals. Conversely, a risk assessment model suggested that triclosan concentrations found in streams do not adversely affect fish.²⁰

Finally, Fraker and Smith examined the effects of triclosan on tadpoles.⁸ They demonstrated that ecologically relevant levels of some PPCPs can have both behavioral and physiological effects on tadpoles. Triclosan, at concentrations found in the environment (2.3 µg/L), lowered tadpole activity level. This lowered activity could affect the tadpole by decreasing its competitive ability in the wild. Furthermore, high concentrations of triclosan (230 µg/L) significantly reduced survival time.

References

1. Adolfsson-Erici M, Pettersson M, Parkkonen J, and Sturve J. Triclosan, a commonly used bactericide found in human milk and in the aquatic environment in Sweden. *Chemosphere*. 2002;46(9-10):1485-1489.
2. ASTM E1241-98. *Standard Guide for Conducting Early Life-Stage Toxicity Tests with Fishes*: ASTM International; 2004.
3. Balmer ME, Poiger T, Droz C, Romanin K, Bergqvist PA, Müller MD, and Buser HR. Occurrence of methyl triclosan, a transformation product of the bactericide triclosan, in fish from various lakes in Switzerland. *Environ Sci Technol*. 2004;38(2):390-395.
4. Bester K. Fate of triclosan and triclosan-methyl in sewage treatment plants and surface waters. *Arch Environ Contam Toxicol*. 2005;49(1):9-17.
5. Boyd GR, Palmeri JM, Zhang S, and Grimm DA. Pharmaceuticals and personal care products (PPCPs) and endocrine disrupting chemicals (EDCs) in stormwater canals and Bayou St. John in New Orleans, Louisiana, USA. *Sci Total Environ*. 2004;333(1-3):137-148.
6. Boyd GR, Reemtsma H, Grimm DA, and Mitra S. Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario, Canada. *Sci Total Environ*. 2003;311(1-3):135-149.
7. Daughton CG. Pharmaceuticals and Personal Care Products (PPCPs) as Environmental Pollutants. *US Environmental Protection Agency* [website]. Available at: <http://www.epa.gov/nerlesd1/chemistry/pharma/index.htm>. Accessed March 17, 2005.
8. Fraker SL and Smith GR. Direct and interactive effects of ecologically relevant concentrations of organic wastewater contaminants on *Rana pipiens* tadpoles. *Environ Toxicol*. 2004;19(3):250-256.
9. Halden RU and Paull DH. Analysis of triclocarban in aquatic samples by liquid chromatography electrospray ionization mass spectrometry. *Environ Sci Technol*. 2004;38(18):4849-4855.
10. Halden RU and Paull DH. Co-occurrence of triclocarban and triclosan in U.S. water resources. *Environ Sci Technol*. 2005;39(6):1420-1426.
11. Houtman CJ, Van Oostveen AM, Brouwer A, Lamoree MH, and Legler J. Identification of estrogenic compounds in fish bile using bioassay-directed fractionation. *Environ Sci Technol*. 2004;38(23):6415-6423.

12. Ishibashi H, Matsumura N, Hirano M, Matsuoka M, Shiratsuchi H, Ishibashi Y, Takao Y, and Arizono K. Effects of triclosan on the early life stages and reproduction of medaka *Oryzias latipes* and induction of hepatic vitellogenin. *Aquat Toxicol.* 2004;67(2):167-179.
13. Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, and Buxton HT. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999-2000: a national reconnaissance. *Environ Sci Technol.* 2002;36(6):1202-1211.
14. Latch DE, Packer JL, Arnold WA, and McNeill K. Photochemical conversion of triclosan to 2,8-dichlorodibenzo-*p*-dioxin in aqueous solution. *J Photochem Photobiol.* 2003;158:63-66.
15. Latch DE, Packer JL, Stender BL, VanOverbeke J, Arnold WA, and McNeill K. Aqueous photochemistry of triclosan: formation of 2,4-dichlorophenol, 2,8-dichlorodibenzo-*p*-dioxin, and oligomerization products. *Environ Toxicol Chem.* 2005;24(3):517-525.
16. Lindström A, Buerge IJ, Poiger T, Bergqvist PA, Müller MD, and Buser HR. Occurrence and environmental behavior of the bactericide triclosan and its methyl derivative in surface waters and in wastewater. *Environ Sci Technol.* 2002;36(11):2322-2329.
17. McAvoy DC, Schatowitz B, Jacob M, Hauk A, and Eckhoff WS. Measurement of triclosan in wastewater treatment systems. *Environ Toxicol Chem.* 2002;21(7):1323-1329.
18. Morrall D, McAvoy D, Schatowitz B, Inauen J, Jacob M, Hauk A, and Eckhoff W. A field study of triclosan loss rates in river water (Cibolo Creek, TX). *Chemosphere.* 2004;54(5):653-660.
19. Orvos DR, Versteeg DJ, Inauen J, Capdevielle M, Rothenstein A, and Cunningham V. Aquatic toxicity of triclosan. *Environ Toxicol Chem.* 2002;21(7):1338-1349.
20. Reiss R, Mackay N, Habig C, and Griffin J. An ecological risk assessment for triclosan in lotic systems following discharge from wastewater treatment plants in the United States. *Environ Toxicol Chem.* 2002;21(11):2483-2492.
21. Rule KL, Ebbett VR, and Vikesland PJ. Formation of chloroform and chlorinated organics by free-chlorine-mediated oxidation of triclosan. *Environ Sci Technol.* 2005;39(9):3176-3185.
22. Sabaliunas D, Webb SF, Hauk A, Jacob M, and Eckhoff WS. Environmental fate of Triclosan in the River Aire Basin, UK. *Water Res.* 2003;37(13):3145-3154.

23. Schipper O. Common household chemicals affect algae. *Environ Sci Technol.* 2003;37(9):162A-164A.
24. Singer H, Muller S, Tixier C, and Pillonel L. Triclosan: occurrence and fate of a widely used biocide in the aquatic environment: field measurements in wastewater treatment plants, surface waters, and lake sediments. *Environ Sci Technol.* 2002;36(23):4998-5004.
25. Tatarazako N, Ishibashi H, Teshima K, Kishi K, and Arizono K. Effects of triclosan on various aquatic organisms. *Environ Sci.* 2004;11(2):133-140.
26. Thompson A, Griffin P, Stuetz R, and Cartmell E. The fate and removal of triclosan during wastewater treatment. *Water Environ Res.* 2005;77(1):63-67.
27. Tixier C, Singer HP, Canonica S, and Müller SR. Phototransformation of triclosan in surface waters: a relevant elimination process for this widely used biocide--laboratory studies, field measurements, and modeling. *Environ Sci Technol.* 2002;36(16):3482-3489.
28. Weigel S, Berger U, Jensen E, Kallenborn R, Thoresen H, and Huhnerfuss H. Determination of selected pharmaceuticals and caffeine in sewage and seawater from Tromsø/Norway with emphasis on ibuprofen and its metabolites. *Chemosphere.* 2004;56(6):583-592.
29. Wilson BA, Smith VH, deNoyelles F, Jr., and Larive CK. Effects of three pharmaceutical and personal care products on natural freshwater algal assemblages. *Environ Sci Technol.* 2003;37(9):1713-1719.

Abbreviations and Acronyms

2,4-DCP	2,4-dichlorophenol
2,8-DCDD	2,8-dichlorodibenzo- <i>p</i> -dioxin
ASTM	American Society for Testing and Materials
EPA	Environmental Protection Agency
g	gram
IC ₅₀	median inhibitory concentration
kg	kilogram
km	kilometer
L	liter
LC ₅₀	median lethal concentration
μg	microgram
mg	milligram
mM	millimolar
ng	nanogram
PCMX	para-chloro-meta-xyleneol
PPCPs	pharmaceuticals and personal care products
TCC	triclocarban
WWTP	wastewater treatment plant