



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

OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC  
SUBSTANCES

MEMORANDUM

DATE: April 17, 2008

**SUBJECT: 5-Chloro-2-(2,4-dichlorophenoxy)phenol (Triclosan):** Risk Assessment for the Reregistration Eligibility Decision (RED) Document. Case No 2340.  
PC Code: **054901. DP Barcode: 373535**

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Attached is the Preliminary Risk Assessment for Triclosan for the purpose of issuing a Reregistration Eligibility (RED) Decision. The disciplinary science chapters and other supporting documents for the Triclosan RED are also included as attachments as follows:

Toxicology Science Chapter for the Reregistration Eligibility Decision Document, T. McMahon, July 2007

Triclosan: Occupational and Residential Exposure Assessment. From Timothy Leighton, Exposure/Risk Assessor, to Tim McMahon, Ph.D., July 2007.

Triclosan: Dietary Exposure Assessments for the Reregistration Eligibility Decision Memorandum. From Najm Shamim, Ph.D. Chemist, to Tim McMahon, Ph.D. Toxicologist April, 2007.

Product Chemistry Chapter for the Triclosan Reregistration Eligibility Decision (RED) Document. From Srinivas Gowda Microbiologist/Chemist, to Mark Hartman, Branch Chief, July 2007.

Environmental Fate Science Chapter for the Triclosan Reregistration Eligibility Decision Document. From Srinivas Gowda, Microbiologist/ Chemist, to Mark Hartman, Branch Chief, July 2007.

Ecological Hazard and Environmental Risk Assessment Chapter. From Genevieve Angle, Biologist, July 2007.

Epidemiology Assessment based on Incident Reports. From J. Chen, Ph.D. Toxicologist, to Tim McMahon, Ph.D. Toxicologist, July 2007.

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## 1.0 Executive Summary

Triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) is a chlorinated aromatic compound that has functional groups representative of both phenols and ethers. It is used as a synthetic broad-spectrum antimicrobial agent in the form of a white to off-white powder. It is practically insoluble in water but is soluble in most organic solvents. Only a small portion of the uses of triclosan are regulated by the U.S. EPA and therefore covered in this document.

Triclosan is used as a bacteriostat, fungistat, mildewistat, and deodorizer. The EPA registered products containing triclosan as the active ingredient (ai) are formulated as ready-to-use, pelleted/tableted, emulsifiable concentrate, soluble concentrate, and impregnated materials. Concentrations of triclosan in these products range widely from 0.69% to >99%. Use sites for triclosan include commercial, institutional and industrial premises and equipment, residential and public access premises, and as a material preservative. As a material preservative, triclosan is used in adhesives, fabrics, vinyl, latex, plastics, polyethylene, polyurethane, synthetic polymers, styrene, floor wax emulsions, rope, textiles, caulking compounds, sealants, coatings, polypropylene, rubber, inks, cellulosic materials, slurries, films and latex paints. The residential and public access premises uses include: brooms, mulch, floors, shower curtains, awnings, tents, mattresses, toothbrushes, toilet bowls, urinals, garbage cans, refuse container liners, insulation, concrete mixtures, grouts, air filter materials, upholstery fabrics, and rugs/carpets. The commercial, institutional and industrial premises and equipment uses include: conveyor belts, fire hoses, dye bath vats and ice making equipment.

There are many other uses under the regulation of the US Food and Drug Administration (FDA) (e.g., hand soaps, toothpaste, antiseptics for wound care, and medical devices) that are not under EPA's regulatory jurisdiction, however, these exposures have been considered in the aggregate risk assessment using population-based biological monitoring data to assess the co-occurrence of uses to develop an aggregate exposure assessment.

### **Toxicology**

The toxicology database for triclosan is complete. Some studies, although cited with certain deficiencies, were considered adequate for regulatory purposes, and thus no new toxicology studies are requested for triclosan. A complete toxicology profile for triclosan can be found in the toxicology chapter .

Acute toxicity studies in experimental animals with technical grade triclosan show that by the oral and dermal routes, triclosan is of low acute toxicity (Toxicity Category IV; MRIDs 43206501 and 94044; 44831105). By the inhalation route of exposure, triclosan was assigned Toxicity Category II for acute exposures and is thus of higher acute toxicity by inhalation exposure than by oral or dermal exposures (MRID 42306902 and 43310501). Triclosan produces moderate irritation to the eyes (MRID 94045) and skin (MRID 42306903) with a Toxicity Category III assigned for both for acute exposures. Triclosan was not a dermal sensitizer in guinea pigs using the Buehler method (MRID 43206502).

Liver toxicity was noted after repeated oral dosing of triclosan to rats, mice, and dogs. In the 90-day rat study, (MRID 43022605, 99.7% a.i.; MRID 133545, % a.i. not stated), fatty metamorphosis and cytomegaly, hypertrophic hepatocytes, vacuolization, inflammation, and pigmentation of Kupffer cells were noted at a dose of 50 mg/kg/day. In the 28-day mouse study, liver cell necrosis and an increase in the liver-body weight ratio were observed at doses of 135 and 158 mg/kg/day for male and female mice respectively (MRID 44389707). In a 90-day oral toxicity study in dogs (MRID 96102), histopathologic examination of tissues from dogs that were killed or died showed evidence of hepatotoxicity resulting in obstructive jaundice at a dose of 25 mg/kg/day.

Dermal irritation is noted after repeated dermal exposure to the technical grade active ingredient (99% a.i.) in a 90-day dermal toxicity study in rats (MRID 43328001) and in two 14-day dermal toxicity studies in rats and mice (MRIDs 44389708 and 44389710). Data from the 90-day rat dermal toxicity study (MRID 43328001) showed irritation at 10 mg/kg/day (500  $\mu\text{g}/\text{cm}^2$ ) and a NOAEL for systemic effects at 40 mg/kg/day. Systemic toxicity was also observed in the mouse study with a NOAEL of 0.6 mg/animal/day.

Repeated exposure by the inhalation route to the assumed technical grade of triclosan (MRID 0087996) resulted in inflammation of the respiratory tract as well as changes in several serum enzymes. Acute purulent inflammation with focal ulceration of the mucous membrane in the nasal cavity and in the trachea were also observed. A LOAEL of 50  $\text{mg}/\text{m}^3$  or 3.21 mg/kg/day was observed in male rats and no NOAEL was established in males.

Developmental toxicity testing of triclosan in rats and rabbits (MRIDs 43817502/43817503 and MRIDs 43820401/43022607) showed no evidence of pre- or postnatal developmental toxicity at any dose level in either study up to and including 300 mg/kg/day. Developmental LOAELs were therefore not identified. In 2-generation reproductive toxicity testing of triclosan in rats showed effects in offspring (decreased viability and weaning index) only at doses producing toxicity in parental animals (decreased body weights) (MRID 40623701).

Chronic toxicity testing of triclosan in baboons (MRID 133230) showed signs of clinical toxicity (vomiting, diarrhea, failure to eat) at a dose of 100 mg/kg/day with a NOAEL of 30 mg/kg/day. In rats, chronic toxicity testing (MRID 42027906;161332) showed decreases in erythrocyte count, hemoglobin concentration, and hematocrit. Serum alanine and aspartate aminotransferase activities were increased in males at 168.0 mg/kg/day, and blood urea nitrogen was increased in females at 217.4 mg/kg/day. Hepatocellular hypertrophy was observed in males at 52.4 mg/kg/day and above. Chronic toxicity testing of triclosan in hamsters (MRID 44874001/44751101) showed increased mortality, decreased weight gain, increased incidence of nephropathy, and histopathologic findings of the stomach and testes of male hamsters at a dose of 250 mg/kg/day with a NOAEL of 75 mg/kg/day.

In carcinogenicity testing of triclosan in hamsters (MRID 44874001/44751101), there was no evidence of a carcinogenic effect. In carcinogenicity testing in rats (MRID 42027906; 161332), there was no evidence of a carcinogenic effect. In public documents available from the FDA, administration of triclosan in the diet to mice at doses of 10, 30, 100, and 200 mg/kg/day resulted in increases in the incidence of liver tumors at 30 mg/kg/day and above. A systemic NOAEL of 10 mg/kg/day was established from the data in this study, based on increased incidence of liver neoplasms in male and female mice at 30 mg/kg/day.

In several mutagenicity tests including Ames *Salmonella* assays (MRIDs 43533301 and 44389705), a mammalian cell gene mutation assay at the thymidine kinase locus (MRID 44389704), a chromosome aberration assay [Broker, et al. (1988)], an *in vivo* bone marrow cytogenetic assay (MRID 43740802), and an *in vitro* DNA synthesis assay [SanSebastian, 1993 ], triclosan was negative for mutagenicity. However, in an *in vitro* cytogenetic assay (MRID 43740801), there was a dose-related increase in the yield of cells with abnormal chromosome morphology. In the presence of S9 activation, nonsignificant but concentration dependent increases in cells bearing exchange figures were also seen.

In a metabolism study in hamsters (MRID 45307501/45307502), urine was the major route of elimination for triclosan radioactivity. Peak plasma and blood concentrations of triclosan-derived radioactivity occurred at one hour post-dose. Area Under the Curve (AUC) measurements indicated that saturation may have been achieved at the high dose, as AUC was not proportional to dose. The major urinary metabolite detected after oral administration was the glucuronide conjugate of triclosan. The major fecal metabolite was parent triclosan. The plasma, kidney, and liver eliminated triclosan equivalent rapidly. Tissue metabolite analyses showed that the glucuronide and sulfate conjugates of triclosan were the major metabolites detected. In a metabolism study in mice, (MRID 45307503), triclosan was eliminated primarily through the feces, via biliary excretion. Bioretention studies indicate that values from  $C_{max}$  to  $1/8C_{max}$  in the liver were higher than those in plasma following repeated administration at both dose levels, indicating that the liver is the target organ. Primary excreted compounds in the urine following single oral exposures included the unmetabolized parent compound and two parent conjugates; fecal excretion was primarily that of the free parent compound.

In metabolism studies conducted in rats, dogs, and rabbits (MRID 149464), results indicated that at least 70% of an oral dose of triclosan is absorbed from the gastrointestinal tract and that biliary secretion and subsequent fecal elimination is a major excretory route in the rat and dog. Urinary excretion appeared to be a major route of elimination in the rabbit. Tissue accumulation was minimal and primarily associated with highly perfused tissues and organs with excretory function. Metabolite data in rats revealed glucuronide conjugates and unchanged parent compound as biliary metabolites.

Biochemical and cell proliferation studies submitted for triclosan (MRIDs 44389702, 44389703, 44389706, 44389701) suggest that triclosan acts as a peroxisome proliferator

and that the hepatotoxic effect is followed by cell regeneration. For chemicals producing increased cell turnover through cytolethality, a threshold can be inferred below which these effects would not occur.

On July 25, 2007, the Health Effects Division's Carcinogenicity Assessment Review Committee met to discuss the carcinogenicity classification for triclosan and additional data submitted conducted with triclosan in support of a mode of action involving peroxisome proliferation as a causative factor in the positive tumorigenic results observed in the mouse carcinogenicity study. **In accordance with the EPA Final Guidelines for Carcinogen Risk Assessment (March 29, 2005), the CARC classified triclosan as "Not Likely to be Carcinogenic to Humans"**. This decision is based on the weight-of-evidence that supports activation of peroxisome proliferator-activated receptor alpha (PPAR $\alpha$ ) as the mode of action for triclosan-induced hepatocarcinogenesis in mice. The data did not support either mutagenesis or cytotoxicity followed by regenerative proliferation as alternative modes of action. While the proposed mode of action for liver tumors in mice is theoretically plausible in humans, hepatocarcinogenesis by this mode of action is quantitatively implausible and unlikely to take place in humans based on quantitative species differences in PPAR $\alpha$  activation and toxicokinetics. The quantification of risk is not required.

### **Dose-Response Assessment**

On March 10, 1998, the Health Effects Division's Hazard Identification Assessment Review Committee reviewed the available toxicology data for triclosan and selected endpoints for use as appropriate in occupational/residential exposure risk assessments. The potential for increased susceptibility of infants and children from exposure to triclosan was also evaluated. On October 31, 2006, the Antimicrobial's Division Toxicity Endpoint Committee met to provide additional endpoints for incidental oral and dermal exposures.

For acute and chronic dietary exposure risk assessments, a NOAEL value of 30 mg/kg/day was selected, based on clinical signs of toxicity (vomiting, diarrhea, failure to eat) at a dose of 100 mg/kg/day in a chronic toxicity study in baboons (MRID 133230). For dietary risk assessments, an uncertainty factor of 100 is assigned (10x inter-species extrapolation, 10x intra-species variation). The hazard-based FQPA safety factor is not applied in this case as there are no existing food use tolerances for triclosan. The resulting acute and chronic Reference Dose value is 0.30 mg/kg/day.

For short-term and intermediate-term incidental oral risk assessments (1-30 days and 30 days - 6 months), a NOAEL value of 30 mg/kg/day was selected, based on clinical signs of toxicity (vomiting, diarrhea, failure to eat) at a dose of 100 mg/kg/day in a chronic toxicity study in baboons (MRID 133230). An uncertainty factor of 100 was assigned to this endpoint (10x inter-species extrapolation, 10x intra-species variation).

For short-term dermal risk assessment (1-30 days), a NOAEL of 0.6 mg/animal (converted to concentration of 100  $\mu\text{g}/\text{cm}^2$  by using the surface area of the applied gauze

(2 x 3 cm or 6 cm<sup>2</sup>) was selected from a 14-day dermal toxicity study in the mouse (MRID 44389708), based on treatment-related dermal irritation at the treatment site and on increased liver weights at 1.5 mg/animal. It is to be noted that the short-term dermal endpoint was derived from a study using the technical grade (99%) test material. Residential uses of triclosan involve exposure to diluted formulations (e.g., 0.5% ai for carpet shampoo further diluted by water). Therefore, the short-term dermal irritation observed for the 99% ai formulation is not applicable for the dermal risk assessment in this case.

For intermediate-term and long-term dermal risk assessments, the endpoint was selected from a 90-day dermal toxicity study in rats with a NOAEL value of 40 mg/kg/day, based on increased occult blood in the urine observed at 80 mg/kg/day..

For inhalation risk assessments, a LOAEL of 50 mg/m<sup>3</sup> (3.21 mg/kg/day) was selected from a 21-day inhalation toxicity study (MRID 0087996), based on increased total leukocyte count and increased serum alkaline phosphatase in male rats at 3.21 mg/kg/day. While this study contained deficiencies that resulted in it not meeting the guideline requirement for a repeat dose inhalation toxicity study, the endpoint was chosen from this study as it was the only data available.

### **FQPA Considerations**

There are no food use tolerances for triclosan. Therefore, a formal FQPA analysis is not needed for this chemical. However, in light of residential exposures to triclosan, the ADTC did note that there was no evidence for neurotoxicity of triclosan in the submitted toxicology database. The data provided no indication of increased sensitivity of rats or rabbits to *in utero* and post-natal exposure to triclosan. Two prenatal developmental toxicity studies, one in rats and one in rabbits, failed to show evidence of developmental toxicity in the absence of maternal toxicity. In the two-generation reproduction study in rats, effects in the offspring were observed only at or above treatment levels which resulted in evidence of parental toxicity.

### **Exposure and Risk**

Based on a review of EPA product labels, triclosan is the active ingredient in products used in paints, textiles (mattresses and clothing) and plastic toys. Exposures also include those uses where there is the possibility of indirect food migration, including paper/pulp use, use in ice-making equipment, adhesives, cutting boards, and counter tops as well use in conveyer belts. In addition to EPA-regulated uses, the aggregate assessment accounts for non-EPA regulated uses of triclosan. Non-EPA uses include FDA uses such as toothpaste, hand soaps, and deodorants.

Although individual EPA-regulated uses have been assessed using standard Agency methodology, the NHANES biological monitoring data is available for assessing aggregate exposure and risk. Therefore, the supporting human exposure chapter for the

triclosan RED characterized exposures from individual EPA-regulated uses but was not needed for the aggregate risk assessment. EPA views the NHANES data as more representative of aggregate exposures than determining probability of co-occurrence of EPA and FDA-regulated uses.

### **Aggregate Risk**

In the case of triclosan, population-based biological monitoring data are available to assess the co-occurrence of uses to develop an aggregate exposure assessment. The population-based biological monitoring data are believed to be a more accurate predictor of aggregate exposure because not only are the data triclosan specific, they are also based on actual consumer use of the various triclosan products as they naturally co-occur. Nonetheless, uncertainties in the biological monitoring data also need to be addressed. Converting spot urine concentrations to dose is a difficult endeavor. The population-based biological monitoring data based on spot urine concentrations used in this assessment were obtained from the National Health and Nutrition Surveys (NHANES).

All exposure durations were assessed using the selected oral NOAEL of 30 mg/kg/day with a target MOE of 100. The oral endpoint was selected to represent the various oral exposure scenarios that are expected from antimicrobial exposure to triclosan. The calculated MOEs are representative of all exposure durations. The results of the NHANES data indicate that 74.6% of the samples had detectable levels of total (free plus conjugated) triclosan. Tables and provide the mean and 99<sup>th</sup> percentiles, respectively, of the (1) spot urine concentration to dose conversion (in units of ug/kg); (2) the pharmacokinetic 54% corrected daily dose; and (3) the MOEs for the three conversion methods. Aggregate exposures and risks are presented for several age groups (all ages combined, ages 6-11, 12-19, 20-59, >=60, Mexican-American, White non-Hispanic, and Black non-Hispanic).

**Based on the results at the mean and 99<sup>th</sup> percentile, the aggregate risks to triclosan from all uses (EPA and FDA) do not trigger a risk of concern. The mean MOEs range from 4,700 to 19,000. The MOEs at the 99<sup>th</sup> percentile range from 260 to 1,500. In fact, applying the lowest (most conservative) percent excreted from the results of the pharmacokinetic data (i.e., 24 percent) to the most conservative dose conversion method (i.e., 24-hour urine void extrapolation assuming the upper percentile of daily urine volumes), the MOE is 120.**

### **Occupational Exposure**

Triclosan short-term dermal irritation exposures and risks were not estimated for occupational handler exposures. Instead, dermal irritation exposures and risks will be mitigated using default personal protective equipment requirements based on the toxicity of the end-use product.

For intermediate-term dermal risks, the MOEs were above the target MOE of 100, and therefore, not of concern except for commercial painters and material preservative use for paper. The intermediate-term MOEs for using a paint brush/roller and an airless sprayer

are 31 and 1, respectively. Because triclosan is used as a material preservative in the paint, the use of chemical resistant gloves on the label is impractical.

For the occupational handler inhalation exposure and risk assessment, the MOEs were below the target of 1000 except for the brush application for paints. The inhalation MOE for commercial use of an airless sprayer for paints is 54, for liquid pour and liquid pump during paint manufacturing 330 and 290, respectively, and for pulp and paper the metering pump is 28.

Based on the low vapor pressure of triclosan and application methods, inhalation post-application exposure are expected to be minimal.

### **Environmental Fate Assessment**

Triclosan is hydrolytically stable under abiotic and buffered conditions over the pH 4-9 range based on data from a preliminary test at 50°C (MRID 420279-08). Photolytically, triclosan degrades rapidly under continuous irradiation from artificial light at 25°C in a pH 7 aqueous solution, with a calculated aqueous photolytic half-life of 41 minutes (MRID 430226-08). One major transformation product was identified, DCP (2,4-dichlorophenol), which was a maximum of 93.8-96.6% of the applied triclosan at 240 minutes post-treatment.

The Agency has used its databases (EPI Suite) and open literature (Toxnet) to conduct the environmental fate risk assessment.

In soil, triclosan is expected to be immobile based on an estimated  $K_{oc}$  of 9,200. Triclosan is not expected to volatilize from soil (moist or dry) or water surfaces based on an estimated Henry's Law constant of  $1.5 \times 10^{-7}$  atm-m<sup>3</sup>/mole. Triclosan partially exists in the dissociated form in the environment based on a pKa of 7.9, and anions do not generally adsorb more strongly to organic carbon and clay than their neutral counterparts. In aquatic environments, triclosan is expected to adsorb to suspended solids and sediments and may bioaccumulate ( $K_{ow}$  4.76), posing a concern for aquatic organisms. There is also a low to moderate potential for bioconcentration in aquatic organisms based on a BCF range of 2.7 to 90.

Hydrolysis is not expected to be an important environmental fate process due to the stability of triclosan in the presence of strong acids and bases. However, triclosan is susceptible to degradation via aqueous photolysis, with a half-life of <1 hour under abiotic conditions, and up to 10 days in lake water. An atmospheric half-life of 8 hours has also been estimated based on the reaction of triclosan with photochemically produced hydroxyl radicals. Additionally, triclosan may be susceptible to biodegradation based on the presence of methyl-triclosan following wastewater treatment. Although these data are limited, they indicate triclosan is not likely to contaminate surface or ground waters due

to its immobility in soils, and susceptibility to photodegradation, and potentially biodegradation, in soil and water.

From published literature studies on the occurrence of triclosan in waste water treatment plants, treatment plant efficiency, and open water measurements of triclosan, the majority suggest that aerobic biodegradation is one of the major and most efficient biodegradation pathways (70-80%) through which triclosan and its by-products are removed from the aquatic environment with actual efficiencies ranging from 53-99% (Kanda et al., 2003) in activated sludge plants and trickle down filtration, ranging from 58-86% (McAvoy et al., 2002). Another pathway of removing triclosan from water in wastewater treatment plants is through the sorption of triclosan and associated by-products to particles and sludge (10-15%) because of the chemical's medium to high hydrophobicity (Agüera et al., 2003; Gomez et al., 2007; Kanda et al., 2003; Lee and Peart, 2002; Bester, 2003 and 2005; Xia et al., 2005). Benchtop fate testing of triclosan found that 1.5-4.5% was sorbed to activated sludge and 81-92% was biodegraded (Federle et al., 2002).

Activated sludge and/or sludge samples examined for triclosan residue in Ohio showed a range of 0.5 to 15.6 µg/g (dry weight) with higher concentrations of triclosan observed in anaerobic sludge as compared to aerobic sludge (McAvoy et al., 2002). Other countries where sludge samples were analyzed for triclosan are as follows: Canada found 370 ng/g (Lee and Peart, 2002); Germany found 1000-8000 ng/g (Bester, 2003 and 2005); Greece found 1,840 ng/g (Gatidou et al. 2007); Spain found 420-5400 ng/g (Morales et al., 2005); and 19 WWTP were analyzed in Australia, which had a range of 90-16,790 ng/g dry weight and a median of 2,320 mg/g (Ying and Kookana, 2007).

Effluent concentrations from wastewater treatment plants in the US were 10-21 ng/L in Louisiana (Boyd et al., 2003); 63 ng/L in the upper Detroit river (Hua et al., 2005); 72 ng/L in Arlington, Virginia (Thomas and Foster, 2004); 110 ng/L in North Texas (Waltman et al., 2006); and the highest was 200-2700 ng/L in Ohio (McAvoy et al., 2002). Effluent concentrations from wastewater treatment plants in other countries were measured to be 160 ng/L (Lee et al., 2003) or 50-360 ng/L in Canada (Lee et al., 2005); 50 ng/L (Bester, 2003), 10-600 ng/L (Bester, 2005), or 180 ng/L (Wind et al., 2004) in Germany; 160 ng/L in Sweden (Bendz et al., 2005); 430 ng/L (31.2 µg/g particulate matter), 1120 ng/L (16.1 µg/g particulate matter), or 230 ng/L (22.4 µg/g particulate matter) in three different WWTP in Greece (Gatidou et al. 2007); 80-400 ng/L in Spain (Gomez et al., 2007); 100-269,000 ng/L in Spain (Mezcua et al., 2004); 0.15±0.08 mg/person in 5 European countries (Paxeus, 2004); 340 or 1100 ng/L, for trickle filtration and activated sludge treatment plant in England (Sabaliunas et al., 2003); 42-213 ng/L in Switzerland (Singer et al., 2002); and from 19 WWTP in Australia the range was 23-434 ng/L with a median concentration of 108 ng/L (Ying and Kookana, 2007).

Triclosan was found in approximately 36 US streams (Klopin et al., 2002) where effluent from activated sludge waste water treatment plants, trickle down filtration, and sewage overflow are thought to contribute to the occurrence of triclosan in open water. For this study, the U.S. Geological Survey surveyed a network of 139 streams across 30 states during 1999 and 2000. The selection of sampling sites was biased toward streams

susceptible to contamination (i.e. downstream of intense urbanization and livestock production). The median concentration was 40 ng/L and the maximum concentration detected was 280 ng/L (Klopin et al., 2002). In another study, storm water canal measurements over a 6 month period in Bayou St. John in Louisiana indicated that triclosan ranged from below the detection level to 29 ng/L (Boyd et al., 2004). Raw drinking water in Southern California was found to have 560 ng/L triclosan and 490 ng/L triclosan in finished water (Loraine and Pettigrove, 2006). Other published data on surface water concentrations of triclosan in the US indicated concentrations of 4 and 8 ng/L in the upper Detroit river (Hua et al., 2005) and 56 ng/L in Arlington, Virginia (Thomas and Foster, 2004). Published data on surface water concentrations of triclosan in other countries indicated concentrations of <3-10 ng/L in Germany (0.3-10 ng/L methyl-triclosan) (Bester, 2005); 19±1.4 ng/L in England (Sabaliunas et al., 2003); 11-98 ng/L in Switzerland (Singer et al., 2002); 30 ng/L in Germany (Wind et al., 2004); and in Australia 75 ng/L (Ying and Kookana, 2007).

### **Ecological/Environmental Risk Assessment**

An ecological risk assessment is not typically conducted for the types of uses registered for triclosan. However, since triclosan has been detected in natural waters, EPA has performed a qualitative environmental risk assessment using monitoring levels of triclosan found in waterways and toxicity values to develop risk quotients (RQs) and compare them to levels of concern (LOCs) for triclosan. LOCs were not exceeded for fish or aquatic plants. There were no acceptable acute toxicity studies for freshwater invertebrates or estuarine and marine organisms nor were there any acceptable chronic toxicity studies available for aquatic organisms. Therefore, risk to these species could not be assessed and data gaps were identified.

### **Endangered Species**

To facilitate compliance with the requirements of the Endangered Species Act subsection (a)(2) the Environmental Protection Agency, Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (U.S. EPA 2004). After the Agency's screening-level risk assessment is performed, if any of the Agency's Listed Species LOC Criteria are exceeded for either direct or indirect effects, a determination is made to identify if any listed or candidate species may co-occur in the area of the proposed pesticide use. If determined that listed or candidate species may be present in the proposed use areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

For certain use categories, the Agency assumes there will be minimal environmental exposure, and only a minimal toxicity data set is required (Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs U.S. Environmental Protection Agency - Endangered and Threatened Species Effects Determinations, 1/23/04, Appendix A, Section IIB, pg.81). Chemicals in these categories therefore do not undergo a full screening-level risk assessment.

Preliminary analysis indicates that there is a potential for triclosan use to overlap with listed species and that a more refined assessment is warranted, to include direct, indirect and habitat effects [the Agency is making this statement because triclosan and triclosan transformation products are being detected in various environmental components (see triclosan environmental fate chapter)].

The more refined assessment should involve clear delineation of the action area associated with proposed use of triclosan and best available information on the temporal and spatial co-location of listed species with respect to the action area. This analysis has not been conducted for this assessment. **An endangered species effect determination will not be made at this time.**

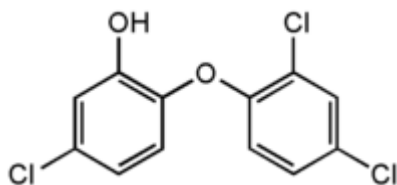
## Incident Reports

There are no reported incidents for triclosan from a search of the available databases.

## 2.0 PHYSICAL/CHEMICAL PROPERTIES AND CHARACTERIZATION

### Chemical Identity:

Chemical Name:	triclosan
Chemical Family:	diphenoxyether
Common/Trade Name:	2,4,4'-Trichloro-2'-hydroxydiphenyl ether Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- 5-Chloro-2-(2,4-dichlorophenoxy)phenol Irgasan DP-300R Irgaguard B1000 VIV-20
CAS Number:	3380-34-5
Molecular Formula:	C <sub>12</sub> H <sub>7</sub> Cl <sub>3</sub> O <sub>2</sub>
Chemical Structure:	



**Table 2-1a Chemical Characteristics for Technical Grade Active Triclosan**

Molecular Weight	289.541
Color	White crystals
Physical State	White crystalline powder
Specific Gravity	1.55 x 10 <sup>3</sup> kg/m <sup>3</sup> at 22°C
Dissociation Constant	pK <sub>a</sub> =8.14 at 20°C
pH	N/A
Stability	Stable at normal conditions
Melting Point	56.5 ° C
Boiling Point	N/A
Water Solubility	0.012 g/l at 20°C
Octanol-Water Partition constant ( LogK <sub>OW</sub> )	4.8 at 25°C
Vapor Pressure	5.2E-6 mm Hg at 25°C 2.2E-6 mm Hg at 20°C

### 3.0 HAZARD CHARACTERIZATION

#### 3.1 Hazard Profile

##### Acute Toxicity

Acute toxicity studies in experimental animals with technical grade triclosan show that by the oral and dermal routes, triclosan is of low acute toxicity (Toxicity Category IV; MRID 43206501 and 94044). By the inhalation route of exposure, triclosan was assigned Toxicity Category II for acute exposures and is thus of higher acute toxicity by inhalation exposure than by oral or dermal exposures (MRID 42306902 and 43310501). Triclosan produces moderate irritation to the eyes (MRID 94045) and skin (MRID 42306903) with a Toxicity Category III assigned for both for acute exposures. Triclosan was not a dermal sensitizer in guinea pigs using the Buehler method (MRID 43206502).

<b>Table 1. Acute Toxicity Profile for Triclosan</b>				
<b>Guideline Number</b>	<b>Study Type/ Test substance (% a.i.)</b>	<b>MRID Number/ Citation</b>	<b>Results</b>	<b>Toxicity Category</b>
870.1100 (§81-1)	Acute Oral- Rat Triclosan (99.7% a.i.)	43206901	LD <sub>50</sub> : >5000 mg/kg	IV
870.1200 (§81-2)	Acute Dermal- Rabbit Triclosan (97% a.i.)	94044	LD <sub>50</sub> : >9300 mg/kg	IV
870.1300 (§81-3)	Acute Inhalation- Rat Triclosan (100.5% a.i.)	42306902, 43310501	LC <sub>50</sub> : >0.15 mg/L	II
870.2400 (§81-4)	Primary Eye Irritation- Rabbit Triclosan (97% a.i.)	94045	moderately irritating	II
870.2500 (§81-5)	Primary Dermal Irritation- Rabbit Triclosan (% a.i. not provided)	42306903	PII: 3.5 at 72 hours	III
870.2600 (§81-6)	Dermal Sensitization- Guinea Pig Triclosan (99.7% a.i.)	43206502	Not a Sensitizer	NA

### 3.2 Dose-Response Assessment

On March 10, 1998 the Health Effects Division’s Hazard Identification Assessment Review Committee reviewed the available toxicology data for triclosan and selected endpoints for use as appropriate in occupational/residential exposure risk assessments. The potential for increased susceptibility of infants and children from exposure to triclosan was also evaluated. On October 31, 2006, the Antimicrobial’s Division Toxicity Endpoint Committee met to provide additional endpoints for incidental oral and dermal exposures. On July 25, 2007, the Health Effects Division Carcinogenicity Assessment Review Committee met and classified triclosan as “not likely to be carcinogenic to humans (HED TXR # 0054799). A summary of the selected endpoints is shown in table 2 below.

<b>Exposure Scenario</b>	<b>Dose Used in Risk Assessment, UF</b>	<b>Special FQPA SF* and Level of Concern for Risk Assessment</b>	<b>Study and Toxicological Effects</b>
<b>Acute Dietary (gen. pop.)</b>	NOAEL = 30 mg/kg UF = 100 <b>aRfD</b> = 0.03 mg/kg/day	FQPA SF = 1x	Chronic Toxicity study in Baboons MRID 133230
<b>Acute Dietary (females 13+)</b>	No appropriate endpoint identified in the database		
<b>Chronic Dietary (all populations)</b>	NOAEL = 30 mg/kg UF = 100 <b>cRfD</b> = 0.03 mg/kg/day	FQPA SF = 1x	Chronic Toxicity study in Baboons MRID 133230 LOAEL = 100 mg/kg/day, based on clinical signs of toxicity
<b>Short-Term/ Intermediate-Term Incidental Oral (1-30 days; 30 days- 6 months)</b>	NOAEL = 30 mg/kg	MOE = 100	Chronic Toxicity study in Baboons MRID 133230 LOAEL = 100 mg/kg/day, based on clinical signs of toxicity
<b>Dermal (short-term)</b>	NOAEL = 0.6 mg/animal (100 $\mu\text{g}/\text{cm}^2$ )	MOE = 100	14-day dermal toxicity study in the mouse MRID 44389708 LOAEL = 1.5 mg/kg/day, based on treatment-related dermal irritation at the treatment site and on increased liver weights
<b>Dermal (intermediate term)</b>	NOAEL = 40 mg/kg UF = 100	FQPA SF = 1x MOE = 100	90-day Dermal Toxicity in Rats MRID 43328001 LOAEL = 80 mg/kg/day, based on increased incidence occult blood in the urine.
<b>Dermal (long-term)</b>	NOAEL = 40 mg/kg UF = 100	FQPA SF = 1x MOE = 100	90-day Dermal Toxicity in Rats MRID 43328001 LOAEL = 80 mg/kg/day, based on increased incidence occult blood in the urine.

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
<b>Inhalation (all durations)</b>	NOAEL = 50 mg/m <sup>3</sup> or 3.21 mg/kg/day Where mg/kg/day = ((0.0087 m <sup>3</sup> /hr * mg/m <sup>3</sup> * 2 hr/day) / 0.271 b.w.	MOE = 1000	21-Day Inhalation Toxicity study in the rat MRID 0087996 LOAEL = 0.115 mg/L, based on increased total leukocyte count and increased serum alkaline phosphatase
<b>Cancer (oral)</b>	Not likely to be carcinogenic to humans (Health Effects Division Carcinogenicity Assessment Review Committee, July 2007).		

UF = uncertainty factor, DB UF = data base uncertainty factor, FQPA SF = special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic), RfD = reference dose, MOE = margin of exposure

### 3.3 FQPA Considerations

There are no food use tolerances for triclosan. Therefore, a formal FQPA analysis is not needed for this chemical. However, in light of residential exposures to triclosan, the ADTC did note that there was no evidence for neurotoxicity of triclosan in the submitted toxicology database. The data provided no indication of increased sensitivity of rats or rabbits to *in utero* and post-natal exposure to triclosan. Two prenatal developmental toxicity studies, one in rats and one in rabbits, failed to show evidence of developmental toxicity in the absence of maternal toxicity. In the two-generation reproduction study in rats, effects in the offspring were observed only at or above treatment levels which resulted in evidence of parental toxicity.

### 3.4 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of

potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCAs has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, triclosan may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

#### **4.0 EXPOSURE ASSESSMENT AND CHARACTERIZATION**

Based on a review of EPA product labels, triclosan is the active ingredient in products used in paints, textiles (mattresses and clothing) and plastic toys. Exposures also include those uses where there is the possibility of indirect food migration, including paper/pulp use, use in ice-making equipment, adhesives, cutting boards, and counter tops as well use in conveyer belts. In addition to EPA-regulated uses, the aggregate assessment accounts for non-EPA regulated uses of triclosan. Non-EPA uses include FDA uses such as toothpaste, hand soaps, and deodorants.

Although individual EPA-regulated uses have been assessed using standard Agency methodology, the NHANES biological monitoring data are available for assessing aggregate exposure and risk. Therefore, the supporting human exposure chapter for the triclosan RED characterized exposures from individual EPA-regulated uses but was not needed for the aggregate risk assessment. EPA views the NHANES data as more representative of aggregate exposures than determining probability of co-occurrence of EPA and FDA-regulated uses. Specific discussion of the individual EPA-regulated uses have been assessed using standard Agency methodology and are presented in the Occupational and Residential Exposure chapter.

#### **5.0 AGGREGATE RISK ASSESSMENT**

In order for a pesticide registration to continue, it must be shown that the use does not result in "unreasonable adverse effects on the environment". Even though no pesticide tolerances have been established for triclosan, EPA has performed an assessment of the aggregate exposure to triclosan. Aggregate exposure is the total exposure to a single chemical (or its residues) that may occur from dietary (i.e., food and drinking water), residential, and other non-occupational sources including triclosan FDA uses such as hand soaps and toothpaste, and from all known or plausible exposure routes (oral, dermal, and inhalation). An aggregate risk assessment was conducted using the single selected

toxicological endpoint for acute dietary, short-term (1-30 days), intermediate-term (1-6 months), and chronic (several months to lifetime) exposure durations. Inhalation aggregate risks are expected to be minimal based on the low vapor pressure of triclosan and uses such as tooth paste, hand soap, impregnated textiles, etc that do not involve inhalation as the primary route of exposure.

In performing aggregate exposure and risk assessments, the Office of Pesticide Programs has published guidance outlining the necessary steps to perform such assessments (General Principles for Performing Aggregate Exposure and Risk Assessments, November 28, 2001; available at <http://www.epa.gov/pesticides/trac/science/aggregate.pdf>). Steps for deciding whether to perform aggregate exposure and risk assessments are listed, which include: identification of toxicological endpoints for each exposure route and duration; identification of potential exposures for each pathway (food, water, and/or residential); reconciliation of durations and pathways of exposure with durations and pathways of health effects; determination of which possible residential exposure scenarios are likely to occur together within a given time frame; determination of magnitude and duration of exposure for all exposure combinations; determination of the appropriate technique (deterministic or probabilistic) for exposure assessment; and determination of the appropriate risk metric to estimate aggregate risk

In the case of triclosan, population-based biological monitoring data are available to assess the co-occurrence of uses to develop an aggregate exposure assessment. The population-based biological monitoring data are believed to be a more accurate predictor of aggregate exposure because not only are the data triclosan specific, they are also based on actual consumer use of the various triclosan products as they co-occur in practice. Nonetheless, uncertainties in the biological monitoring data also need to be addressed. Converting spot urine concentrations to estimated dose is a difficult endeavor. The population-based biological monitoring data based on spot urine concentrations used in this assessment were obtained from the National Health and Nutrition Surveys (NHANES).

## **5.1 National Health and Nutrition Surveys (NHANES) Data for Triclosan**

### **5.1.1 NHANES Data and Dose Conversion**

The following information has been excerpted from Cohen (2008). The National Health and Nutrition Surveys (NHANES) are a series of US national surveys of the health and nutrition status of the non-institutionalized civilian population conducted by the Centers for Disease Control and Prevention. As part of the 2003-2004 NHANES, urinary concentrations ( $\mu\text{g/L}$ ) of triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) were measured on a random sample of 2,517 participants of ages 6 and over. These

measurements represent concentrations in spot urine samples. The corresponding human dose (mg/kg/day) was not measured or estimated by NHANES. The NHANES urinary metabolite concentration data collection efforts were not designed to directly determine the dose and CDC has not reported dose estimates for triclosan based on NHANES measurement data. The NHANES 2003-2004 data were obtained from the NHANES website: [www.cdc.gov/nchs/nhanes.htm](http://www.cdc.gov/nchs/nhanes.htm)

EPA evaluates health effects in terms of toxicity endpoints that represent an exposure level in mg or  $\mu\text{g}$  per kilogram body weight that is not expected to be associated with adverse health effects. The conversion of measured spot urine concentrations to daily doses can be difficult because of variable dilution caused by wide fluctuations in fluid intake and excretion. Dose calculation is also difficult because there is no way to determine from the NHANES data from what route of exposure (i.e., oral, dermal, inhalation) and when (i.e., duration and time interval prior to measurement) the exposure to triclosan occurred, and because of uncertainty and variability in the absorption, distribution, metabolism, and excretion (ADME) parameters. If NHANES collected total daily urine excretion for each participant, then that participant's dose could be more accurately estimated by multiplying the triclosan concentration by the total daily urine volume and then dividing by the body weight. However, NHANES only collected spot urine samples so that total urine volume was not measured.

In the absence of total urine volume data, various methods have been proposed to estimate the dose from the measured spot urine concentration. The methods have been categorized into two main groups: one that uses measured pesticide concentrations in urine directly and the other that standardizes urinary concentrations on the basis of creatinine, a by-product of metabolism. There is some debate on whether creatinine is less variable than urinary output. Therefore, at this time, results of both methods are presented. The dose conversion methods are summarized below:

- Mage et al. (2004, 2007) use the estimated daily creatinine excretion for a demographic group; the triclosan concentration is divided by the creatinine concentration, multiplied by the daily creatinine excretion in  $\mu\text{g}/\text{day}$ , and divided by the body weight.
- Schafer et al. (2004) use the estimated daily urine excretion in L/day and the average body weight for a demographic group; the triclosan concentration is multiplied by the daily urine excretion in L/day, and divided by the average body weight. Because the data were available in NHANES, actual body weights of subjects were used instead of average body weights as described by PANNA (2004).
- The EPA Office of Research and Development (ORD) does not currently recommend an approach for converting spot urine concentration to a dose. However, the approach used by some ORD researchers is to use the estimated daily urine excretion in L/kg-day for a demographic group; the triclosan concentration is multiplied by the estimated daily urine excretion in L/kg-day.

Urine volumes (mean and upper percentile) from Geigy (1981) were used in this method.

Detailed procedures and assumptions used by EPA/OPP/AD to convert spot urine concentrations into dose to assess the triclosan aggregate risks are provided by Cohen (2008). Cohen (2008) provided the dose conversion from spot urine samples leaving the correction for the pharmacokinetics of triclosan to be done at a later date (see Section 6.1.2 below for pharmacokinetic correction).

### 5.1.2 Pharmacokinetics of Triclosan

A correction factor to account for the disposition of triclosan, derived from the data of Sandborgh-Englund (2006) was applied to the biological (urine) monitoring data provided by Cohen (2008) and used in this assessment. Sandborgh-Englund (2006) dosed 10 subjects (5M/5F) ranging from 26 to 42 years of age with a single oral dose of 4 mg of triclosan in mouthwash solution. Pre-exposure monitoring to establish baseline exposure levels was also determined. Results indicate that urinary excretion among individuals is variable for triclosan. Urinary excretion ranged from 24 to 83 percent (median of 54 percent) of the administered dose of triclosan in urine in 4 days. The data also indicate that the majority of urinary excretion occurred within 24 hours as illustrated in Figure 1. The urinary excretion half life of triclosan in this study was determined to be 11 hours. Therefore, 54 percent excretion, corrected for baseline exposures, was used by EPA in this assessment to convert the urine concentrations from NHANES to a dose using estimated 24 hour urine void volumes as described by Cohen (2008). The conversion is facilitated by the linear excretion kinetics observed for triclosan in this study. Based on the above, the pharmacokinetic equation used to calculate the triclosan dose is as follows:  $\text{Triclosan dose (mg/kg/day)} / 0.54$ .

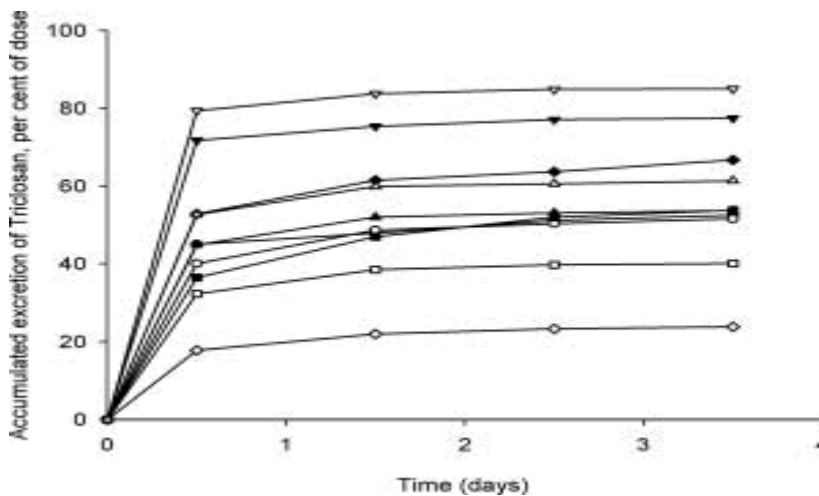


Figure 1. Triclosan Excretion in Urine (taken from Sandborgh-Englund (2006))

### **5.1.3 Uncertainties Associated with the Dose Conversion**

Several uncertainties exist in the aggregate assessment for triclosan that arise from using the biological monitoring data from NHANES. However, these uncertainties are balanced (and perhaps even offset) by (1) the relatively large data set obtained from NHANES; (2) assumptions used by Cohen (2008) for the dose conversion; (3) the characterization of the dose at the lowest (most conservative) urinary excretion; (4) the short urinary excretion half life 11 hours; and (5) the inclusion of the upper percentile of exposure. The following uncertainties and data limitations are noted for the aggregate assessment:

- It is assumed that the ADME parameters are the same across all individuals within the NHANES study and are constant within individuals over time.
- Sandborgh-Englund (2006) reported urinary excretion over 4 days post dose. However, from the graphical presentation of the data (raw data not reported) the profile of urinary excretion of triclosan indicates that the results at 24 hours are similar to those at 4 days. The urinary excretion half life for triclosan is reported in the text of the study (not taken from the graph) as 11 hours.
- The urinary excretion of triclosan presented in Sandborgh-Englund (2006) is highly variable (ranging from 24 to 83 percent). The median value reported of 54% urinary excretion has been used by EPA in the dose estimates. Additionally, to further characterize the uncertainty in the urinary excretion, risks are also discussed using the full range of urinary excretion values.
- NHANES urinary metabolite concentration data are not collected in a way to directly determine the dose, and CDC has not reported dose estimates for triclosan based on NHANES measurement data. In order to determine how sensitive the estimated dose was to urinary excretion volume, one of the dose conversion methods (Geigy 1981 95% urine volume upper bound estimate) is used to estimate a 24 hour urinary excretion volume for all individuals in the NHANES data set.
- Dose calculation is also difficult because there is no way to determine from the NHANES data from what route of exposure (i.e., oral, dermal, inhalation) and when (i.e., duration and time interval prior to measurement) the exposure to triclosan occurred. However, the unique aspects of triclosan -- short half life in urine and widespread daily use of triclosan products -- lend themselves to represent long-term measurements of exposure from a nationally representative population sample such as NHANES.

## **5.2 Acute, Short-term, Intermediate-term, and Chronic Aggregate Risks**

The NHANES results are believed to be representative of a range of acute to chronic exposures to children and adults because of the relatively short half-life of triclosan in urine (i.e., 11 hours) and the often daily use of triclosan products such as hand soaps and tooth paste. The upper range of exposures is important because of the

uncertainties in converting the spot urine concentrations to a dose; because the pharmacokinetic data appears to be highly variable for triclosan; and because the use of triclosan by the NHANES population is unknown. Interpreting the NHANES data for triclosan as representing a range of acute to chronic exposures is also supported by the fact that the 2,517 samples selected for analyses of triclosan were randomly selected from the total NHANES random population of 9,643, and therefore, “...*the representative design of the survey was maintained*” (Calafat et al 2007). Given the uncertainties in aggregating screening-level single use exposure estimates and assumptions on co-occurrence of uses, the NHANES data are viewed to be a reasonable data set to use for predicting aggregate risks.

All exposure durations were assessed using the selected oral NOAEL of 30 mg/kg/day with a target MOE of 100. The oral endpoint was selected to represent the various oral exposure scenarios that are expected from antimicrobial exposure to triclosan. The calculated MOEs are representative of all exposure durations. The NHANES data show that 74.6% of the samples had detectable levels of total (free plus conjugated) triclosan. Tables 5.1 and 5.2 provide – for each of the three basic concentration to dose conversion methods -- the mean and 99<sup>th</sup> percentiles, respectively, of the (1) spot urine concentration to dose conversion prior to correcting for the 54% triclosan urinary excretion (in units of ug/kg/day); (2) the pharmacokinetic 54% corrected daily dose converted to units of mg/kg/day; and (3) the MOEs. Aggregate exposures and risks are presented for the following age groups and subpopulations:

- All age groups;
- Ages 6-11;
- Ages 12-19
- Ages 20-59
- Ages >=60
- Male
- Females
- Mexican-American
- White, non-Hispanic
- Black, non-Hispanic

The three basic conversion methods used in this risk characterization are (1) Mage et al (2007) with an obesity correction factor; (2) Schafer et al (2004) using actual body weights from subjects; and (3) Geigy (1981) values for both a mean and 95<sup>th</sup> percentile of daily urine excretion volume. Based on the results at the mean and 99<sup>th</sup> percentile of the dose, the aggregate risks to triclosan from all uses (EPA and FDA) do not trigger a risk of concern. The mean MOEs range from 4,700 to 19,000. The MOEs at the 99<sup>th</sup> percentile of the dose range from 260 to 1,500. In fact, applying the lowest (most conservative) percent urinary excretion from the results of the pharmacokinetic data (i.e., 24 percent) to the most conservative dose conversion method (i.e., Geigy’s 95<sup>th</sup> percentile of daily urine volumes), the MOE is 120. In conclusion, even with the considerable uncertainties in converting spot urine concentration to dose, the NHANES data as analyzed for triclosan

sufficiently characterizes the aggregate risks as meeting the definition of not resulting in unreasonable adverse effects.

**Table 5.1. Acute, Short, Intermediate-, and Long-term Aggregate Risks for Triclosan (Mean)**

Groups	Method: Mage (2007) Obese Correct- based Dose  [Creatinine Correction]			Method: Schafer (2004) Actual BW- based Dose  [Urinary Volume Correction]			Method: Geigy 1981 [Urinary Volume Correction]					
							Mean Urine Volume-based Dose			95% Urine Volume-based Dose		
	ug/kg/d	mg/kg/d	MOE	ug/kg	mg/kg/d	MOE	ug/kg	mg/kg/d	MOE	ug/kg/d	mg/kg/d	MOE
All	1.373	0.0025	11801	1.5700	0.0029	10318	1.551	0.0029	10442	2.413	0.0045	6714
6-11	0.872	0.0016	18582	1.0511	0.0019	15412	0.901	0.0017	17986	1.304	0.0024	12426
12-19	1.431	0.0027	11318	1.7404	0.0032	9308	2.189	0.0041	7400	3.361	0.0062	4820
20-59	1.543	0.0029	10501	1.7187	0.0032	9426	1.635	0.0030	9911	2.562	0.0047	6322
>= 60	1.013	0.0019	15996	1.2108	0.0022	13380	1.152	0.0021	14065	1.806	0.0033	8972
Male	1.684	0.0031	9618	2.0316	0.0038	7974	1.963	0.0036	8254	2.997	0.0056	5405
Female	1.076	0.0020	15062	1.1306	0.0021	14329	1.160	0.0021	13969	1.857	0.0034	8726
Mexican-American	1.863	0.0035	8694	2.2781	0.0042	7111	2.220	0.0041	7297	3.455	0.0064	4689
White, Non-Hispanic	1.355	0.0025	11956	1.4850	0.0028	10909	1.477	0.0027	10969	2.303	0.0043	7035
Black, Non-Hispanic	1.082	0.0020	14967	1.5665	0.0029	10342	1.512	0.0028	10714	2.327	0.0043	6962

See Cohen (2008) for details of the dose conversion methods (Mage 2007 is based on creatinine excretion correction and both Schafer (2004) and Geigy 1981 are based on urine volume excretion corrections).

Groups (demographics) are based on the available data in NHANES.

Doses in units of ug/kg/day are based on the spot urine conversions to daily dose without being corrected for the pharmacokinetics of triclosan.

Doses in units of mg/kg/day = [dose (ug/kg/day) x 0.001 mg/ug unit conversion] / 0.54 (representing the median urinary excretion of triclosan of 54%).

Geigy (1981) 95% urine volume is the upper percentile of daily urine volume.

**Table 5.2. Acute, Short, Intermediate-, and Long-term Aggregate Risks for Triclosan (99th Percentile)**

Groups	Method: Mage (2007) Obese Correct- based Dose			Method: Schafer (2004) Actual BW- based Dose			Method: Geigy 1981 [ <i>Urinary Volume Correction</i> ]					
	<i>[Creatinine Correction]</i>			<i>[Urinary Volume Correction]</i>			Mean Urine Volume-based Dose			95% Urine Volume-based Dose		
	ug/kg/d	mg/kg/d	MOE	ug/kg/d	mg/kg/d	MOE	ug/kg/d	mg/kg/d	MOE	ug/kg/d	mg/kg/d	MOE
All	15.51	0.029	1044	23.59	0.044	687	23.56	0.0436	688	38.06	0.070	426
6-11	10.85	0.020	1493	24.62	0.046	658	9.70	0.0180	1670	14.17	0.026	1143
12-19	16.63	0.031	974	25.46	0.047	636	28.77	0.0533	563	46.48	0.086	349
20-59	19.08	0.035	849	29.07	0.054	557	29.87	0.0553	542	48.25	0.089	336
>= 60	14.42	0.027	1123	17.15	0.032	945	14.78	0.0274	1096	22.70	0.042	714
Male	18.96	0.035	855	35.15	0.065	461	35.20	0.0652	460	54.07	0.100	300
Female	14.74	0.027	1099	17.77	0.033	912	17.62	0.0326	920	28.47	0.053	569
Mexican-American	20.56	0.038	788	42.37	0.078	382	40.64	0.0753	399	62.42	0.116	260
White, Non-Hispanic	14.98	0.028	1081	16.30	0.030	994	18.97	0.0351	854	29.13	0.054	556
Black, Non-Hispanic	13.72	0.025	1181	26.12	0.048	620	28.25	0.0523	573	45.64	0.085	355

See Cohen (2008) for details of the dose conversion methods (Mage 2007 is based on creatinine excretion correction and both Schafer (2004) and Geigy 1981 are based on urine volume excretion corrections).

Groups (demographics) are based on the available data in NHANES.

Doses in units of ug/kg/day are based on the spot urine conversions to daily dose without being corrected for the pharmacokinetics of triclosan.

Doses in units of mg/kg/day = [dose (ug/kg/day) x 0.001 mg/ug unit conversion] / 0.54 (representing the median urinary excretion of triclosan of 54%).

Geigy (1981) 95% urine volume is the upper percentile of daily urine volume.

## 6.0 CUMULATIVE RISK

FQPA (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

AD did not perform a cumulative risk assessment as part of this RED for triclosan because AD has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of triclosan.

On this basis, the Registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether triclosan shares a common mechanism of toxicity with any other substance. If AD identifies other substances that share a common mechanism of toxicity with triclosan, AD will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment.

The Health Effects Division, Office of Pesticide Programs, has recently developed a framework proposed for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on January 16, 2002 (67 FR 2210-2214) and is available from the OPP Website at: [http://www.epa.gov/pesticides/trac/science/cumulative\\_guidance.pdf](http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf). In the guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed.

Before undertaking a cumulative risk assessment, AD will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

## 7.0 OCCUPATIONAL EXPOSURE AND RISK

A complete explanation of the occupational exposure and risk assessment can be found in the supporting disciplinary chapter entitled Triclosan: Occupational and Residential Exposure Assessment. Summary information is provided in this section.

The exposure scenarios assessed for representative uses of triclosan selected by EPA are shown in Table 7.1. The table also shows the maximum application rate associated with the representative use and the appropriate EPA Registration number for the product label. It should be noted that for the calculation of application rates in which 8.34 lb/gal is noted, the product is assumed to have the density of water because no product-specific density is available.

The occupational handler scenarios included in Table 7.1 were assessed to determine inhalation exposures. The general assumptions and equations that were used to calculate occupational handler inhalation risks are provided in Section 1.2 of the Occupational and Residential Exposure Chapter. The majority of the scenarios were assessed using CMA data and Equations 1-3. However, for the occupational scenarios in which CMA data were insufficient, other data and methods were applied.

Triclosan dermal irritation exposures and risks were not estimated for occupational handler exposures. Instead, dermal irritation exposures and risks will be mitigated using default personal protective equipment requirements based on the toxicity of the end-use product.

<b>Table 7.1. Representative Exposure Scenarios Associated with Occupational Exposures to Triclosan</b>				
Representative Use	Method of Application	Exposure Scenario	Example Registration #	Application Rate
<b>Commercial/Industrial/Institutional Premises (Use Category III)</b>				
HVAC coil applications	Airless sprayer	ST/IT Handler: Inhalation	82523-1	6.1E-4 lb ai/10 ft <sup>2</sup>  (0.85 pints/10 ft <sup>2</sup> x 1 gal/8 pts x 8.34 lb/gal x 0.69% ai)
Painting (commercial painters)	Paint brush, Airless sprayer	ST/IT Handler: Inhalation	42182-1	0.1 lb ai/gallon  [up to 1% product x 99% ai x 10 lb/gal paint density = 0.099 lb ai/gallon of paint]
<b>Material Preservatives (Use Category VII)</b>				
Paint	Liquid pour, Powder	ST/IT Handler: inhalation	42182-1	0.1 lb ai/gallon  [up to 1% product x 99% ai x 10 lb/gal paint density = 0.099 lb ai/gallon of paint]
<b>Industrial processes and water systems (Use Category VIII)</b>				
Pulp and Paper	Metered pump	ST/IT Handler: Inhalation	70404-5	2% ai by weight of paper product  (2% product by weight x 99% ai for paper mulch )  Note : other labels for paper and paper board have lower rates, 42182-1 and 3090-165)

The resulting inhalation exposures and MOEs for the representative occupational handler scenarios are presented in Table 6.2. The calculated MOEs were above the target MOE of 100 for all scenarios, except for the commercial painters (both by brush and airless sprayer).

**Table 6.2. Short- and Intermediate-Term Inhalation Risks Associated with Occupational Handlers**

Exposure Scenario	Method of Application	Unit Exposure (mg/lb a.i.)		Application Rate	Quantity Handled/Treated per day	Daily Dose (mg/kg/day) <sup>a</sup>		MOE <sup>b</sup> (Target MOE = 100)	
		Inhalation	Dermal			Inhalation	Dermal	Inhalation	Dermal
<b>Commercial, Institutional and Industrial Premises and Equipment (Use Site Category III)</b>									
HVAC	Airless sprayer	0.83	38	6.1E-4 lb ai/10ft <sup>2</sup>	Large building 1000 ft <sup>2</sup>	0.00072	0.033	4,500	1,200
Painting (commercial)	Paint brush	0.26	180	0.1 lb ai/gal	5 gallons	0.002	1.3	1,600	31
	Airless sprayer	0.83	38		50 gallons	0.059	2.7	54	1
<b>Material Preservatives (Use Site Category VII)</b>									
Paint (manufacturing process)	Liquid pour	0.00346	0.135 (gloves)	0.99% ai	20,000 lbs	0.0098	0.38	330	110
	Liquid pump	0.000403	0.00629 (gloves)		200,000 lbs	0.011	0.18	290	220
<b>Industrial Processes and Water Systems (Use Site Category VIII)</b>									
Pulp and Paper	Metering pump	0.000403	0.00629 (gloves)	2% ai	500 tons	0.115	1.8	28	22

a Daily dose (mg/kg/day) = [unit exposure (mg/lb a.i.) x absorption factor (1 for inhalation and 1 for dermal) x application rate x quantity treated / Body weight (70 kg).

b MOE = NOAEL (mg/kg/day) / Daily Dose [Where inhalation LOAEL = 3.21 mg/kg/day for all inhalation exposure durations and the IT dermal NOAEL is 40 mg/kg/day from a dermal route-specific study]. Target MOE = 100.

## 7.1 Occupational Post-application Exposures

Occupational post-application dermal and inhalation exposures are assumed to be negligible.

## 7.2 Data Limitations/Uncertainties

There are several data limitations and uncertainties associated with the occupational handler and post application exposure assessments as noted in the occupational and residential exposure chapter. These are reproduced here and include:

- Surrogate dermal and inhalation unit exposure values were taken from the proprietary Chemical Manufacturers Association (CMA) antimicrobial exposure study (USEPA, 1999: DP Barcode D247642) or from the Pesticide Handler Exposure Database (USEPA, 1998). Since the CMA data are of poor quality, the Agency requires that confirmatory data be submitted to support the occupational scenarios assessed in this document.

- The quantities handled/treated were estimated based on information from various sources, including HED’s Standard Operating Procedures (SOPs) for Residential Exposure Assessments (USEPA, 2000 and 2001), and personal communication with experts. The individuals contacted have experience in these operations and their estimates are believed to be the best available without undertaking a statistical survey of the uses. In certain cases, no standard values were available for some scenarios. Assumptions for these scenarios were based on AD estimates and could be further refined from input from registrants.

## 8.0 ENVIRONMENTAL RISK

### 8.1 Ecological Hazard

The toxicity endpoints presented below are based on the results of ecotoxicity studies submitted to EPA to meet the Agency’s data requirements for the uses of triclosan.

#### A. Toxicity to Terrestrial Animals

##### (1) Birds, Acute

The results of three acute oral toxicity studies, submitted for triclosan, are provided in the following table:

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/kg)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Mallard duck ( <i>Anas platyrhynchos</i> )	Triclosan 99.7%	LD <sub>50</sub> = >2150 NOAEL = 2150	Relatively nontoxic	Yes (core) - 14-day test duration - 19 weeks of age	430226-03
Bobwhite quail ( <i>Colinus virginianus</i> )	<b>Triclosan</b> <b>99.7%</b>	LD <sub>50</sub> = 825 NOAEL = <147	Slightly toxic	Yes (core) - 14-day test duration - 21 weeks of age	430226-02
Bobwhite quail ( <i>Colinus virginianus</i> )	<b>Triclosan</b> <b>3.89%</b>	LD <sub>50</sub> = >2000 NOAEL = N.R.	Relatively nontoxic	Yes (core for a formulated product)	410089-10

These three acceptable acute oral toxicity studies indicate that triclosan is slightly toxic to relatively nontoxic to birds on an acute oral basis. The guideline requirement OPPTS 850.2100/(71-1) is satisfied.

**(2) Birds, Subacute**

This testing was required for triclosan. The results of two subacute dietary toxicity studies, submitted for triclosan, are provided in the following table:

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (ppm)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Bobwhite quail ( <i>Colinus virginianus</i> )	Triclosan 99.7%	LC <sub>50</sub> (diet) = >5000 NOAEC = 1250	Relatively nontoxic	Yes (core) - 8-day test duration - 13 days of age	430226-04
Bobwhite quail ( <i>Colinus virginianus</i> )	Triclosan 3.89%	LC <sub>50</sub> (diet) = >5000 NOAEC = N.R.	Relatively nontoxic	Yes (core for formulated product) - 8-day test duration - 7-10 days of age	410089-11

The results of these two acceptable studies indicate that triclosan is relatively nontoxic to avian species through subacute dietary exposure. These studies fulfill guideline requirement OPPTS 850.2100/ (71-2a – Bobwhite quail/71-2b – Mallard duck).

**B. Toxicity to Aquatic Animals**

The Agency requested that aquatic toxicity studies be conducted with triclosan since, under typical use conditions, it may be introduced into the aquatic environment.

**(1) Freshwater Fish, Acute**

In order to establish the acute toxicity of triclosan to freshwater fish, the Agency requires freshwater fish toxicity studies using the TGAI. The preferred test species are rainbow trout (a coldwater fish) and bluegill sunfish (a warm water fish). The results of 5 freshwater fish acute studies submitted for triclosan are presented in the following table:

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Rainbow Trout ( <i>Oncorhynchus mykiss</i> )	Triclosan 99.3%	LC <sub>50</sub> = 0.288 NOAEC = 0.100	Highly toxic	Yes (core) - 96-hr test duration - static test system	439693-01
Fathead minnow ( <i>Pimephales promelas</i> )	Triclosan 99.7%	LC <sub>50</sub> = 0.26 LOEC = 0.18 NOAEC = 0.10	Highly toxic	No (supplemental) - 96-hr test duration - static test system - nominal concentrations not verified	430460-01
Bluegill sunfish ( <i>Lepomis macrochirus</i> )	Triclosan 3.89%	LC <sub>50</sub> = 37.2 NOAEC = N.R.	Slightly toxic	Yes (core for formulated product) - 96-hr test duration - static test system	410089-13
Rainbow Trout ( <i>Oncorhynchus mykiss</i> )	Triclosan 3.89%	LC <sub>50</sub> = 23.4 NOAEC = N.R.	Slightly toxic	Yes (core for formulated product) - 96-hr test duration - static test system	410089-12

Freshwater acute toxicity tests indicate that triclosan is highly toxic to slightly toxic to fish on an acute basis. These studies fulfill guideline requirement OPPTS 850.1075 (72-1a&b). Because acute toxicity to fish is <1.0 mg/L, the environmental hazard section of triclosan labels must state: “This pesticide is toxic to fish.”

(2) Freshwater Invertebrates, Acute

The results of the two acute studies submitted for triclosan are provided in the following table:

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
Waterflea ( <i>Daphnia magna</i> )	Triclosan 99.7%	EC <sub>50</sub> = 0.39 NOAEC = 0.10	Highly toxic	No (supplemental) - 48-hr test	430460-02

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Toxicity Category	Satisfies Guidelines/ Comments	Reference (MRID No.)
		(a.i.)		duration - static test system - nominal concentrations not verified	
Waterflea ( <i>Daphnia magna</i> )	Triclosan 3.89%	LC <sub>50</sub> = 0.42 NOAEC = N.R.	Highly toxic	No (supplemental)  - 48-hr test duration - static test system - lack of pH and DO measurements and formulated product used	410089-14
Waterflea ( <i>Daphnia magna</i> )					423221-02

The results of these studies indicate that triclosan is highly toxic to freshwater invertebrates. These studies **do not** fulfill guideline requirement OPPTS 850.1010 (72.2a). Because the acute aquatic invertebrate toxicity values are < 1.0 mg/L, the environmental hazard section of triclosan labels must state: “This pesticide is toxic to aquatic invertebrates.”

### (3) Estuarine and Marine Organisms, Acute

Acute toxicity testing with estuarine and marine organisms using the TGAI is required when the end-use product is intended for direct application to the marine/estuarine environment or effluent containing the active ingredient is expected to reach this environment. The preferred fish test species is the sheepshead minnow. The preferred invertebrate test species are mysid shrimp and eastern oysters. At this time this testing is not required for triclosan, but is dependent upon the results of environmental fate data which may be required. (See triclosan environmental fate chapter and comments above on potential data requirements). No studies have been submitted to fulfill these data requirements (OPPTS 850.1075/(72-3a), OPPTS 850.1035/(72-3c) and OPPTS 850.1025/(72-3b)).

### (4) Aquatic Organisms, Chronic

Chronic toxicity testing (fish early life stage and aquatic invertebrate life cycle) is required for pesticides when certain conditions of use and environmental fate apply. The preferred freshwater fish test species is the fathead minnow. The preferred freshwater invertebrate is *Daphnia magna*. At this time this testing is not required for triclosan, but is dependent upon the results of environmental fate data which may be required. (See triclosan environmental fate chapter and comments above on potential data requirements).

The results of one toxicity study submitted for triclosan is presented in the following table:

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
Waterflea ( <i>Daphnia magna</i> )	Triclosan % purity unknown	LOEC = <0.1388 NOAEC = N.R.	No (supplemental) - 21-day test duration - <b>static renewal test system</b> - growth not measured as a	437407-01

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
			chronic endpoint - % a.i. not given - raw data missing - concentration analysis insufficient	

No fathead minnow study has been submitted. The study on the waterflea does not fulfill the guideline requirement for a chronic aquatic invertebrate study (OPPTS 850.1300).

### C. Toxicity to Plants

Non-target plant phytotoxicity testing is required for pesticides when certain conditions of use and environmental fate apply. At this time this testing is not required for triclosan, but is dependent upon the results of environmental fate data which may be required. (See triclosan environmental fate chapter and comments above on potential data requirements). However, testing has been conducted with triclosan on several aquatic plant species. Testing is normally conducted with one species of aquatic vascular plant (*Lemna gibba*) and four species of algae: (1) freshwater green alga, *Selenastrum capricornutum*, (2) marine diatom, *Skeletonema costatum*, (3) freshwater diatom, *Navicula pelliculosa*, and (4) bluegreen cyanobacteria, *Anabaena flos-aquae*. The rooted aquatic macrophyte rice (*Oryza sativa*) is also tested in seedling emergence and vegetative vigor tests.

Four studies that evaluate the toxicity of triclosan to freshwater aquatic plants have been submitted. Results of these studies are presented in the following table:

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
Marine Diatom ( <i>Skeletonema costatum</i> )	Triclosan 99.5%	EC <sub>50</sub> = >0.066 NOEC = 0.0126	Yes (core) - 96-hour test duration - static test system	444228-01
Freshwater Diatom ( <i>Navicula</i> )	Triclosan 99.5%	EC <sub>50</sub> = 0.016 NOEC = 0.005	Yes (core) - 96-hour test duration	444228-01

Species	Chemical, % Active Ingredient (a.i.) Tested	Endpoint (mg/L)	Satisfies Guidelines/ Comments	Reference (MRID No.)
<i>pelliculosa</i> )			- static test system	
Bluegreen Cyanobacteria ( <i>Anabaena flos-aquae</i> )	Triclosan 99.5%	EC <sub>50</sub> = 0.0012 NOEC = N.R.	Yes (core)  - 96-hour test duration - static test system	444228-01
Duckweed ( <i>Lemna gibba</i> )	Triclosan 99.5%	EC <sub>50</sub> = >0.0625 NOEC = 0.0125	Yes (core)  - 7-day test duration - static test system	444228-01

The guideline requirement for an algal toxicity test (850.5400, 123-2) is partially fulfilled. One additional algal toxicity test under 850.5400 is outstanding: a test with the freshwater green alga, *Selenastrum capricornutum*. The other non-target aquatic plant toxicity requirement, floating freshwater aquatic macrophyte duckweed (*Lemna gibba*) – guideline 850.4400 - is satisfied. Studies on the rooted freshwater macrophyte rice (*Oryza sativa*) – 850.4225 and 850.4250 (2 tests on seedling emergence and vegetative vigor) -- have not been submitted.

## 8.2 Environmental fate and Transport

Triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol] is a white crystalline powder with low solubility in water (12 ppm). Triclosan is hydrolytically stable under abiotic and buffered conditions over the pH 4-9 range based on data from a preliminary test at 50°C. Photolytically, triclosan degrades rapidly under continuous irradiation from artificial light at 25°C in a pH 7 aqueous solution, with a calculated aqueous photolytic half-life of 41 minutes. One major transformation product has been identified, DCP (2,4-dichlorophenol), which was a maximum of 93.8-96.6% of the applied triclosan at 240 minutes post-treatment.

In soil, triclosan is expected to be immobile based on an estimated K<sub>oc</sub> of 9,200. Triclosan is not expected to volatilize from soil (moist or dry) or water surfaces based on an estimated Henry's Law constant of 1.5 x 10<sup>-7</sup> atm-m<sup>3</sup>/mole. Triclosan exists partially in the dissociated form in the environment based on a pK<sub>a</sub> of 7.9, and anions do not generally adsorb more strongly to organic carbon and clay than their neutral counterparts. In aquatic environments, triclosan is expected to adsorb to suspended solids and sediments and may bioaccumulate (K<sub>ow</sub> 4.76), posing a concern for aquatic organisms. There is a low to moderate potential for bioconcentration in aquatic organisms based on a BCF range of 2.7 to 90.

Hydrolysis is not expected to be an important environmental fate process due to the stability of triclosan in the presence of strong acids and bases. However, triclosan is susceptible to degradation via aqueous photolysis, with a half-life of <1 hour under abiotic conditions, and up to 10 days in lake water. An atmospheric half-life of 8 hours has also been estimated based on the reaction of triclosan with photochemically produced hydroxyl radicals. Additionally, triclosan may be susceptible to biodegradation based on the presence of methyl-triclosan following wastewater treatment.

Of the published literature studies on the occurrence of triclosan in waste water treatment plants, treatment plant efficiency, and open water measurements of triclosan, the majority suggest that aerobic biodegradation is one of the major and most efficient biodegradation pathways (70-80%) through which triclosan and its by-products are removed from the aquatic environment, with actual efficiencies ranging from 53-99% (Kanda *et al.*, 2003) in activated sludge plants, and trickle down filtration ranging from 58-86% (McAvoy *et al.*, 2002). Another pathway of removing triclosan from water in wastewater treatment plants is through the sorption of triclosan and associated by-products to particles and sludge (10-15%) because of the chemical's medium to high hydrophobicity. Benchtop fate testing of triclosan found that 1.5-4.5% was sorbed to activated sludge and 81-92% was biodegraded (Federle *et al.*, 2002).

### 8.3 Environmental Exposure and Risk

The ecotoxicity test values (measurement endpoints) used in the acute and chronic risk quotients are derived from required studies. Examples of ecotoxicity values derived from short-term laboratory studies that assess acute effects are: (1) LC<sub>50</sub> (fish and birds), (2) LD<sub>50</sub> (birds and mammals), (3) EC<sub>50</sub> (aquatic plants and aquatic invertebrates) and (4) EC<sub>25</sub> (terrestrial plants). Examples of toxicity test effect levels derived from the results of long-term laboratory studies that assess chronic effects are: (1) LOAEC (birds, fish, and aquatic invertebrates), and (2) NOAEC (birds, fish and aquatic invertebrates). For birds and mammals, the NOAEC generally is used as the ecotoxicity test value in assessing chronic effects, although other values may be used when justified. However, the NOAEC is used if the measurement endpoint is production of offspring or survival.

#### Risk Presumptions for Terrestrial Animals

Risk Presumption	RQ	LOC
<b>Birds and Wild Mammals</b>		
Acute Risk	EEC <sup>1</sup> /LC50 or LD50/sqft <sup>2</sup> or LD50/day <sup>3</sup>	0.5
Acute Restricted Use	EEC/LC50 or LD50/sqft or LD50/day (or LD50 < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC50 or LD50/sqft or LD50/day	0.1
Chronic Risk	EEC/NOAEC	1

<sup>1</sup> abbreviation for Estimated Environmental Concentration (ppm) on avian/mammalian food items  
<sup>2</sup>  $\frac{\text{mg/ft}^2}{\text{LD50} * \text{wt. of bird}}$       <sup>3</sup>  $\frac{\text{mg of toxicant consumed/day}}{\text{LD50} * \text{wt. of bird}}$

**Risk Presumptions for Aquatic Animals**

Risk Presumption	RQ	LOC
Acute Risk	EEC <sup>1</sup> /LC50 or EC50	0.5
Acute Restricted Use	EEC/LC50 or EC50	0.1
Acute Endangered Species	EEC/LC50 or EC50	0.05
Chronic Risk	EEC/MATC <sup>2</sup> or NOAEC	1

<sup>1</sup> EEC = (ppm or ppb) in water

<sup>2</sup> MATC = maximum allowable toxicant concentration

**Risk Presumptions for Plants**

Risk Presumption	RQ	LOC
<b>Terrestrial and Semi-Aquatic Plants</b>		
Acute Risk	EEC/EC25	1
Acute Endangered Species	EEC/EC05 or NOAEC	1
<b>Aquatic Plants</b>		
Acute Risk	EEC <sup>1</sup> /EC50	1
Acute Endangered Species	EEC/EC05 or NOAEC	1

1 EEC = (ppb/ppm) in water

Triclosan was found in approximately 36 US streams (Klopin et al., 2002), where effluent from activated sludge waste water treatment plants, trickle down filtration, and sewage overflow are thought to contribute to the occurrence of triclosan in open water. For this study, the U.S. Geological Survey surveyed a network of 139 streams across 30 states during 1999 and 2000. The selection of sampling sites was biased toward streams susceptible to contamination (i.e. downstream of intense urbanization and livestock production). The median concentration of triclosan was 40 ng/L and the maximum concentration detected was 280 ng/L (Klopin *et al.*, 2002).

From the toxicity tables in section I above, the highest toxicity in an acceptable fish study was achieved in a study on the rainbow trout (*Oncorhynchus mykiss*). The LC<sub>50</sub> value obtained in this study was 0.288 mg/L (MRID 439693-01). There were no acceptable acute toxicity studies for freshwater invertebrates or estuarine and marine organisms nor were there any acceptable chronic toxicity studies available for aquatic organisms. Therefore, risk to these species cannot be assessed. The highest toxicity in an acceptable aquatic plant toxicity study was achieved in a study on the bluegreen cyanobacteria (*Anabaena flos-aquae*). The EC<sub>50</sub> value obtained in this study was 0.0012 mg/L and no NOEC was reported (MRID 444228-01).

For aquatic animals the LOC ranges from 0.05 for endangered species to 1 for chronic risks. Comparing the maximum concentration of triclosan found in US streams (280 ng/L or 0.00028 mg/L) to the highest toxicity found in a fish acute study (0.288 mg/L), an RQ of 0.00097 is obtained. This is less than all LOCs for aquatic animals and therefore the potential for triclosan to cause adverse effects on fish is not high.

For aquatic plants the LOC is 1. Comparing the maximum concentration of triclosan found in US streams (280 ng/L or 0.00028 mg/L) to the highest toxicity found in aquatic plants (0.0012 mg/L), an RQ of 0.23 is obtained. This is less than the LOC and therefore the potential for acute risk to aquatic plants from triclosan is not high.

#### **8.4 Endangered Species Consideration**

Section 7 of the Endangered Species Act, 16 U.S.C. Section 1536(a)(2), requires all federal agencies to consult with the National Marine Fisheries Service (NMFS) for marine and anadromous listed species, or the United States Fish and Wildlife Services (FWS) for listed wildlife and freshwater organisms, if they are proposing an "action" that may affect listed species or their designated habitat. Each federal agency is required under the Act to insure that any action they authorize, fund, or carry out is not likely to jeopardize the continued existence of a listed species or result in the destruction or adverse modification of designated critical habitat. To jeopardize the continued existence of a listed species means "to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of the species." 50 CFR. § 402.02.

To facilitate compliance with the requirements of the Endangered Species Act subsection (a)(2) the Environmental Protection Agency, Office of Pesticide Programs has established procedures to evaluate whether a proposed registration action may directly or indirectly reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of any listed species (U.S. EPA 2004). After the Agency's screening-level risk assessment is performed, if any of the Agency's Listed Species LOC Criteria are exceeded for either direct or indirect effects, a determination is made to identify if any listed or candidate species may co-occur in the area of the proposed pesticide use. If determined that listed or candidate species may be present in the proposed use areas, further biological assessment is undertaken. The extent to which listed species may be at risk then determines the need for the development of a more comprehensive consultation package as required by the Endangered Species Act.

For certain use categories, the Agency assumes there will be minimal environmental exposure, and only a minimal toxicity data set is required (Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs U.S. Environmental Protection Agency - Endangered and Threatened Species Effects Determinations, 1/23/04, Appendix A, Section IIB, pg.81). Chemicals in these categories therefore do not undergo a full screening-level risk assessment, and are considered to fall under a no effect determination.

A preliminary analysis indicates that there is a potential for triclosan use to overlap with listed species and that a more refined assessment is warranted, to include direct, indirect and habitat effects.<sup>1</sup> The more refined assessment should involve clear delineation of the action area associated with proposed use of triclosan and best available information on the temporal and spatial co-location of listed species with respect to the action area. This analysis has not been conducted for this assessment. **An endangered species effect determination will not be made at this time.**

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<sup>1</sup> The Agency is making this statement because triclosan and triclosan transformation products are being detected in various environmental components (see triclosan environmental fate chapter).

## **9.0 INCIDENT REPORT ASSESSMENT**

The Following databases were consulted for poisoning incidence data on OPP:

- 1) Office of Pesticides Programs (OPP) Incident Data System (IDS)
- 2) Poison Control Centers
- 3) California Department of Pesticide Regulations
- 4) National Pesticide Telecommunications Network (NTPT)
- 5) Published Scientific Literature on Incidences

### **9.1 OPP's Incident Data System (IDS)**

There were no reported incidents from examination of this database.

### **9.2 Poison Control Center**

There were no reported incidents from examination of this database

### **9.3 California Data- 1982-through 2003.**

There were no reported incidents from examination of this database

### **9.4 National Pesticide Telecommunications Network (NPTN)**

There were no reported incidents from examination of this database

### **9.5 Hazardous Substances Data Bank (HSDB)**

There were no reported incidents from examination of this database.

## 10.0 References

### Ecotox REFERENCES

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