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High Production Volume (HPV) Chemical Challenge Program Data Availability and Screening Level Assessment

for

Triclocarban

CAS #: 101-20-2

Prepared for the HPV Challenge Program by:
The TCC Consortium
December 27, 2002

High Production Volume (HPV) Chemical Challenge Program
Data Availability and Screening Level Assessment

Triclocarban
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Abbreviations:

BCF	Bioconcentration factor
CAS	Continuous Activated Sludge or Chemical Abstract Service
E-FAST	Exposure and Fate Assessment Screening Tool
GC/MS	Gas chromatography/mass spectroscopy
LC	Liquid chromatography
MSHA	Mine Safety and Health Administration
NIOSH	National Institute of Occupational Safety and Health
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NOEL	No Observed Effect Level
MOE	Margin Of Exposure
OECD	Organization for Economic Cooperation and Development
PEC	Predicted Environmental Concentration
PNEC	Predicted No Effect Concentration
SIDS	Screening Information Data Set
WWTP	Wastewater treatment plant

[1] Executive Summary

[1.1] Sponsor Companies

The Triclocarban (TCC) Consortium, managed by the Soap and Detergent Association (SDA), includes the following member companies: Bayer Corporation and Clariant Corporation BU-IV Biocides.

[1.2] CAS Number: **101-20-2**

[1.3] Substance Name: Triclocarban
TCC
Urea, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)
3,4,4'-Trichlorocarbanilide

[1.4] Structure and Synthesis

($C_{13}H_9Cl_3N_2O$):

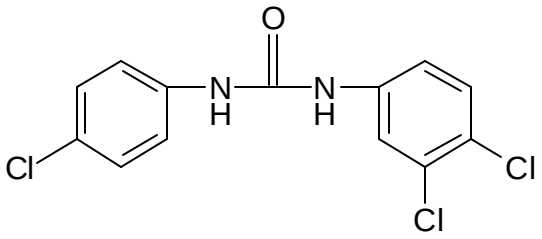

Figure 1. Structure of Triclocarban

There are two commercial routes used for the production of TCC:

1) 4-chlorophenyl isocyanate [CAS# 104-12-1] is reacted with 3,4-dichloroaniline [CAS# 95-76-1] to give TCC.
   or
2) 3,4-dichlorophenyl isocyanate [CAS# 102-36-3] is reacted with 4-chloroaniline [CAS# 106-47-8] to give TCC.

The purity specification in the draft USP monograph for TCC is: not less than 97.0% w/w. The purity of commercial production is > 98% w/w.

[1.5] Production Volume

Total tonnage of CAS# 101-20-2 [Urea, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl] reported in the 1998 IUR, from EPA's info on non-confidential report, was greater than 500,000 to 1,000,000 pounds/year (250 - 500 metric tonnes/year).

[1.6] Use Pattern and Function

TCC is an anti-microbial active ingredient used globally in a wide range of personal cleansing products that include deodorant soaps, detergents, cleansing lotions, and wipes. In North America, TCC is used exclusively as an antimicrobial and preservative in bar and liquid soaps and body washes.

[1.7] Environmental Screening Level Assessment

TCC is slightly soluble in water and non-volatile. It has been demonstrated to be inherently biodegradable and extensively removed (98%) during wastewater treatment through a combination of sorption and biodegradation processes. The potential for TCC to bioaccumulate in fish is low, having a bioconcentration factor (BCF) of 137 (whole fish wet weight) and 13 (muscle), indicating that TCC is readily metabolized and excreted.

The environmental fate of TCC during the main phase of its life-cycle (processing, and consumer use) was modeled using Exposure and Fate Assessment Screening Tool (E-FAST), a U.S. EPA screening level exposure assessment model. In addition, extensive environmental monitoring of TCC in wastewater, sewage treatment facilities and in surface water has been conducted over the last 20 years. Predicted Environmental Concentrations (PEC) from the environmental modeling work and field measurements range from 0.0013 to 0.050 µg/L, depending on the assessment scenario.

TCC has been the subject of extensive acute and chronic ecotoxcity studies that have included algae, aquatic invertebrates, and fish. Aquatic invertebrates were found to be the sensitive taxa to TCC exposure from this data-set. The ecotoxicity endpoint employed in the TCC aquatic risk characterization was a 7-day *Ceriodaphnia* study that resulted in a chronic No Observed Effect Concentration (NOEC - defined as the highest concentration that causes an effect that is not statistically significantly different from the controls) of 1.46 µg/L. Given the extensive acute and chronic ectotoxicity database for TCC, the U.S. EPA recommends an assessment factor of 10 be applied to the chronic toxicity value in order to account for various uncertainties in the measured data. This results in a Predicted No Effect Concentration (PNEC) of 0.146 µg/L.

The risk to the aquatic environment is characterized by comparing the PEC to the PNEC. If the concentration in the surface water is less than the no effect concentration, then the potential for adverse effects is low. Integrating all the information currently available, the modeled and measured TCC surface water PEC does not exceed the PNEC. The risk characterization ratios (PEC/PNEC) range from 0.009 to 0.34 depending on the scenario used. The higher PEC/PNEC values are from scenarios where low surface water dilution of treated wastewater occurs. These

ratios, which are all less than 1, confirm that the potential for adverse environmental effects from the use TCC is very low.

[1.8] Human Health Screening Level Assessment

An extensive database of toxicology studies exists on TCC. These studies include both Screening Information Data Set (SIDS) and beyond-SIDS endpoints, and collectively demonstrate that this material possesses a low order of toxicity. Acute toxicity studies show that TCC is not measurably toxic by the oral or dermal routes. Studies indicate this material can be slightly irritating to eyes and non-irritating to the skin. TCC did not produce sensitization when investigated in 50 human volunteers using the Shelanski Patch Test method. TCC was also neither a primary irritant or a fatiguing agent.

The potential for systemic toxicity and functional alterations resulting from repeated exposure to TCC was evaluated in subchronic and chronic toxicity studies by the oral exposure route in rats. No adverse effects were seen in rats dosed at 1000 mg/kg bw/day for 30 days. A chronic (24 month) oral study in rats demonstrated testicular degeneration, anemia, and microscopic changes in various organs at 75 mg/kg bw/day. A No Observed Effect Level (NOEL) was established at 25 mg/kg bw/day. A three generation oral study in rats demonstrated no effect on mating indices and male fertility at all doses tested. The pregnancy rates for all groups (except second litter of the F1 generation at the highest dose) were comparable to the control group. No treatment-related effects were seen on any pups from all generations.

An assessment of the *in vitro* genotoxicity potential of TCC shows no evidence of mutagenic or clastogenic activity. A carcinogenicity study in rats demonstrated no evidence of a dose-related increase in tumor incidence at any site.

In summary, the toxicological profile of TCC indicates that the material has a low order of toxicity, based on a variety of acute, sub-chronic, and chronic studies.

[1.8.1] Exposure Data

TCC is used in personal cleansing products as an antimicrobial ingredient. Based on this use, workers and consumers may be exposed to TCC although the type of exposure for these two populations is different.

Worker Exposure

For workers, inhalation and dermal exposure to TCC during the production, formulation, or transportation process is limited due to the low volatility of TCC and the industrial hygiene standards and personal protective equipment that are utilized as a standard practice in production facilities. Employee exposure is minimized through engineering controls and good industrial hygiene practices. Processing experience with a variety of ingredients in the manufacturing of personal cleansing products confirms that these practices are effective in minimizing worker exposure.

Consumer Exposure ***(Direct Exposure)***

The potential for consumer exposure to TCC is very limited. Based on the chemistry and low level of deposition there is negligible consumer exposure to this material under recommended use situations (see Table 1.2). This assessment is based on a thorough attempt to identify the intended and reasonably foreseeable uses for personal care products containing this material and to assess those resultant exposures. The most relevant and anticipated exposure for TCC to consumers is by dermal exposure. Dermal exposure can result from hand, face or body washing with either bar soap, liquid soap, or body wash containing TCC. Due to the rinse-off nature of this product type, a low level of deposition of the material is anticipated. For example, the consumer is estimated to be exposed to only 1.4% of the applied TCC when a bar soap containing 1.5% TCC is used under normal circumstances (North-Root et al., 1984). Based on the results of a Soap and Detergent Association Use and Exposure Survey (SDA, 2002), bar soaps contain levels of TCC which range from 0.5 to 5% in the final formulation, liquid soaps contain TCC at levels ranging from 1 to 5% and body washes may contain from 0.1 – 0.5% in the final formulation. It is worth noting that the range of TCC in product identified here for the exposure assessment is broad due to the reporting ranges used in the SDA survey. Actual concentrations in bar soaps are expected to be limited to a maximum of 1.5%. Regardless, the upper end of each range for TCC was used to estimate the "worst case" exposure where washing the face, hands and body was assumed for each of these product types. Hence, a bar soap containing 5% TCC is estimated to result in exposure of 0.001 mg TCC/kg bw/day. Exposure from liquid soaps used for washing the hands and body also result in an estimate of 0.001 mg TCC/kg bw/day. Body washes formulated with TCC contain the lowest level of this ingredient and under the "worst case" scenario may result in an exposure of 0.0001 mg TCC/kg bw/day. For these dermal exposures, an absorption value of 0.39% was used based on published work conducted by Scharpf et al. in 1975. No inhalation exposure to the consumer is expected due to the low vapor pressure of TCC. Additionally, there is no anticipated oral exposure under recommended use conditions.

Consumer Exposure ***(Indirect Exposure)***

No inhalation exposure is anticipated due to the low vapor pressure of TCC. Exposure calculations based on estimates of TCC in drinking water using the EPA's E-FAST model resulted in estimated values of 1.38×10^{-6} mg/kg bw/day. E-FAST provides screening level estimates of concentrations of chemicals released to the environment from consumer products and is designed to provide high end to bounding estimates of exposure as is appropriate for screening level risk characterizations. Indirect exposure to TCC from ingestion of fish was also determined to be negligible because the potential for TCC to bioconcentrate is minimal based on a BCF of 138 (whole fish wet weight) and 13 (muscle).

Children's Exposure ***(Direct Exposure)***

Exposure of children to TCC is anticipated based on the recommended use of the personal cleansing products that utilize TCC. As with adults, the dermal route is the main pathway by which children would be exposed to TCC. For all exposure assessments, a child's body weight of 10 kg was assumed based on data released by the Center for Disease Control in 2002

(National Health and Nutrition Examination Survey Results (NHANES), 2002). A 10 kg child represents a 95th percentile 7 month old boy. Additionally, for these dermal exposures, an assumption of 0.39% absorption is made based on published work (Scharpf et al., 1975). Hence, a bar soap containing 5% TCC is estimated to result in exposure of 0.005 mg TCC/kg bw/day. Exposure from liquid soaps used for washing the hand and body result in an estimate of 0.006 mg TCC/kg bw/day. Body washes formulated with TCC contain the lowest level of this ingredient and under the "worst case" scenario may result in an exposure of 0.0004 mg TCC/kg bw/d.

Children's Exposure ***(Indirect Exposure)***

No inhalation exposure is anticipated due to the low vapor pressure of TCC. There may be accidental ingestion of bars, liquid soaps or body washes containing TCC by children; however, these would be infrequent and would result in mild transient symptoms, if any are present, such as nausea, vomiting and/or diarrhea. Such effects would be consistent with the effects observed following accidental ingestion of other surfactant based products and could be attributed to the surfactant and not TCC.

Summary of Human Health Assessment:

The data summarized above demonstrate that TCC has an acceptable safety profile for use in personal cleansing products. The risk to human health is characterized by comparing the estimated human exposure to the NOEL from animal studies. The amount by which the NOEL exceeds the estimated exposure is referred to as the margin of exposure (MOE). The MOE should be sufficiently large to account for several sources of uncertainty and variability in extrapolating data from animal studies to humans. Based on the data presented, no adverse effects for humans are expected via any relevant exposure route. The "worst-case" dermal exposure to TCC would result from use of a liquid soap containing TCC for all hand and body washings daily by a 10 kg child. This scenario results in an estimated exposure of 0.006 mg TCC/kg bw/day (see "Children's Exposure" section above for more details). For potential oral exposure, if one assumes that TCC would be present in drinking water and not removed in wastewater treatment facilities, the calculated exposure using E-FAST would be 1.38×10^{-6} mg/kg bw/day. The NOEL in the oral chronic study was 25 mg/kg bw/day. Comparing the estimated oral exposure to the oral NOEL results in an MOE of many orders of magnitude difference, even after accommodating inter- and intra-species variation. In evaluating this conservative estimate, the MOE is acceptable.

[1.9] HPV Endpoint Data Assessment

Each of the reports obtained was reviewed to determine adequacy according to EPA criteria and reliability per Klimisch *et al.* (1997). Robust summaries were prepared for SIDS endpoints, as well as several relevant beyond SIDS endpoints, with available and reliable data for TCC. These summaries are provided in Appendix A and are identified in Table 1.1.

Table 1.1. HPV Endpoint Data Assessment

ENDPOINT	Data Available	Data Reliable *
Physical Chemical Characteristics		
Melting Point	Yes	Yes
Boiling Point	Yes	Yes
Vapor Presure	Yes	Yes
Partition Coefficient	Yes	Yes
Water Solubility	Yes	Yes
Environmental Fate		
Photodegradation	Yes	Yes
Stability in Water	Yes	Yes
Transport (Fugacity)	Yes	Yes
Biodegradation	Yes	Yes
Ecotoxicity		
Acute Toxicity to Fish	Yes	Yes
Acute Toxicity to Aquatic Invertebrates	Yes	Yes
Acute Toxicity to Aquatic Plants	Yes	Yes
Mammalian Toxicity		
Acute Toxicity	Yes	Yes
Genetic Toxicity: Ames	Yes	Yes
Genetic Toxicity: Chromosome Aberration	Yes	Yes
Repeated Dose Toxicity	Yes	Yes
Reproductive Toxicity	Yes	Yes
Developmental Toxicity/Teratogenicity	Yes	Yes
Non-SIDS Endpoints		
Eye Irritation	Yes	Yes
Skin Irritation	Yes	Yes
Skin Sensitization	Yes	Yes
Carcinogenicity	Yes	Yes

* In accordance with the HPV Guidelines (U.S. EPA, 1999) (i.e. Determining Adequacy of Existing Data) (U.S. EPA, 1999), data reliability was established following the criteria described by Klimisch and others (1997).

[1.10] Sponsor's Conclusions and Recommendation

The available data on TCC hazard and exposure demonstrates that there is negligible likelihood of harm to man and the environment during manufacture of TCC and formulation and use of personal cleansing products containing TCC (See Tables 1.2 and 1.3). Data for all SIDS and other relevant endpoints are available, reliable and demonstrate that the material possesses a low order of toxicity. Aquatic PEC/PNEC ratios for TCC ranged from 0.009 to 0.34 and confirm that the potential for adverse effects to the environment are very low. Exposure to TCC in the workplace is limited due to low vapor pressure of TCC and through engineering controls and good industrial hygiene practices. Consumer evaluations indicate that MOE are acceptable and calculations supporting these estimates are conservative. Considering the completeness, accuracy, and relevance of both the hazard and exposure evaluations, TCC is concluded to be sufficiently studied and recommended as a low priority for further work.

Table 1.2. Consumer Risk Characterization

ROUTE	EXPOSURE	RESULTING DOSE*	NOEL	MOE
Dermal				
bar soap	0.1 mg /kg bw/day	0.005 mg/kg bw/day	25 mg/kg bw/day	5000
liquid soap	0.11 mg/kg bw/day	0.006 mg/kg bw/day	25 mg/kg bw/day	4167
bodywash	0.07 mg/kg bw/day	0.0004 mg/kg bw/day	25 mg/kg bw/day	62,500
Oral				
Drinking water	Not applicable	1.38×10^{-6} mg/kg bw/day**	25 mg/kg bw/day	18,115,942

* The resulting dose takes into account the estimated dermal absorption of TCC of 0.39% based on a published report (Scharpf et al, 1975).

** The resulting dose was calculated using EPA's E-FAST model.

Table 1.3. Environmental Risk Characterization

	PEC (? g/L)	PNEC (? g/L)	PEC/PNEC ($10^{th}/50^{th}$ percentile)
Measured	0.050 (high end)	0.146	0.34
Calculated	0.0013 (median) 0.017 (high end)	0.146 0.146	0.009 0.116

[2] Environmental Assessment

[2.1] Introduction

The environmental hazard assessment is based on a combination of modeling, laboratory studies and actual field monitoring to establish the key environmental fate pathways and characterize TCC ecotoxicity. Each of the study reports used for this assessment was reviewed to determine adequacy according to U.S. EPA criteria and reliability as per Klimisch et al. (1997). Robust summaries were prepared for each report with the scores assigned according to the guidelines recommended by the U.S. EPA (U.S. EPA, 1999) for each study type. These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. Robust summaries for endpoints with available and reliable data for TCC are provided in Appendix A (IUCLID data set). Data essential for the environmental risk characterization of TCC is summarized in Tables 2.1 to 2.3.

Table 2.1. Physical/Chemical Property Data

PARAMETER	RESULT	Unit	REFERENCE
Molecular Weight	315.6	g/mol	Hawley's Chemical Dictionary, 11th ed.
Melting Point	250	°C	Hawley's Chemical Dictionary, 11th ed.
Boiling Point	>300	°C	MPBWIN ver1.65, EPIWIN Estimation Program; adapted Stein and Brown Method
Density	650	kg/m^3	Bayer AG data
Vapor Pressure	<1	hPa at 50°C	Bayer AG data ; MPBWIN ver1.65, EPIWIN Estimation Program; Modified Grain Method
Partition Coeffiecient	4.2	Log P_{ow}	OECD Guideline 117, Bayer AG data
Water Solubility	11	mg/L @ 20 degree C	Directive 92/69/EEC, A.6; Bayer AG data

Table 2.2. Environmental Fate and Pathway Data

ENVIRONMENTAL FATE and PATHWAY	RESULTS	PROTOCOL
Photodegradation	50% after 0.5 days; not likely a significant degradation mechanism given low vapor pressure	Calculated AopWin v 1.89, EPIWIN Estimation Program
Hydrolysis	Half-life > 1 year	HYDROWIN v1.67, EPIWIN Estimation Program
Organic Carbon-Normalized Sorption Coefficient (Koc) Koc = Kd/foc	Activated sludge: 54,800 (Kd=17,320 L/kg, foc=0.316) Lagoon effluent: 111,965 (Kd=45.346, foc=0.405) Simulated river water: 111,965 (Kd=45.346, foc=0.405)	Other: based on batch equilibrium sorption experiments (Procter & Gamble Report #E98-001)
Biodegradation	0% after 28 days	OECD Guideline 301C
	100% after 10 hours; 50% mineralization of 4-chloroaniline and 3,4-dichloroaniline rings	Other: Shake-flask method with adapted activated sludge (Gledhill, 1975)
Ultimate Removability	98% removal of TCC; 56% mineralized as CO_2	Continuous activated sludge (CAS) (Gledhill, 1975)
Transport and Distribution between Environmental Compartments	Water: 70.2% Sediment: 29.8% Air: 0% Soil: 0%	Calculated Fugacity Level II Type (local exposure, EQC model) (Mackay et al., 1996)

Table 2.3. Environmental Toxicity Data*

ECOTOXICITY	SPECIES	RESULT	PROTOCOL
Toxicity to Aquatic Plants (Algae)	***Navicula pelliculosa***	Minimum Algistatic Concentration (MAC, 5 day) = 6 ?g/L	Method based on Payne and Hall (1979), Monsanto study #BP-90-9-151R
Chronic Toxicity to aquatic Invertebrates	***Ceriodaphnia dubia***	NOEC (21 day) = 1.46 ?g/L	OECD Guideline 202
Chronic toxicity to fish	***Pimephales promelas***	NOEC (35 day) = 5 ?g/L	Critcal Life Stage Test (Monsanto, 1992)

*Only the key studies essential for the environmental risk characterization of TCC are presented in the table. Please see Appendix A for Robust Summaries of these studies and Appendix B for the complete list of all available ecotoxicity studies.

[2.2] Fugacity Modeling

Fugacity modeling was performed to estimate the transport and distribution of TCC into environmental compartments. Given that TCC is predominantly used in personal care products with a down-the-drain disposal route, water is the main entry compartment for this chemical. To model the partitioning of TCC upon its entry to the aquatic compartment, Level III EQC model (Mackay et al., 1996) was used with the chemical input parameters shown in Table 2.1. TCC is not readily biodegradable, however, it is biodegradable inherently, with the mineralization rate of 50% after 10 hour incubation in adapted domestic activated sludge (Gledhill, 1975, Table 2.2). For this type of substance, the Interim U.S. EPA Guidance recommends using an aquatic half-life ($t_{½}$) of 100 days in multimedia models. Likewise, following the recommendations of the Guidance, the half-lives for the sediment and soil compartments were 100 days and 400 days, respectively. The EQC model predicted that 70% of TCC released to the aquatic compartment would stay there, with the rest partitioning to sediment (Table 2.2). The fraction partitioning to the atmosphere is negligible. Thus, the aquatic compartment is the key environmental compartment for TCC. The environmental risk characterization of TCC presented in this document therefore focuses on the aquatic compartment.

[2.3] Environmental Fate

[2.3.1] Summary of Biodegradation Data

Even though TCC is not readily biodegradable, it was shown to biodegrade in adapted activated sludge, with 100% loss of the parent compound and 50% mineralization rate (Gledhill, 1975). This is supported by the data from the Continuous Activated Sludge (CAS) study, where the removal of TCC was 98% with mineralization (measured as CO_2) accounting for 56% of the total loss (Gledhill, 1975).

[2.3.2] Removal of TCC in Wastewater Treatment Plants

Calculated:

Sorption to activated sludge and biodegradation are expected to be the key removal processes of TCC during wastewater treatment. For compounds with inherent biodegradation test results between 20 and 70%, the Interim U.S. EPA Guidance recommends using a wastewater treatment half-life of 30 hours, which corresponds to a biodegradation rate (k1) of 0.023/hour. The measured sorption coefficient (Kd) of TCC in activated sludge is 17,320 (Table 2.2). The parameters were used in the AS-Treat model to calculate the removal of TCC during wastewater treatment. AS-Treat is a customized version of the SimpleTreat model (Struijs, 1996) allowing for the direct use of Kd and k1. The model predicted the total removal rate of TCC of 63.4%, of which 59.7% was via sorption to sludge and 3.75% due to degradation. This calculated removal rate was lower than the measured removal rates in the CAS study and monitoring studies (see below), probably due to the conservative biodegradation rate used in the model (the CAS study showed that at least 56% of the total removal was due to biodegradation (Table 2.2.) compared to 3.75% predicted by the model).

Monitoring:
TCC removal values obtained from actual measurements taken from activated sludge systems in the U.S. and Europe are presented in Table 2.4. Based on a combination of the CAS study results (Table 2.2.) and monitoring data, an activated sludge removal estimate of 94% was established for this assessment.

Table 2.4. Removal of TCC in Trickling Filter (TF) and Activated Sludge (AS) wastewater treatment plants based on environmental monitoring data in the U.S. and UK.

TREATMENT	Influent µg/l	Effluent µg/l	Removal (%)	Basis
Trickling Filter	15 (n = 6)	5 (n = 6)	65 (n = 3)*	Dayton OH (MSL-1759)
Trickling Filter	27	2	93*	North East/Pensacola FL (MSL-1441)
Trickling Filter	-	7 (n = 3)	-	South East/Lubbock TX (MSL-1442)
TF ($^2/_3$) + AS ($^1/_3$)	50	12	76*	Montclair/Pensacola FL (MSL-1441)
Trickling Filter	0.4	0.076	81	U.K. Stretford Plant (Shuguang Ma 1997)
Trickling Filter	16.3	4.82	70	Glendale OH (Shuguang Ma 1997)
Average TF			**77**	
Activated Sludge	42	5	88*	Main Street/Pensacola FL (MSL-1441)
Activated Sludge	-	4 (n = 3)	-	#1 & #2/Bakersfield CA (MSL-1442)
Activated Sludge	200	~ 6	98	CAS data (Gledhill, 1975)
Activated Sludge	14.5	0.54	96	Polk Run (Shuguang Ma 1997)
Average AS	-	-	**94**	

*Calculated removals were based on analysis of grab samples. These removals should be considered only an indication of actual removal rates because large fluctuations in influent concentrations as a function of time are expected.

[2.3.3] Ecosystem Exposures Related to Manufacturing and Formulation of Triclocarban- Containing Products

Manufacture:
There is no TCC manufacture in the U.S.; TCC is imported to the formulation facilities. Hence, this document only discusses the manufacturing processes of the major importers. Total estimated TCC volume imported to the U.S., as identified though information from EPA's non-confidential 1998 IUR, is 250 - 500 metric tonnes/year.

Formulation:
TCC is received by the production facilities in 500 kg "supersacks". With the current 3-shift production process, 10 supersacks are used per week, or 260,000 kg per year, approximately one third total U.S. volume. TCC enters the totally closed, dust-free and dedicated production process at the mixer phase. Product at this process stage is a low moisture (~10%) solid being extruded through the product line by rotating screws and air. Only two processes remain after TCC addition, milling and packing. Both processes have dust control measures to contain TCC-containing product (~1%). Waste TCC is kept to a minimum by recycling finish product shavings, dust control systems, and a totally enclosed production process. There is no TCC-containing wastewater disposal from cleaning or production processes. A minimum amount of bulk TCC may be spilled with the opening of each supersack. This material is swept up immediately and disposed to the solid waste stream. This waste material does not enter the aquatic compartment and does not affect the assessment presented in this document.

[2.3.4] Ecosystem Exposures Related to Consumer Use and Disposal of Products Containing TCC

[2.3.4.1] Usage in Consumer Products

The total estimated TCC volume imported to the U.S., from EPA's non-confidential 1998 IUR, is 250 - 500 metric tonnes/year. However, the volume used in the environmental and human health assessments was set at 750 metric tones/year as this represents the upper range of reporting in the 1990 IUR and could represent the upper range of use in the U.S.

[2.3.4.2] Consumer Product Releases - Influent Concentration

The concentration of TCC in the effluent from consumer homes is calculated assuming per capita water use is 364 l/cap/day and a U.S. population of 250 million people (defaults from U.S. EPA E-FAST Down-the-Drain scenario). Assuming no loss of TCC in the sewage collection and conveyance system, the influent concentration to the wastewater treatment plant is assumed to be equal to the effluent concentration from the home.

The influent concentration (I) is calculated using the equation:

$$\mathbf{I = D/ (a)(b)(c)}$$

where:

D = amount of chemical used per year in consumer products
a = number of days in year
b = water used per capita, and
c = total population

Using this equation the influent concentration of TCC is calculated as:

I = 750,000 kg/yr (10E6mg/kg)/(365 d/y)(364 l/cap/day)(2.5E8 people)
I = 0.02258 mg/L
I = 22.6 µg/L

The average measured influent TCC concentration at a Dayton, OH trickling filter wastewater treatment plant (WWTP) was 15.4 µg/L based on samples collected over a three day period (MSL-1759) and influent levels at three treatment plants in Pensacola, FL ranged from 27 to 50 µg/L (MSL-1441). These measurements were made in the 1980's. More recently, influent concentrations at two U.S. treatment plants were 14.55 and 16.32 ?g/L for an activated sludge and trickling filter plant, respectively. These measured influent concentrations are comparable to measurements made approximately 15 years ago and demonstrate that TCC use has remained constant in the US. The average of the measured influent concentration was 15.4 ug/L, agreeing quite nicely with the predicted values. The slight discrepancy between the predicted value and the actual measured values can be explained in part by: 1) loss of TCC during wastewater conveyance systems (sorption/biodegradation); and/or 2) not all of the manufacturing volume of TCC is disposed down-the-drain.

[2.3.4.3] Summary of Predicted and Measured Surface Water Concentrations

Predicted Concentrations:
The U.S. EPA Exposure E-FAST model was used to calculate the concentrations of TCC in surface waters. The key input parameters in the down-the-drain exposure scenario of the model were the estimated TCC usage rate in the U.S. (750 t/y, section 2.3.4.2) and the wastewater treatment removal rate of 94% (section 2.3.2). The predicted median surface water concentration of TCC was 0.0013 ?g/L, and the high-end concentration was 0.017 ?g/L.

Measured Concentrations:
Illustrated in Figure 2.1 is the distribution of TCC concentrations measured in U.S. freshwater environments during the 1979 (78 sites) and 1982 (30 sites) samplings (MSL-1264 & ES-84-SS-6). These data indicate that > 90% of the freshwater surface waters in the U.S. contained a TCC concentration of < 0.05 µg/L.

Less intensive sampling efforts were also conducted during 1985 and 1987 at six locations previously sampled during 1979 and 1982. TCC concentrations ranged from <0.001 µg/L to 0.194 µg/L for the 1985 sampling (MSL-5342). The range of concentrations observed during the 1987 sampling was <0.074 µg/L to 0.228 µg/L (MSL-7813). The use of a less sensitive analytical method for the 1987 sampling limits comparisons to previous data. Data from 1985 and 1987 are summarized in the Table 2.5. Note that the concentrations in the table are given in nanograms/litre and are measured using liquid chromatography (LC) and gas

chromatography/mass spectroscopy (GC/MS). Many of the locations sampled during this period did not have advanced wastewater treatment in place. Improved wastewater treatment systems in these areas would likely improve TCC removal in wastewater and result in decreased levels of TCC in WWTP effluents.

Based on the results from the monitoring studies in 1979, 1982, 1985 and 1987, the TCC concentration of 0.05 ?g/L should be regarded as a high-end predicted concentration in surface waters (PEC). Given that the consumption of TCC has remained constant over the last 15 years (see section 2.3.4.2), this estimate should also adequately reflect the present situation. This estimate is slightly higher than the calculated concentrations of TCC using the E-FAST model and is likely due to the fact that sites more prone to contamination by industrial and household chemicals were selected for environmental monitoring studies.

Robust Summaries of the monitoring studies mentioned in this section are presented in Appendix A of this document.

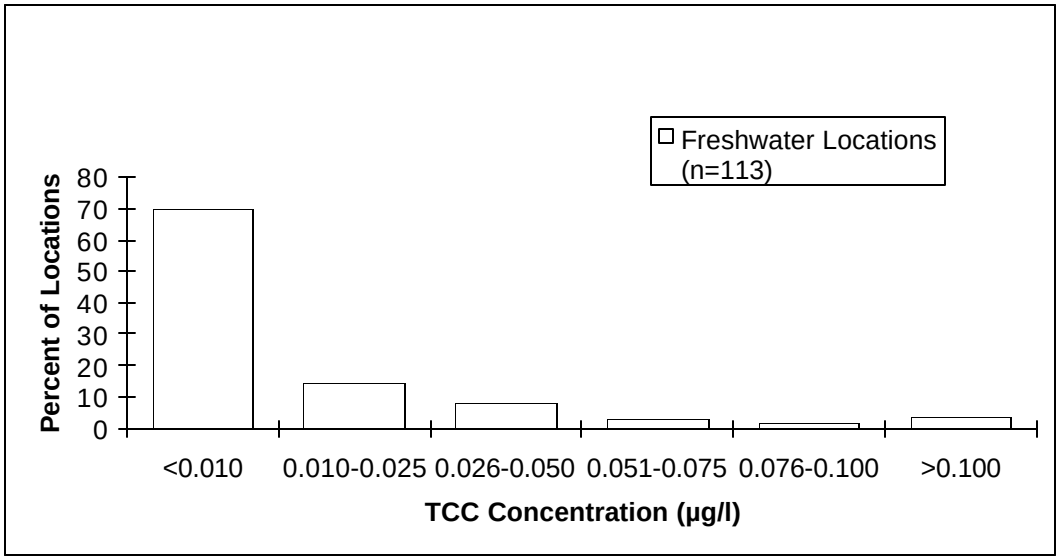

Figure 2.1 Measured Concentrations of TCC in U.S. Surface Waters in 1979 and 1982.

Table 2.5. Measured Concentrations of TCC in U.S. Surface Waters in 1985 and 1987.

SITE	LC (ng/l)	GC/MS (ng/l)
Fall 1987		
Delaware River (Philadelphia Harbour) PA	98 – 179	<74 – 218
Delaware River (Easton) PA	<81	-
Conn. River (Glastonbury) CN	<81	-
Conn. River (Hartford) CN	<81 – 228	-
Charles River (Needham) MA	<81 – 118	<74
Charles River (Boston Harbour) MA	<81	-
Fall 1985		
Delaware River (Philadelphia Harbour) PA	57 – 110	100 - 194
Delaware River (Easton) PA	2 – 15	26 - 134
Conn. River (Glastonbury) CN	24 – 32	58 - 81
Conn. River (Hartford) CN	23 – 41	34 - 57
Charles River (Needham) MA	<1 – 9	<20
Charles River (Boston Harbour) MA	51 – 89	63 - 77

[2.4] Ecotoxicity

The key ecotoxicity data for TCC are summarized in Table 2.3 above, and the complete list of all available studies are presented in Appendix B. Robust summaries of these studies are presented in Appendix A.

The most sensitive taxa to TCC exposure are aquatic invertebrates. This conclusion is supported by both acute and chronic toxicity information from testing done on a wide range of organisms. The ecotoxicity endpoint employed in the TCC aquatic risk characterization was a 7 day *Ceriodaphnia* study conducted in aged, blended water (Procter & Gamble, ABC # 43812). This endpoint was chosen as it represents an organism from the taxa that is most sensitive to TCC exposure and it is an end point that was developed using standard chronic toxicity test methods. This study resulted in a NOEC of 1.46 µg/L and was completed in 1997 by ABC Labs, Columbia, Mo. TCC exposure concentrations were determined using LC/MS by ABC Analytical. TCC levels that show an adverse effect to fish, the next most sensitive taxa, are at least an order of magnitude greater than those observed for aquatic invertebrates.

Given the abundance of acute and chronic aquatic toxicity data on TCC covering all the key taxonomic categories (algae, invertebrates, fish), an application factor of 10 was deemed appropriate for use in this risk characterization, resulting in the aquatic Predicted No-Effect Concentration (PNEC) of 0.146 ? g/L.

[2.5] Environmental Screening Level Assessment

Environmental risk characterization of TCC in the aquatic compartment (ratios of PEC/PNEC) is presented in Table 2.6. Based on both calculated and measured concentrations of TCC, the ratio of PEC/PNEC is below 1. It can be concluded, therefore, that TCC is safe for the aquatic environment at its current rate of consumption.

Table 2.6. Risk Characterization of TCC.

	PEC (? g/L)	PNEC (? g/L)	PEC/PNEC (10^{th}/50^{th} percentile)
Measured	0.050 (high end)	0.146	0.34
Calculated	0.0013 (median)	0.146	0.009
	0.017 (high end)	0.146	0.116

[3] Human Health Assessment

[3.1] Introduction

Each of the reports obtained was reviewed to determine adequacy according to EPA criteria and reliability per Klimisch *et al.* (1997). Robust summaries were prepared for each report with Klimisch scores assigned according to the guidelines recommended by the EPA (U.S. EPA, 1999) for each study type. Robust study summaries for SIDS endpoints, as well as several relevant beyond SIDS endpoints, with available and reliable (according to Klimisch criteria) data for TCC are provided in Appendix A and are summarized in Tables 3.1. and 3.2.

Table 3.1. Summary of SIDS Endpoints

ENDPOINT	SPECIES	RESULTS	PROTOCOL
Acute Oral Toxicity	Rat	LD_{50} >2000 mg/kg bw	Directive 84/449/EEC, B.1
Acute Dermal Toxicity	Rabbit	LD_{50} >10000 mg/kg bw	Other (Monsanto Study # Y-63-23)
Repeat Dose Toxicity	Rat	NOAEL = >1000 mg/kg bw	Oral gavage, exposure: 5days/week/30days, 10 rats/sex/group
Genetic Toxicity: Gene mutation	*Salmonella typhimurium* strains TA 98, 100, 1535, 1537	negative	OECD Guideline 471, With and without metabolic activation
Genetic Toxicity: Chromosome Aberration	Chinese hamster ovary (K-1) cells	negative	EPA OPPTS 870.5375, With and without metabolic activation
Reproductive Toxicity	Rat	NOAEL P = 3000 ppm NOAEL F1 = 1000 ppm NOAEL F2 = 3000 ppm	Three generation reproduction study
Developmental Toxicity	Rat	NOAEL >3000 ppm	Three generation reproduction study

Table 3.2. Summary of Beyond SIDS Endpoints

ENDPOINT	SPECIES	RESULTS	PROTOCOL
Eye Irritation	Rabbit	Slightly-irritating	undiluted, 24 hr. (modified Draize)
Skin Irritation	Rabbit	Non-irritating	25% suspension in corn oil, 24 hr. occluded (Draize)
Sensitization	Human	Not- sensitizing	Shelanski method (Monsanto Study #SH-63-7)
Carcinogenicity	Rat	No evidence of dose-related increase in tumors at any site	EPA OTS 798.3320

[3.2] Summary of Hazard Assessment

The following toxicology data are provided in support of the use of TCC in consumer soaps. A summary of each study is presented below. Additional information on these studies, in the form of robust summaries, is provided in Appendix A.

SIDS Endpoints

[3.2.1] Acute Oral Toxicity in Rats

An acute oral LD_{50} toxicity study was conducted on TCC. A single dose of 2000 mg/kg bw test material was administered in polyethylene glycol 400 to rats by oral gavage. All animals (5 rats/sex/group) were observed for mortality and clinical signs at 0.5, 1, 2, and 4 hours after dosing and daily thereafter for 14 days.

There were no deaths in any group, therefore the oral LD_{50} for male and female rats is > 2000 mg/kg bw.

[3.2.2] Acute Dermal Toxicity in Rabbits

The acute percutaneous toxicity of TCC was investigated in rabbits. The diluted compound was applied in increasing doses at 0.2 fractional log intervals to the closely clipped, intact skin of New Zealand white male and female rabbits. The treated areas were covered with plastic strips and the animals placed in wooden stocks for periods up to 24 hr, after which time they were

assigned to individual cages. Observations were made for toxic symptoms and, since there were no deaths, no autopsies were performed. The dermal LD_{50} of TCC is greater than 10,000 mg/kg bw.

[3.2.3] Subchronic (30 day) Oral Study

A subchronic feeding study was conducted to assess the potential for systemic toxicity after repeated exposure to TCC. The test substance was administered as a 25% aqueous solution at 500 or 1000 mg/kg bw by gavage, 5 days per week for a thirty day period. Food consumption and weight gain were recorded weekly and observations were made for outward symptoms of toxicity such as reduced activity and non-grooming. At the end of the 30 day period, representative animals from each group were sacrificed.

The feeding of TCC to rats at a daily level of 1000 mg/kg bw, five days per week for thirty days, was not detrimental insofar as could be determined by food consumption, growth data, and tissue examination.

[3.2.4] Mutagenicity - Salmonella Reverse Mutation Assay (Ames Test)

The mutagenicity potential of TCC was evaluated using the *Salmonella* Reverse Mutation Assay (OECD Guideline 471) in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537. Test material concentrations ranged from 8-5000 ?g/plate in the preliminary toxicity dose range-finding studies and 125-4000?g/plate in the definitive studies. Appropriate positive, solvent and sterility controls were used.

The results of the Ames test indicate that under the condition of these studies, the test material did not show any evidence of mutagenic potential in any of the tester strains in the presence or absence of Arochlor-induced rat S9 liver microsomes.

[3.2.5] *In Vitro* Chromosomal Aberration Study

The objective of this study was to evaluate the clastogenic potential of TCC as manifested by the production of chromosomal abnormalities such as deletions, exchanges, rings and breaks in exposed Chinese hamster ovary (CHO-K1) cells. Mitomycin C and Cyclophosphamid were used as positive controls in the non-activated study and activated study, respectively. Test material concentrations ranged from 33-2000 ?g/ml in the study.

The study results indicate that the compound has no clastogenic potential under the conditions of this test.

[3.2.6] Reproductive and Developmental Toxicity

A study was conducted to determine the reproductive and teratogenic potential of TCC in rats in a three generation oral feeding study. TCC was administered for 60 days prior to initiation of mating in the parental generation and 80 days prior to initiation of mating in the F1 and F2 generations at one of the following doses: 250, 500, 1000, or 3000 ppm.

Body weights and food consumption were measured weekly during the study. Observations for mortality and adverse effects were done twice daily. Detailed physical exams were done weekly on all generations. All animals dying spontaneously or killed in a moribund condition were examined and tissues preserved in 10% formalin. Dead or stillborn pups were given a gross postmortem exam and preserved in 70% ethanol. All adult males and females were given a gross postmortem exam and tissues preserved. At weaning (day 21), pups not chosen as future parents were sacrificed and examined with only grossly abnormal tissues preserved. Data were analyzed between control and treated groups.

No treatment-related effect was evident on mortality or physical in-life evaluations. Body weight and food consumption were not adversely affected by treatment throughout the study. Mating indices and male fertility were not adversely affected by treatment for all generations. Pregnancy rates were comparable to controls for dose groups 250 - 1000 ppm. The pregnancy rate was unusually low for the high dose group (3000 ppm) during the second litter interval of the F1 generation only.

The Reproductive No Observed Adverse Effect Level (NOAEL) for Parental and F2 generations = 3000 ppm; NOAEL for the F1 generation = 1000 ppm. No treatment-related effects were seen on any pups from all generations (including dead pups). Litter viability and survival rates were comparable to controls. The NOAEL for teratogencity was greater than 3000 ppm.

Beyond SIDS Endpoints

[3.2.7] Primary Eye Irritation in Rabbits

TCC was evaluated for the potential to cause eye irritation by placing 20.0 mg of finely ground sample in the conjunctival sac of the right eye of each of three albino rabbits. The eyes were rinsed with warm isotonic saline solution after 24 hours. Observations for irritation were made over a period of several days. The data was scored according to the method of Draize.

The maximum average score was 7.3 out of a possible 110. TCC is considered slightly irritating to the eyes of rabbits.

[3.2.8] Primary Dermal Irritation in Rabbits

A dermal irritation study was conducted on TCC in rabbits. Finely ground powder as a 25% suspension in corn oil was applied to the clipped intact skin of albino rabbits and removed after

24 hours. The application was covered with plastic strips to retard evaporation and avoid contamination. Observations were made over a period of several days for irritation.

According to Draize scoring, the compound was classified as non-irritating.

[3.2.9] Dermal Sensitization

A dermal sensitization study was conducted on TCC in 50 human volunteers. Fifty (50) mg of substance was applied to the gauze portion of patches that were applied to the back of 50 subjects for 24 hours and repeated for 15 applications (with 24 hour rest periods between each repeat application). After a 2 week rest period, a challenge application of 50mg was applied to the same site of each subject for a 24 hour exposure period. Subjects were observed for reactions.

TCC was neither a primary irritant, a fatiguing agent, nor a sensitizer to any of the 50 subjects.

[3.2.10] Carcinogenicity test

A 24 month oral feeding study was conducted in male and female Sprague-Dawley rats according to EPA OTS 798.3320 guideline. TCC was administered ad libitum at doses calculated to be 25, 75, and 250 mg/kg body weight.

No evidence of a dose related increase in tumor incidence at any site. No statistically significant difference in tumor incidence between controls and high dose animals (except for a significant reduction in incidence of fibroadenomas and papillary carcinomas in high dose females).

[3.3] Worker Exposure Assessment

There is potential for occupational exposure to this material by workers who either produce the raw material or formulate TCC-containing products. The potential routes of exposure that are most relevant during manufacture of TCC and formulation of TCC-containing products are dermal and inhalation exposure.

[3.3.1] Manufacturing Facility

For workers, exposure to TCC during the production or transportation process is limited due to the low volatility of TCC and the industrial hygiene standards and personal protective equipment that are utilized as a standard practice in production facilities. Employee exposure is minimized through engineering controls and good industrial hygiene practices.

[3.3.2] Formulation Facility

The potential for worker exposure during the manufacture of bar soaps, liquid soaps or body washes containing TCC is minimized through engineering controls, a closed system operation, administrative procedures and personal protective equipment such as safety glasses or goggles, rubber gloves and other protective clothing as appropriate to prevent skin contact. Also, a NIOSH/MSHA (National Institute of Occupational Safety and Health/Mine Safety and Health Administration) approved dust respirator is recommended if the inhalation of dust is possible. A behavior observation and safety sampling system is in place as part of standard operating procedures to reinforce compliance with safe practices.

[3.4] Consumer Residential Exposure Assessment

Consumer residential exposure to TCC from product use is expected to be limited based on the use pattern for the product and chemistry of TCC. The potential for consistent consumer exposure to TCC exists through possible lifetime use of personal cleansing products (e.g., bar soaps, liquid soap, and body washes) that may contain TCC. Consumer exposure with the bar soap and body wash forms containing TCC is expected to be the same as or less than with the liquid form. The potential routes of consumer exposure are discussed below and are followed by calculations to estimate the most relevant exposures. Consumer monitoring studies have not been performed, as modeled estimates suffice for this material.

[3.4.1] Dermal Exposure

Dermal exposure to TCC is the major route of exposure due to the fact that TCC is utilized in personal cleansing products. Such dermal exposure can occur to the 1) face, 2) hands, and/or 3) body during the cleansing process.

Under typical cleansing conditions TCC containing products are utilized in 'rinse-off' scenarios. It follows that the majority of TCC to which an individual is initially exposed is anticipated to be washed away with the rinse water. In addition, these cleansing exposures are generally of very short duration, which is not considered in the calculations.

The FDA (OTC, 1978) used the following Maibach experiment to estimate absorption at 14% and for calculating safety factors. Maibach demonstrated that when radio-labeled TCC was dissolved in acetone and applied to human skin for 24 hours and not rinsed, up to 14% was excreted by the end of 10 days (Maibach, 1986). However the conditions used (i.e., use of an acetone solution) and the assumption that the absorption was instantaneous, are not directly comparable to TCC exposure as a result of actual product use. In a 'single showering study' conducted by Scharpf *et al.* (1975), TCC was measured directly under product use conditions. These investigators showed that approximately 0.2% of an applied dose of TCC (from 7 grams of a 2% TCC bar soap) was excreted in the first 24 hours. Only 0.39% TCC was absorbed after six days.

A summary of the risk characterization exposure estimates is included in the table below and in more detail in the following section. These exposure estimates are based on a child whose body weight is 10 kg (see children's exposure section for more detail) and a worst case scenario of 5% TCC in product. Additionally, no correction was made for the fact that the habits and practices data gathered by the SDA was based on adult use only. Thus, no correction for a difference in surface area and product usage amounts was included in this exposure estimate calculation, adding another level of conservatism.

Table 3.3. Consumer Dermal-Based Exposure Assessment

ROUTE:	EXPOSURE	RESULTING DOSE
Dermal		
bar soap	0.1 mg /kg bw/day	0.005 mg/kg bw/day
liquid soap	0.11 mg/kg bw/day	0.006 mg/kg bw/day
bodywash	0.07 mg/kg bw/day	0.0004 mg/kg bw/day

[3.4.1.1] Bar Soap

[3.4.1.1.1] Bar Soap – hands

The exposures for hands, face and body are added together for bar soap use to account for a worst case scenario.

Exposure during bar soap use on the hands is given by the following equation (AIHA, 2001):

$$\frac{\text{(Use /day)(grams used/ use)(\% product retained on skin)(\% absorbed dermally)(CF)}}{\text{BW}}$$

Where: CF: conversion factor (1000 mg/g)
BW: body weight

Assumptions:

1. Product is used an average of 6 times/day for hand washing (SDA, 2002)
2. The average mass of bar soap utilized per hand wash use = 0.36 g (SDA, 2002)
3. The amount of TCC retained on the skin after rinse off use = 1.4% (North-Root et al., 1984).
4. The amount of TCC absorbed = 0.39% (Sharpf et al., 1975)
5. The conversion factor = 1000 mg/kg
6. The 95th percentile body weight for a 7 month old male = 10 kg (NHANES, 2002)

$$\text{Exposure} = \frac{\text{(6 uses /day)(0.36 grams / use) (1.4 \% product retained on skin)(0.39\% absorbed)(1000 mg/g)}}{\text{10 kg bw}}$$

Exposure = 0.012 mg/kg bw/day for hand washing

[3.4.1.1.2] Bar Soap - face

Exposure during bar soap use on the face is given by the following equation (AIHA, 2001):

$$\frac{\text{(Use /day)(grams used/ use)(\% product retained on skin)(\% absorbed dermally)(CF)}}{\text{BW}}$$

Where: CF: conversion factor (1000 mg/g)
BW: body weight
Assumptions:

1. Product is used an average of 1 times/day for face washing (SDA, 2002)
2. The average mass of bar soap utilized per face wash use = 2.7 g (SDA, 2002)
3. The amount of TCC retained on the skin after rinse off use = 1.4% (North-Root et al., 1984).
4. The amount of TCC absorbed = 0.39% (Sharpf et al., 1975)
5. The conversion factor = 1000 mg/kg
6. The 95th percentile body weight for a 7 month old male = 10 kg (NHANES, 2002)

Exposure =

$$\frac{\text{(1 uses /day)(2.7 grams / use) (1.4 \% product retained on skin)(0.39\% absorbed)(1000 mg/g)}}{\text{10kg bw}}$$

Exposure = 0.015 mg/kg bw/day for face washing

[3.4.1.1.3] Bar Soap – body

Exposure during bar soap use is given by the following equation (AIHA, 2001):

$$\frac{\text{(Use /day)(grams used/ use)(\% product retained on skin)(\% absorbed dermally)(CF)}}{\text{BW}}$$

Where: CF: conversion factor (1000 mg/g)
BW: body weight
Assumptions:

1. Product is used an average of 1.53 times/day for body washing (SDA, 2002)
2. The average mass of bar soap utilized per body wash use = 8.6 g (SDA, 2002)
3. The amount of TCC retained on the skin after rinse off use = 1.4% (North-Root et al., 1984).
4. The amount of TCC absorbed = 0.39% (Sharpf et al., 1975)
5. The conversion factor = 1000 mg/kg
6. The 95th percentile body weight for a 7 month old male = 10 kg (NHANES, 2002)

Exposure =

$$\frac{\text{(1.53 uses /day)(8.6 grams /use)(1.4 \% product retained on skin)(0.39\% product absorbed)(1000 mg/g)}}{\text{10kg bw}}$$

Exposure = 0.072 mg/kg bw/day for body washing

Thus, **total exposure** to TCC under a worst case scenario for bar soap use =
(Exposure to TCC from hand washing + face washing + body washing) =
(0.012 + 0.015 + 0.072 mg/kg bw/day) = 0.10 mg /kg bw/day

The resulting dose is calculated by:
(exposure) x (the maximum amount of TCC in the product) =
(0.10 mg/kg bw/day) x (5%) = 0.005 mg/kg bw/day

The **MOE** is calculated by:
(NOEL for 2 year oral gavage) / resulting dose =
(25 mg/kg bw/day) / (0.005 mg/kg bw/day) = **5000**

[3.4.1.2] Liquid Soap

[3.4.1.2.1] Liquid Soap –Hands

The exposures for hands and body are added together for liquid soap use to account for a worst case scenario. No face washing is generally anticipated for this product type.

Exposure during liquid soap use is given by the following equation (AIHA, 2001):

$$\frac{\textbf{(Use /day)(grams used/ use)(\% product retained on skin)(\% absorbed dermally)(CF)}}{\textbf{BW}}$$

Where: CF: conversion factor (1000 mg/g)
BW: body weight
Assumptions:

1. Product is used an average of 8 times/day for hand washing (SDA, 2002)
2. The average mass of bar soap utilized per hand wash use = 1.7 g (SDA, 2002)
3. The amount of TCC retained on the skin after rinse off use = 1.4% (North-Root et al., 1984).
4. The amount of TCC absorbed = 0.39% (Sharpf et al., 1975)
5. The conversion factor = 1000 mg/kg
6. The 95th percentile body weight for a 7 month old male = 10 kg (NHANES, 2002)

Exposure =

$$\frac{\text{(8 uses /day)(1.7 grams / use) (1.4 \% product retained on skin)(0.39\% absorbed)(1000 mg/g)}}{\text{10kg bw}}$$

Exposure = 0.074 mg/kg bw/day for hand washing

[3.4.1.2.2] Liquid Soap - body

Exposure during liquid soap use is given by the following equation (AIHA, 2001):

$$\frac{\text{(Use /day)(grams used/ use)(\% product retained on skin)(\% absorbed dermally)(CF)}}{\text{BW}}$$

Where: CF: conversion factor (1000 mg/g)
BW: body weight
Assumptions:

1. Product is used an average of 0.57 times/day for body washing (SDA, 2002)
2. The average mass of bar soap utilized per body wash use = 11.8 g (SDA, 2002)
3. The amount of TCC retained on the skin after rinse off use = 1.4% (North-Root et al., 1984).
4. The amount of TCC absorbed = 0.39% (Sharpf et al., 1975)
5. The conversion factor = 1000 mg/kg
6. The 95th percentile body weight for a 7 month old male = 10 kg (NHANES, 2002)

Exposure =

$$\frac{\text{(0.57 uses /day)(11.8 grams /use) (1.4 \% product retained on skin)(0.39\% absorbed)(1000 mg/g)}}{\text{10 kg bw}}$$

Exposure = 0.037 mg/kg bw/day for body washing

Thus, **total exposure** under a worst-case scenario for liquid soap use =
(Exposure to TCC from hand washing) + (Exposure to TCC from body washing) =
(0.074 mg/kg bw/day) + (0.037 mg/kg bw/day) = **0.11 mg /kg bw/day**

The resulting dose is calculated by:
(exposure) x (the maximum amount of TCC in the product) =
(0.11 mg/kg bw/day) x (5%) = 0.006 mg/kg bw/day

The **MOE** is calculated by:
(NOEL for 2 year oral gavage) / resulting dose =
(25 mg/kg bw/day) / 0.006 = **4166**

[3.4.1.3] Body Wash

No separate face and hand washing are expected for this product type.

Exposure during body wash use is given by the following equation (AIHA, 2001):

$$\frac{\text{(Use /day)(grams used/ use)(\% product retained on skin)(\% absorbed dermally)(CF)}}{\text{BW}}$$

Where: CF: conversion factor (1000 mg/g)
BW: body weight
Assumptions:

1. Product is used an average of 1 times/day for body washing (SDA, 2002)
2. The average mass of bar soap utilized per body wash use = 12 g (SDA, 2002)
3. The amount of TCC retained on the skin after rinse off use = 1.4% (North-Root et al., 1984).
4. The amount of TCC absorbed = 0.39% (Sharpf et al., 1975)
5. The conversion factor = 1000 mg/kg
6. The 95th percentile body weight for a 7 month old male = 10 kg (NHANES, 2002)

Exposure =

$$\frac{\text{(1 use /day)(12 grams /use) (1.4 \% product retained on skin)(0.39\% absorbed)(1000 mg/g)}}{\text{10kg bw}}$$

Exposure = 0.07 mg/kg bw/day for body washing

Thus, the resulting dose to TCC under a worst case scenario for body wash use =
(exposure from body wash) x (maximum amount of TCC in product)
(0.07 mg/kg bw/day)(0.5%) = 0.0004 mg/kg bw/day

The **MOE** is calculated by:
(NOEL for 2 year oral gavage) / resulting dose =
(25 mg/kg bw/day) / 0.0004 = **62,500**

[3.4.2] Oral Exposure

There is no anticipated oral exposure under normal use conditions. There is little potential for TCC to be present in drinking water because it is extensively removed during wastewater treatment processes, is biodegradable, and sorptive. Drinking water samples from twelve metropolitan areas in the U.S. had non-detectable concentrations of TCC (<0.010 µg/L) and confirm this conclusion (Werner and Sehnert, 1980; Monsanto Study Number MSL-1264). Even though the potential for TCC exposure from drinking water is minimal, the E-FAST model was used to conservatively estimate the concentration of TCC in drinking water. The E-FAST results were used in the drinking water exposure calculation because the drinking water monitoring

study consisted of a limited number of samples. The results of this model indicate the high end (10% percentile) drinking water results to be 1.36 x 10^{-6} mg TCC /kg bw/day.

Ingestion of fish is another potential indirect oral exposure pathway for TCC. The log Pow for TCC is 4.2, a value that approaches a level where bioaccumulation in fish is a potential concern. However, actual measured TCC bioconcentration factors (BCFs) in channel catfish ranged from 13 (muscle) to 137 (whole fish) and are much lower than would be expected from a material with a log Pow of 4.2 (Lakinger et al. 1980, Monsanto Report #MSL-1277). The low measured TCC BCFs were the result of rapid metabolism of TCC and excretion of its metabolites. These data suggest that TCC does not bioconcentrate in fish to any significant degree and that measurable oral TCC exposure from ingestion of fish is not likely.

The other potential for oral exposure would only occur following accidental ingestion of the product, which would be a one time or infrequent acute exposure. Based on information collected from a consumer telephone service, Poison Control Centers and national emergency rooms, when accidental swallowing does occur there are usually no symptoms reported. Occasionally, when symptoms do occur they include nausea, vomiting, or diarrhea, which are mild and transient in nature. These symptoms are not specific to TCC since they would arise from accidental exposure to a surfactant-based personal cleansing product containing TCC and are symptoms consistent with ingestion of surfactant-based products.

[3.4.3] Inhalation Exposure

Consumer inhalation exposure during product use is limited primarily by the low vapor pressure of TCC. Consequently, there is no potential for inhalation from the liquid forms. In addition there is very little dust involved in transferring a bar of soap from the package to the consumer use, so the potential for inhalation exposure from this action is negligible.

[3.5] Human Health Screening Level Assessment

The available data summarized in this document demonstrate that TCC has an acceptable safety profile for use in personal cleansing products. The risk to human health is characterized by comparing the estimated exposure to the NOEL from animal studies. The amount by which the NOEL exceeds the estimated exposure is referred to as the MOE and this should be sufficiently large to account for several sources of uncertainty and variability in extrapolating data from animal studies to humans. The worst-case scenario for dermal exposure to TCC from the use of a personal cleansing product leads to an estimated dose of 0.006 mg/kg bw/day. In comparing this conservative estimate to the results from the oral chronic study where the NOEL is 25 mg/kg bw/day, the high MOE indicates there is no safety concern associated with consumer use of TCC-containing products. For potential oral exposure, if one assumes conservatively that TCC would be present in drinking water and not removed in wastewater treatment facilities, the calculated TCC exposure using E-FAST would be 1.38 x 10^{-6} mg/kg bw/day. Comparing the estimated oral exposure to the oral NOEL results in a MOE of many orders of magnitude, even

after accommodating inter- and intra-species variation. Based on the data presented, no adverse effects for humans are expected via any relevant exposure route.

Table 3.4. Consumer Risk Characterization

ROUTE:	EXPOSURE	Resulting Dose*	NOEL	MOE
Dermal				
bar soap	0.1 mg /kg bw/day	0.005 mg/kg bw/day	25 mg/kg bw/day	5000
liquid soap	0.11 mg/kg bw/day	0.006 mg/kg bw/day	25 mg/kg bw/day	4167
bodywash	0.07 mg/kg bw/day	0.0004 mg/kg bw/day	25 mg/kg bw/day	62,500
Oral				
drinking water	Not applicable	1.38×10^{-6} mg/kg bw/day	25 mg/kg bw/day	18,115,942

* The resulting dose takes into account the estimated dermal absorption of TCC of 0.39% based on a published report (Scharpf et al, 1975).

[4] References

(studies that are referenced in the text and appear in the IUCLID dataset are not included in this list of references)

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APPENDIX B

ACUTE ECOTOXICITY DATA FOR TCC

Compartment	Common Name	Species	Acute Endpoint	Duration	Value (µg/l)	Source
Freshwater	Water flea	*Daphnia magna*	LC_{50} (static)	48-hr	13	Monsanto MSDS
Freshwater	Water flea	*Daphnia magna*	LC_{50} (dynamic)	48-hr	10 - 20	Monsanto MSDS
Freshwater	Water flea	*Daphnia magna*	LC_{50} (static) 0.1 mg/l LAS	24-hr	16	BN-80-418 (BW-78-11-347)
Freshwater	Water flea	*Daphnia magna*	LC_{50} (static) 0.1 mg/l LAS	48-hr	10	BN-80-418 (BW-78-11-347)
Freshwater	Water flea	*Ceriodaphnia dubia*	EC_{50} (static)	48-hr	3.1	SLS 87-12-2582
Freshwater	Rainbow trout	*Oncorhynchus mykiss*	LC_{50}	96-hr	120	Monsanto MSDS
Freshwater	Bluegill sunfish	*Lepomis macrochirus*	LC_{50} (static)	96-hr	77	Monsanto MSDS
Freshwater	Bluegill sunfish	*Lepomis macrochirus*	LC_{50} (dynamic)	96-hr	>12	Monsanto MSDS
Freshwater Benthic	Midge larvae	*Chironomid sp.*	LC_{50}	48-hr	60 - 100	Monsanto MSDS
Estuarine/Marine	Eastern oyster embryo	*Crassostrea sp.*	LC_{50}	48-hr	6	Monsanto MSDS
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (dynamic)	24-hr	42	BN-80-463 (BP-80-9-152R)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (dynamic)	48-hr	30	BN-80-463 (BP-80-9-152R)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (dynamic)	72-hr	21	BN-80-463 (BP-80-9-152R)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (dynamic)	96-hr	15	BN-80-463 (BP-80-9-152R)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static)	96-hr	13	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 10 ppm SS	96-hr	10	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 50 ppm SS	96-hr	11	BN-80-465 (BP-79-10-157)

Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 100 ppm SS	96-hr	10	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 1,000 ppm Sewage	96-hr	10	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 5,000 ppm Sewage	96-hr	10	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 10,000 ppm Sewage	96-hr	10	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LC_{50} (static) + 100 ppm SS & 10,000 ppm Sewage	96-hr	8	BN-80-465 (BP-79-10-157)
Estuarine/Marine	Clam eggs	*Mercenaria mercenaria*	-	48-hr	32	Davis & Hidu (1979)

CHRONIC ECOTOXICITY DATA FOR TCC

Compartment	Common Name	Species	Chronic Endpoint	Duration	Value (µg/l)	Source
Freshwater	Green algae	*Selenastrum sp.*	Minimum Algistatic Concentration (~LOEC)	5-d	36	BN-80-464 (BP-90-9-151R)
Freshwater	Green algae	*Selenastrum sp.*	NOEC	5-d	30	BN-80-464 (BP-90-9-151R)
Freshwater	Blue-green algae	*Microcystis sp.*	Minimum Algistatic Concentration (~LOEC)	5-d	>32	BN-80-464 (BP-90-9-151R)
Freshwater	Blue-green algae	*Microcystis sp.*	NOEC	5-d	>32	BN-80-464 (BP-90-9-151R)
Freshwater	Diatom	*Navicula sp.*	Minimum Algistatic Concentration (~LOEC)	5-d	7.8	BN-80-464 (BP-90-9-151R)
Freshwater	Diatom	*Navicula sp.*	NOEC	5-d	6.0	BN-80-464 (BP-90-9-151R)
Freshwater	Water flea	*Ceriodaphnia dubia*	NOEC Mortality & Reproduction	7-d	1.46	Procter & Gamble ABC # 43812
Freshwater	Water flea	*Daphnia magna*	LOEC Mortality & Reproduction	21-d	4.7	Procter & Gamble ABC #44442
Freshwater	Water flea	*Daphnia magna*	NOEC Mortality & Reproduction	21-d	2.9	Procter & Gamble ABC #44442

Freshwater	Water flea	*Daphnia magna*	LOEC 50 ppm SS & 100,000 ppm Sewage Mortality	28-d	15.0	BN-80-416 (BW-79-11-559)
Freshwater	Water flea	*Daphnia magna*	NOEC 50 ppm SS & 100,000 ppm Sewage Mortality	28-d	7.5	BN-80-416 (BW-79-11-559)
Freshwater	Fathead minnow	*Pimephales promelas*	NOEC	-	5.0	Monsanto MSDS
Freshwater	Fathead minnow	*Pimephales promelas*	LOEC	-	10.0	Monsanto MSDS
Freshwater Benthic	Midge larvae	*Chironomid sp.*	NOEC (water)	-	>1.3<3.0	Monsanto MSDS
Freshwater Benthic	Midge larvae	*Chironomid sp.*	NOEC (sediment)	-	<2,760	Monsanto MSDS
Freshwater Benthic	Midge larvae	*Chironomid sp.*	NOEC (food)	-	>85,000	Monsanto MSDS
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LOEC Mortality & Reproduction	28-d	0.12	BN-80-463
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	NOEC Mortality & Reproduction	28-d	0.06	BN-80-463
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	EC_{50} (dynamic) Reproduction	28-d	0.209	XX-92-9893 (SS-91-0022)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LOEC (dynamic) Reproduction	28-d	0.125	XX-92-9893 (SS-91-0022)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	NOEC (dynamic) Reproduction	28-d	0.062	XX-92-9893 (SS-91-0022)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LOEC (dynamic) Growth	28-d	0.500	XX-92-9893 (SS-91-0022)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	NOEC (dynamic) Growth	28-d	0.250	XX-92-9893 (SS-91-0022)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	LOEC (dynamic) 100 ppm SS & 10,000 ppm Sewage Mortality	28-d	0.6	BN-80-462 (BP-79-10-154R)
Estuarine/Marine	Mysid shrimp	*Mysidopsis bahia*	NOEC (dynamic) 100 ppm SS & 10,000 ppm Sewage Mortality	28-d	0.4	BN-80-462 (BP-79-10-154R)
Estuarine/Marine	Clam larvae	*Mercenaria mercenaria*	-	12-d	37	Davis & Hidu (1979)