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OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES

Triclosan

Occupational and Residential Exposure Assessment

Office of Pesticide Programs
Antimicrobials Division
U.S. Environmental Protection Agency

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EXECUTIVE SUMMARY

This document is the Occupational and Residential Exposure Chapter of the Reregistration Eligibility Decision (RED) document for triclosan. It addresses the potential risks to humans that result from the use of triclosan in occupational and residential settings. The National Health and Nutrition Surveys (NHANES) biological monitoring data are available for assessing aggregate exposure and risk. EPA views the NHANES data as the most reliable and representative assessment of aggregate exposures to determine probability of co-occurrence of EPA- and FDA-regulated uses. Although the aggregate exposure/risk assessment using the NHANES data provides an encompassing review of triclosan-treated products, it does not include exposures to children under the age of 6 years old. Children under the age of 6 years exhibit unique activities that do not occur at older ages. Therefore, a separate estimate for children under the age of 6 years old that exhibit behaviors representative of high-end exposures to triclosan-treated products have been included.

Triclosan is used as a bacteriostat, fungistat, mildewstat, 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%. The EPA registered products are used in commercial/ institutional/industrial, residential and public access, and material preservatives. The residential use includes a direct application to HVAC coils (limited to commercial applicators). Additionally, triclosan is registered to be used as a material preservative in such products as paints (in-can preservative), polymers and plastics (e.g., toys, tooth brushes, etc), and textiles and fabrics (e.g., footwear, clothing, etc). There are many other FDA uses of triclosan (e.g., hand soaps, toothpaste) that are not under EPA's regulatory jurisdiction. These exposures have been considered in this chapter as well as in the aggregate assessment within the risk assessment chapter for triclosan. The general population biological monitoring data from NHANES does not allow for the separation of exposures attributed to EPA- versus FDA-regulated uses.

The toxicological endpoint selected for the oral route of exposure for all exposure durations (i.e., acute to long-term) is from a chronic toxicity study. The effects observed in the chronic study include clinical signs of toxicity include vomiting, failure to eat, and diarrhea in primates. The inhalation endpoint selected to represent all durations is based on a 21-day rat inhalation study with a LOAEL of 50 mg/m^3. The adverse effect for this endpoint is based on increased total leukocyte count and increased serum alkaline phosphate observed in the male rat. No short-term dermal endpoint for systemic effects was selected for triclosan, since no systemic effects were identified in the available data. A short-term dermal irritation endpoint was identified. The short-term irritation endpoint was determined, however, from a 14-day dermal toxicity in mice. Irritation was observed at 0.6 mg/kg/day equivalent to 100 $\mu g/cm^2$. The dermal study was based on a 99% ai formulation. However, all of the residential uses of triclosan are diluted. Therefore, the short-term dermal irritation observed for the 99% ai formulation does not reflect the dilute use patterns. The intermediate- and long-term dermal endpoint was determined from the 90-day dermal rat study. The route-specific dermal NOAEL from this study is 40 mg/kg/day based on increased incidence occult blood in the urine. Because the toxicological endpoints selected for inhalation, dermal, and oral routes of exposure are not female-specific, a body weight of 70 kilograms is used in the assessment. EPA's level of concern (LOC) for occupational and residential triclosan dermal and oral routes of exposures is 100 (i.e., a margin of exposure (MOE) less than 100 exceeds the level of concern). The level of concern is based on 10x for interspecies extrapolation and 10x for intraspecies variation. The LOC for the inhalation route of exposure is 1000 based on10x for interspecies extrapolation, 10x for intraspecies variation, and a 10x for the

use of a LOAEL.

This occupational and residential assessment was based on examination of product labels describing their uses. It has been determined that exposure to residential handlers is restricted to the registered end use product that is for paint containing triclosan as an in-can preservative. Occupational handlers may be exposed in the manufacturing of other products (e.g., plastics, textiles) and during commercial HVAC coil applications and commercial painters. Post-application exposures are likely to occur in residential settings from contacting treated articles such as textiles and fabrics and plastic products such as toys. Additionally, infants can be exposed via nursing and breathing and/or contacting triclosan-contaminated dust.

To assess the handler risks, EPA used surrogate unit exposure data from the Chemical Manufacturers Association (CMA) antimicrobial exposure study and the Pesticide Handlers Exposure Database (PHED). Post application/bystander exposures were assessed using the NHANES biological monitoring data from the general population for ages 6+ years old as well as bounding estimates for infants using EPA's standard assumptions (e.g., Health Effects Division's (HED) *Standard Operating Procedures (SOPs) for Residential Exposure Assessment*). The aggregate for children under 6 years old is based on the 6 to 12 month old age category. The infant aggregate includes the results of the 6-11 year old age group from NHANES combined with bounding estimates of infant-specific activities such as nursing, object-to-mouth, and hand-to-mouth.

Residential Handler Risk Summary

The residential handler dermal exposure scenarios are best represented by the short-term duration (i.e., painting is intermittent in nature). The short-term dermal duration toxicological endpoint is based on dermal irritation observed during the dosing of mice with a 99% ai product. The in-can paint preservation (1 % ai) is not considered to be as irritating as the more concentrated test substance. The short-term dermal exposures are believed to exhibit minimal skin irritation. This is supported by the lack of incident data and a bounding estimate of film thickness on the skin compared to the dermal irritation endpoint.

For the residential handler inhalation assessment, the inhalation risks were calculated by comparing the daily inhalation dose to the short-term inhalation endpoint. The inhalation MOE of 4,000 is above the target MOE of 1000 for the paint brush scenario. However, for the airless sprayer scenario the inhalation MOE of 180 is below the target MOE, and therefore, is of concern. Mitigation options include reducing the application rate in paint or removing the use.

Residential Post Application/Bystander Risk Summary

The residential post-application assessment is protective of long-term exposures. The results of the NHANES aggregate risks using the most conservative methodology option assessed for those 6+ years old indicate mean MOEs ranging from 4,700 to 19,000. At the 99th percentile the MOEs range from 260 to 1,700. These MOEs are above the target MOE of 100. The NHANES aggregate risks include exposure to both EPA- and FDA-regulated uses.

For infants 6 to 12 months old, the mean NHANES 6-11 year old MOEs combined with bounding estimates for infant-specific activities for nursing, object-to-mouth, and hand-to-mouth exposures indicate an aggregate MOE of 390. At the 99th percentile NHANES distribution

combined with the infant-specific activities indicate a MOE of 290. These MOEs are above the target MOE of 100. Clearly, including exposures to the FDA-regulated soaps and toothpaste for 6-11 year olds is a conservative assessment of exposure from these products to 6 to 12 month olds. Future refinements to the infant aggregate should focus on this portion of the total exposure.

Based on the low vapor pressure of triclosan and the lack of aerosol generation over time by the application methods (excluding bystanders in the vicinity of airless spraying of paint which triggers risks of concern), inhalation exposure is expected to be minimal. This expectation is confirmed by the MOEs estimated to be in the millions for breathing triclosan-treated dust.

The dermal irritation potential of diluted uses of triclosan impregnated into textiles/fabrics and plastics are also expected to be minimal. This expectation is supported by the low incidents of irritation as well as the screening-level assessment provided herein. The dermal systemic effects were also investigated for children and adults contacting treated articles. The systemic dermal MOE using conservative assumptions is at or above the target MOE for dermal effects.

Occupational Handler Risk Summary

The 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 products. For occupational uses it is OPP practice to mitigate dermal irritation by requiring the user to wear PPE (e.g., chemical resistant gloves and clothing). Mitigating with PPE is only a viable option for pesticide-labeled products (i.e., a label is needed to inform workers to wear PPE). Therefore, EPA can direct workers using pesticide-labeled products (concentrated form) at the manufacturing setting to wear PPE to mitigate dermal irritation. Conversely, for in-can material preservatives there is no pesticide label that goes with the preserved product to inform the workers/painters that PPE is needed (i.e., there is no pesticide label on a can of paint). Thus PPE is not a viable option to mitigate exposure to products preserved by triclosan such as the in-can paint use.

For the intermediate-term dermal risks, the MOE were above the target MOE of 100, and therefore, not of concern except for commercial painters and material preservative use for paper which will require a closed delivery system. 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 MOE of 1000 for all scenarios 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. For the pulp and paper use a closed delivery system will be required.

Occupational Post Application/Bystander Risk Summary

Based on the low vapor pressure of triclosan and the lack of aerosol generation over time by the application methods, inhalation post-application exposures are expected to be minimal.

1.0 INTRODUCTION

1.1 Purpose

In this document, EPA's Antimicrobials Division (AD) presents the results of its review of the potential human health effects of occupational and residential exposure to triclosan (5-chloro-2-(2,4 dichlorophenoxy) phenol). This information is for use in EPA's development of the triclosan Reregistration Eligibility Decision (RED) document.

1.2 Criteria for Conducting Exposure Assessments

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete. For triclosan, both criteria are met. Toxicological endpoints were selected for short-, intermediate-, and long-term dermal, inhalation, and oral exposures to triclosan. There is the potential for exposure in a variety of occupational and residential settings. Therefore, risk assessments are required for occupational and residential handlers as well as for occupational and residential post application exposures that can occur as a result of triclosan use.

In this document, handler scenarios were assessed by using *unit exposure* data to estimate occupational and residential handlers' exposures. *Unit exposures* are estimates of the amount of exposure to an active ingredient a handler receives while performing various handler tasks and are expressed in terms of micrograms or milligrams (1 mg = 1,000 µg) of active ingredient per pounds of active ingredient handled. A series of unit exposures have been developed that are unique for each scenario typically considered in assessments (i.e., there are different unit exposures for different types of application equipment, job functions, and levels of protection). The *unit exposure* concept has been established in the scientific literature and also through various exposure monitoring guidelines published by the USEPA and international organizations such as Health Canada and OECD (Organization for Economic Cooperation and Development).

Using surrogate unit exposure data, maximum application rates from labels, and EPA estimates of daily amount handled, exposures and risks to handlers were assessed. The exposure/risks were calculated using the following equations:

Daily Exposure: Inhalation and dermal handler exposures are estimated for each applicable handler task with the application rate, quantity treated/handled in a day, and the applicable inhalation unit exposure using the following formula:

Daily Inhalation or dermal Exposure: $E = UE \times AR \times AT$ **(Eq. 1)**

Where:

E	=	Amount (mg ai/day) that is available for inhalation and dermal exposure;
UE	=	Unit exposure value (mg ai/lb ai) derived from August 1998 PHED data or from 1992 CMA data;
AR	=	Maximum application rate based on a logical unit treatment, such as acres (A), square feet (sq. ft.), gallons (gal), or cubic feet (cu. ft). Maximum values are generally used (lb ai/sq ft, lb ai/gal, lb ai/cu ft); and

AT	=	Normalized application area based on a logical unit treatment such as square feet (sq ft/day), gallons (gal/day), or pounds of articles/products to be treated for material preservatives.

Daily Dose: The inhalation dose is calculated by normalizing the daily exposure by body weight and adjusting, if necessary (not needed for triclosan because of the availability of a dermal route-specific study), with an appropriate dermal absorption factor. Daily dose was calculated using the following formula:

Daily Dose: $$ADD = \frac{E \times ABS}{BW} \quad \textbf{(Eq. 2)}$$

Where:

ADD	=	Average daily dose or the absorbed dose received from exposure to a chemical in a given scenario (mg active ingredient/kg body weight/day);
E	=	Amount (mg ai/day) that is available for inhalation or dermal exposure;
ABS	=	A measure of the amount of chemical that crosses a biological boundary; and
BW	=	Body weight determined to represent the population of interest in a risk assessment (kg).

Margins of Exposure: Non-cancer inhalation risks for each applicable handler scenario are calculated using a Margin of Exposure (MOE). This is the ratio of the daily inhalation dose or dermal dose to the toxicological endpoint of concern.

Margins of Exposure: $$MOE = \frac{\text{NOAEL } or \text{ LOAEL}}{ADD} \quad \textbf{(Eq. 3)}$$

Where:

MOE	=	Margin of exposure, value used to represent risk or how close a chemical exposure is to being a concern (unitless);
NOAEL or LOAEL	=	Systemic toxicity level where no observed adverse effects (NOAEL) or where the lowest observed adverse effects (LOAEL) occurred in the study (mg ai/kg body weight/day); and
ADD	=	Average daily inhalation or dermal dose in a given scenario (mg ai/kg body weight/day).

1.3 Chemical Identification

Triclosan (5-Chloro-2-(2,4-dichlorophenoxy)phenol) was first registered with the EPA on June 19, 1969. Triclosan is a diphenyl ether derivative. The CAS number is 3380-34-5 and the molecular structure is provided in Figure 1.

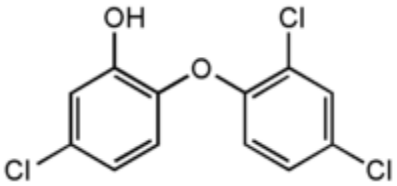

Figure 1. Molecular Structure of Triclosan

1.4 Physical/Chemical Properties

Table 1.2 shows physical/chemical characteristics that have been reported for triclosan.

Table 1.2. Physical/Chemical Properties of Triclosan	
Parameter	Triclosan
Molecular Weight	290
Density	1.55E3 kg/m3 at 22 ˚C
Boiling Point	Solid
Water Solubility	12 ppm
Vapor Pressure	5.2E-6 mm Hg at 25 ˚C

2.0 USE INFORMATION

2.1 Formulation Types and Percent Active Ingredient

Triclosan is used as a bacteriostat, fungistat, mildewstat, and deodorizer. The products containing triclosan as the active ingredient (a.i) 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%.

2.2 Summary of Use Pattern and Formulations

The Agency determines potential exposures to handlers of the product by identifying exposure scenarios from the various application methods that are plausible, given the label uses. Based on a review of product labels, triclosan is the active ingredient in products used in the following Use Site Categories:

- (III) Commercial, institutional and industrial premises and equipment,
- (IV) Residential and public access premises, and
- (VII) Material preservatives,

Specific uses within these use categories are identified in Table 2.1. Examples of EPA registered uses for triclosan include application during manufacturing of textiles and fabrics, plastics, paints, etc. Additionally, FDA uses of triclosan include products such as hand soaps, deodorants, and toothpaste. Although the FDA uses are out of the scope of EPA's jurisdiction,

exposures to these products are included in the overall aggregate assessment and cannot be separately presented using the NHANES data.

Table 2.1 illustrates the uses of triclosan. These scenarios were selected to be representative of the vast majority of uses and are believed to provide high-end degrees of dermal, inhalation, or incidental ingestion exposure. The representative scenarios assessed in this document are shown in Table 4.1 (residential) and Table 6.1 (occupational).

Table 2.1. Potential Use Scenarios Based on Product Labels for Triclosan.

Use Site Category	Example Use Sites	Scenarios
Use Site Category III Commercial/ Institutional/Industrial	Conveyor belts, fire hoses, dye bath vats, ice making equipment, HVAC coils	• Application to HVAC coils • Painting (commercial painters)
Use Site Category IV Residential and Public Access Premises	Treated articles	• Painting • Exposure to treated articles (e.g., clothing, mattress, plastic toys)
Use Site Category VII Material Preservatives	Used in the production of various household, institutional and industrial items	• adhesives • paints (latex) • textiles (cotton, wool, nylon, rayon, linen, fiber filling, mattress ticking) • polymers and plastics

3.0 SUMMARY OF TOXICITY DATA

3.1 Acute Toxicity

The acute toxicity data for triclosan are summarized below in Table 3.1 (USEPA, 2007).

Table 3.1. Acute Toxicity Profile for Triclosan

Guideline Number	Study Type/ Test substance (% a.i.)	MRID Number/ Citation	Results	Toxicity Category
870.1100 (§81-1)	Acute Oral- Rat Triclosan (99.7% a.i.)	43206501	LD_{50}: >5000 mg/kg	IV
870.1200 (§81-2)	Acute Dermal- Rabbit Triclosan (97% a.i.)	42306902 Phase III summary 92084037	LD_{50}: >9300 mg/kg	IV

Table 3.1. Acute Toxicity Profile for Triclosan				
Guideline Number	**Study Type/ Test substance (% a.i.)**	**MRID Number/ Citation**	**Results**	**Toxicity Category**
870.1300 (§81-3)	Acute Inhalation- Rat Triclosan (100.5% a.i.)	42306902, 43310501	LC_{50}: >0.15 mg/L	II
870.2400 (§81-4)	Primary Eye Irritation- Rabbit Triclosan (97% a.i.)	Phase III summary 92084040	PIS: 92/110 (24 hours), 82/110 (72 hours)	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 Summary of Toxicity Endpoints

Table 3.2 summarizes the toxicological endpoints for Triclosan (USEPA, 2007).

Table 3.2. Summary of Toxicological Dose and Endpoint Selection for Triclosan.

Exposure Scenario	Dose Used in Risk Assessment	Hazard-based Uncertainty Factors	Study and Toxicological Effects
Acute Dietary (gen. pop.)	NOAEL = 30 mg/kg	Inter-species extrapolation = 10x; Intra-species variation = 10x; Data Base (special sensitivity) = 1x; Target MOE = 100x	Chronic Toxicity study in Baboons MRID 257773. Effects of clinical signs of toxicity include vomiting, failure to eat, and diarrhea.
Acute Dietary (females 13+)	Endpoint not identified in the database		
Chronic Dietary (all populations)	NOAEL = 30 mg/kg	Inter-species extrapolation = 10x; Intra-species variation = 10x; Data Base (special sensitivity) = 1x; Target MOE = 100x	Chronic Toxicity study in Baboons MRID 257773. Effects of clinical signs of toxicity include vomiting, failure to eat, and diarrhea.

Exposure Scenario	Dose Used in Risk Assessment	Hazard-based Uncertainty Factors	Study and Toxicological Effects
Short-Term/ Intermediate-Term Incidental Oral (1-30 days; 30 days- 6 months)	NOAEL = 30 mg/kg	Inter-species extrapolation = 10x; Intra-species variation = 10x; Data Base (special sensitivity) = 1x; Target MOE = 100x	Chronic Toxicity study in Baboons MRID 257773 Effects of clinical signs of toxicity include vomiting, failure to eat, and diarrhea.
Dermal (short-term)	NOAEL = 0.6 mg/animal @ 99.3% active ingredient (100 $\mu g/cm^2$)	Inter-species extrapolation = 3x; Intra-species variation = 3x; Data Base (special sensitivity) = 1x; Target MOE = 10x	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
Dermal (intermediate term)	NOAEL = 40 mg/kg	Inter-species extrapolation = 10x; Intra-species variation = 10x; Data Base (special sensitivity) = 1x; Target MOE = 100x	90-day dermal toxicity study in rats. MRID 43328001. LOAEL = 80 mg/kg/day, based on increased incidence occult blood in the urine.
Dermal (long-term)	NOAEL = 40 mg/kg	Inter-species extrapolation = 10x; Intra-species variation = 10x; Data based (lack of chronic dermal study) = 3x; Data Base (special sensitivity) = 1x; Target MOE = 300x	90-day dermal toxicity study in rats. MRID 43328001. LOAEL = 80 mg/kg/day, based on increased incidence occult blood in the urine.
Inhalation (all durations)	LOAEL = 50 mg/m3 or 3.21 mg/kg/day UF = 1000 Where mg/kg/day = ((0.0087 m3/hr * mg/m3 * 2 hr/day) /0.271 b.w.	Inter-species extrapolation = 10x; Intra-species variation = 10x; Lack of NOAEL = 10; Data Base (special sensitivity) = 1x; Target MOE = 1000x	21-Day Inhalation Toxicity study in the rat. MRID 0087996. Effects seen in males at LOAEL include increased total leucocyte count and increased serum alkaline phosphatase.
Cancer (oral)	Not likely to be carcinogenic to humans (Health Effects Division Carcinogencity Assessment Review Committee, July 2007).		

UF = uncertainty factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed

adverse effect level, MOE = margin of exposure

3.3 Other Toxicological Considerations

There are no existing tolerances or tolerance exemptions for Triclosan under 40 CFR 180, and there are no food additive clearances from the Food and Drug Administration. However, there are expected exposures of infants and children to triclosan. Therefore, the data on developmental, reproductive, and neurotoxic effects of triclosan were examined for any susceptibility issues. There is no indication of developmental or reproductive effects in offspring of rats or rabbits to *in utero* and post-natal exposure to triclosan.

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." There is some evidence that triclosan disrupts thyroid hormone homeostasis and interacts with the androgen and estrogen receptors. The available evidence is summarized in the risk assessment chapter.

Further research is needed on the effect of triclosan on thyroid homeostasis and relevance of any perturbations in homeostasis of thyroid hormone levels for human risk. It is not readily apparent from the available toxicology database for triclosan that the effects observed are the direct result of perturbations of thyroid homeostasis. The Agency, however, is aware that research is ongoing on endocrine effects of triclosan, and this further research may require future modification to the existing assessment for triclosan.

4.0 RESIDENTIAL EXPOSURE ASSESSMENT

4.1 Summary of Registered Uses

There are no EPA registered products containing triclosan that can be applied directly by the homeowner. There is a homeowner application of triclosan when it is used as an in-can preservative for latex paint (e.g., EPA Reg. No. 42182-1). Articles treated with triclosan as a bacteriostat in occupational settings (e.g., EPA Reg. No. 70404-5) may also have the potential for post-application residential exposure. Triclosan-treated articles that may routinely be used in the residential market include, but are not limited to, material preservative uses in mattresses, clothing, bibs, tooth brush bristles, plastic toys, garbage bags, paper, playground equipment, sponges, furniture, footwear, etc. Additionally, triclosan can be used to control/prevent/inhibit the growth of fungi/mildew/mold/bacteria on coils in residential heating, ventilating, and air conditioning (HVAC) systems (e.g., EPA Reg. No. 82523-1). HVAC coil applications of triclosan are restricted to service contractors only. There are no homeowner applications to HVAC coils. The aerosols from spraying the coils are expected to create minimal inhalation exposure throughout the house.

Table 4.1 presents the maximum application rate associated with the representative uses and the EPA Registration number for the corresponding product label(s). 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.

Table 4.1. Representative Uses Associated with Residential Exposure to Triclosan.			
Representative Use	Application Method	Example Registration Number	Application Rate
Paint (Latex)	Brush and airless sprayer	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]
Textiles	NA[a]	70404-5	Round to 2% ai in finished textiles and mattresses. (Rates range up to the finished product containing 2% formulated product by weight. Triclosan product contains 99% ai.)
Plastic	NA[a]	42182-1	0.5% ai (0.1% to 0.5% product x 99% ai) **Note: labels need to clarify that toys are limited to 0.5%**

(a) The handlers scenarios were not assessed because the products can only be applied occupationally.

4.2 Residential Handler Exposures

Handler exposures are assessed for the in-can preservative use in paint. Dermal exposures for the short-term duration were not assessed because no systemic dermal toxicity was observed. Dermal irritation was observed in the toxicity study using a test substance containing 99 percent active ingredient (ai). Residential uses are at or below 1 to 2 percent ai are not expected to cause irritation. The lack of incident data also support this assumption.

The scenarios were assessed using PHED data along with the equations in Section 1.2, "Criteria for Conducting Risk Assessment." A summary of the PHED data are presented in Appendix A.

Unit Exposure Values: Unit exposure values were taken from the PHED data presented in HED's Residential SOPs (USEPA, 1997).

- For the ***airless sprayer*** scenario, the PHED inhalation unit exposure value for a residential handler applying a pesticide using an airless sprayer was used. The unit exposure value (0.83 mg/lb ai) represents a handler using an airless sprayer to stain the exterior of a house.

- For the ***brush/roller*** scenario**,** the PHED inhalation unit exposure value for a residential handler is based on applying a fungicide in paint to bathroom walls using a paint brush. The unit exposure value is 0.28 mg/lb ai.

Quantity handled/treated: The quantities handled/treated were estimated based on information from various sources, including EPA estimates.

- For the ***brush/roller*** in ***paint applications***, it is assumed that 20 lbs (approximately 2 gallons) of treated paint will be used. This is based on the 90th percentile value of 8 gallons of latex paint used per year divided by the mean frequency of 4 painting events/year.
- For the ***airless sprayer*** in ***paint applications***, it is assumed that 150 lbs (approximately 15 gallons) of treated paint will be used. This is based on the coverage of 200 ft^2/gallon and a house size of 40 x 30 x 20 ft (surface area of 2,800 ft^2).

Duration of Exposure: The duration of exposure for most handler homeowner uses is believed to be best represented by the short-term duration (1 to 30 days). The reason that short-term duration was chosen to be assessed is because painting is episodic in nature, not daily. In addition, homeowners are assumed to use different products with varying activities, not exclusively triclosan treated products (e.g., in-can paint preservative).

Results

The resulting short-term inhalation exposures and MOEs for the painting scenarios are presented in Table 4.2. The calculated inhalation MOEs are above the target MOE of 1000 for the paint brush but below the target MOE for the airless sprayer (i.e., MOE = 180). Therefore, the risk exceeds EPA's level of concern for painting. Personal protective equipment (PPE) such as respirators is not a viable mitigation option for residential paint uses for an in-can preservative.

Table 4.2 Triclosan Short-Term Residential Handler Inhalation Exposures and MOEs

Exposure Scenario Application Method	Application Method	Application Rate[a]	Quantity Handled/ Treated per day[b]	Unit Exposure (mg/lb a.i.)	Daily Dose (mg/kg/day) [c]	MOE [d] (Target MOE = 1000)
Painting	Paint brush	0.1 lb ai/gal	2 gallons	0.28	0.0008	4,000
	Airless sprayer		15 gallons	0.83	0.018	180

a Application rates are the maximum application rates determined from EPA registered labels for triclosan.

b Amount handled per day values are estimates or label instructions.

c Daily dose (mg/kg/day) = [unit exposure (mg/lb a.i.) x application rate (% a.i. weight or lb ai/gal) x quantity treated (lb/day or gal/day) x absorption factor (1.0 for inhalation)]/ Body weight (70 kg for inhalation).

d MOE = LOAEL / Daily Dose. [Where short-term inhalation LOAEL = 50 mg/m^3 or a dose of 3.21 mg/kg/day]. Target MOE = 1000.

4.3 Residential Post-application Exposures

Based on a review of EPA-registered product labels, triclosan is the active ingredient in textiles and fabrics (e.g., mattresses and clothing/bibs) and plastic products (e.g., toys, cutting

boards, etc). 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 post application assessment also includes an aggregate assessment of the FDA uses such as toothpaste, hand soaps, and deodorants. This assessment includes both EPA- and FDA-registered uses because of the biological monitoring methodology used to collect the samples from the general population does not allow us to separate the contribution of individual products to total exposure.

The National Health and Nutrition Surveys (NHANES) biological monitoring data are available for triclosan to assess aggregate exposure and risk. EPA views the NHANES monitoring data as most representative assessment of aggregate exposures to daily use products. 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 for ages 6 years and older. The population-based biological monitoring data are 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.

Although the aggregate exposure/risk assessment using the NHANES data provides an encompassing review of all triclosan-treated products, it does not include exposures to children under the age of 6 years old. Children under the age of 6 years exhibit unique activities that do not occur at older ages. Therefore, a separate estimate for children under 6 years old has been included. Finally, dermal and inhalation route-specific assessments are also presented below.

4.3.1 National Health and Nutrition Surveys (NHANES) Data for Triclosan

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 (µg/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

EPA evaluates health effects in terms of toxicity endpoints that represent an exposure level in mg or µg 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 excretion is less variable (i.e., more consistent within an individual) 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 specific individuals based on their anthropometric measurements and demographic characteristics (e.g, age, sex, race (Black, non-Hispanic or not), height, weight, and obesity (based on the BMI)). The triclosan concentration is divided by the creatinine concentration in the urine, multiplied by the estimated daily creatinine excretion in μg/day specific to the individual being considered, 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 raw data were available in NHANES, actual (measured) body weights of subjects were used instead of average body weights as described by Schafer et al. (2004).

- The EPA Office of Research and Development (ORD) does not currently recommend any single 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 (as opposed to L/day above) for a demographic group; the triclosan urinary concentration is multiplied by the estimated daily urine excretion in L/kg-day. Two variations of this approach are used. Both mean and the 95th%ile urine volumes 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 within this risk assessment.

4.3.1.1 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. 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 correction used to estimate the total triclosan dose (i.e., corrected for triclosan

excretion) equals the urinary concentration derived dose (mg/kg/day) for the 3 basic conversion methods divided by the median value of the triclosan excretion in urine (i.e., 0.54).

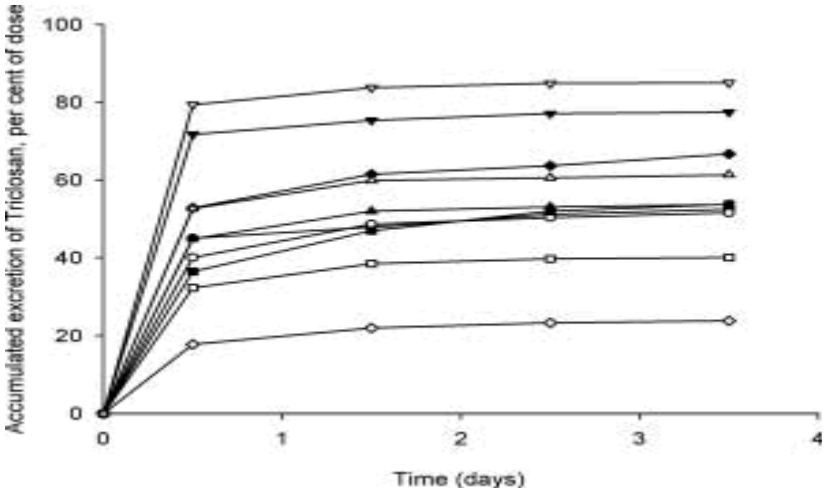

Figure 1. Triclosan Excretion in Urine (taken from Sandborgh-Englund (2006))

4.3.1.2 Uncertainties Associated with the Dose Conversion

Several uncertainties exist in the aggregate assessment for triclosan that arise from using the biological monitoring using spot urine samples from NHANES. Therefore, EPA used conservative assumptions to err on the side of overestimating the potential dose. Conservatisms used in the assessment include: (1) assumptions used by Cohen (2008) for the dose conversion (e.g., 95th percentile of urinary volume assumed for all individuals); (2) the characterization of the risks if one were to assume the pharmacokinetics of triclosan at the lowest (most conservative) urinary excretion (urinary excretion ranged from 24 to 83 percent with a median of 54 percent); and (3) the inclusion of these conservative assumptions even at the upper percentile of exposure. Future refinements to using the NHANES data for the triclosan risk assessment should focus on refining these parameters. 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.

4.3.2 Aggregate Risks

4.3.2.1 Children (6 years) to Adults

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 4.3 and 4.4 provide – for each of the three basic concentration to dose conversion methods -- the mean and 99th 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 95th percentile of daily urine excretion volume. Based on the results at the mean and 99th 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 99th 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 95th 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 4.3. 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 4.4. Acute, Short, Intermediate-, and Long-term Aggregate Risks for Triclosan (99th Percentile)

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/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.

4.3.2.2 Infants

While NHANES data are measured exposures that represent the real world co-occurrence of triclosan-treated products, it is necessary to use screening-level deterministic assessments as well as to make assumptions of potential co-occurrence of triclosan-treated products for younger children. USEPA (2005), an internally and externally scientific peer reviewed document, provides the basis of the age group selection: *"This document recommends a set of age groupings based on current understanding of differences in lifestage behavior and anatomy and physiology that can serve as a starting set for consideration by Agency risk assessors and researchers. In specific situations, it is recognized that exposure factors data may not be available for many of the recommended age groupings or that a specific age group may not need to be the subject of a particular assessment, so flexibility and professional judgment are essential in applying these generic age groupings."* One age group was selected to represent behavioral activities of children younger than 6 years old that are exposed to triclosan-treated products.

An assessment of infants in the 6 to 12 month old age group has been selected to represent the high end of exposure activities of children less then six years old to triclosan-treated products. This age group is considered the high end of exposure based on the characteristics discussed in Table 2 presented in USEPA (2005) and the likelihood of these activities co-occurring. USEPA (2005) indicates that this age group includes behaviors that would lend themselves to potentially expose children to triclosan-treated products. Characteristics of children at this age that potentially exposes children to triclosan that would not have been captured by the 6-11 year old age category in NHANES include nursing, increasingly likely to mouth nonfood items, and *"development of personal dust clouds"* as a characteristic relevant to inhalation exposure.

The younger age groups recommended by USEPA (2005) such as birth to 3 months and 3 to 6 months are less likely to be the high exposure groups to triclosan because of less contact with treated objects (not to say there is no contact, but the 6 to 12 month age group are *"increasingly likely to mouth nonfood items"*). The older age groups recommended by USEPA (2005) include 12 to 24 months and 2 to less than 6 years old. These age groups reflect the cessation of nursing and a reduction in hand-to-mouth activities. The activities in the 12 to 24 month age group as well as the 2 to 6 year age group reflect decreasing frequency of mouthing of objects, nursing, etc and decreasing potential for co-occurrence (e.g., nursing) in comparison to the 6 to 12 month old age group.

Infant-specific activities resulting in potential exposures that are not accounted for by the 6-11 year old age group in NHANES that are likely to co-occur include:

- Nursing (i.e., triclosan-contaminated breast milk);
- Object-to-mouth exposures (e.g., mouthing of plastic items such as toys, combs & brushes, playground equipment);
- Hand-to-mouth exposure (e.g., residues in dust stuck to children's hands); and
- Inhalation of triclosan-contaminated dust.

Other potential exposure pathways for infants in the 6 to 12 month old age group that are captured – and overestimated for the 6 to 12 month olds -- by the NHANES age groups 6-11 years old include:

- Brushing teeth with triclosan-treated tooth paste;
- Washing hands with triclosan-treated antibacterial soap;
- Exposure to impregnated fabrics and textiles such as clothing/sportswear, blankets, mattresses, tooth brush bristles, etc. that may be treated with triclosan;
- Exposure to impregnated polymers and plastics such as food contact surfaces (e.g.,

cutting boards, conveyor belts, counter and table tops).

Infant-specific Exposure Pathways

Nursing

As indicated by the NHANES biological monitoring data set, a substantial portion of the population has triclosan excreted in the urine. Therefore, mothers expose nursing infants to triclosan-contaminated breast milk. Dayan (2007) reports a breast milk concentration of 35.8 ug of triclosan per kilogram whole breast milk. Limited information is available in this study on the actual results of the breast milk sampling. The breast milk was obtained *"…anonymously after collection by the Mothers Milk Banks for routine purposes"* from 62 mothers from California and Texas. The breast milk concentration ranged from two non detect samples up to 2100 ug/kg lipid (as opposed to whole milk). Dayan (2007) does not report individual data points but summarizes the data as *"…the mean of the concentrations in the 5 samples with the highest levels… 1742 ug/kg lipid, corresponding to 35.8 ug/kg whole breast milk."* Using the same ratio by Dayan (2007) of lipids to whole milk, the maximum level reported, 2100 ug/kg lipid, corresponds to 43.2 ug/kg whole breast milk.

USEPA's (2002) Child-specific Exposure Factors Handbook recommends nursing ingestion rates. The mean breast milk intake for a 1 to 6 month old is 742 ml/day (upper percentile is estimated as the mean plus two standard deviations yielding a value of 1033 ml/day). The mean breast milk intake for a 12 month old is 688 ml/day (upper percentile is 980 ml/day).

An infant's estimated daily dose of triclosan-contaminated breast milk is the product of the breast milk concentration multiplied by the daily intake volume. The following equation is used to determine the daily dose.

$$PDD = \frac{BM\ (concentration) \times CF1 \times CF2 \times SP \times BM\ (intake)}{BW}$$

where:

PDD	=	potential daily dose (mg/kg/day);
BM (concentration)	=	Breast milk conc. (ug/kg whole breast milk);
BM (intake)	=	Breast milk intake (ml/day)
SP	=	Specific gravity of breast milk (1.03).
CF1	=	Conversion factor of 0.001 mg/ug.
CF2	=	Conversion factor of 0.001 kg/ml.
BW	=	body weight of an infant (kg).

Assumptions

- As a bounding estimate, the maximum breast milk concentration in whole breast milk from 62 mothers reported by Dayan (2007) is assumed (i.e., 43.2 ug/kg whole breast milk).
- As a bounding estimate, the upper percentile (i.e., mean plus two standard deviations) of breast milk intake is assumed for a 1 to 6 month old to represent the 6 to 12 month old infant (i.e., 1033 ml/day).
- Specific gravity of breast milk 1.03 (KellyMom.com).
- The body weight of a 6 to 11 month old infant is 9 kg (average of the male and female body weights rounded to a whole number) (USEPA 2002).

The daily dose for an infant 6 to 12 months old is estimated to be 0.005 mg/kg/day. The MOE is 6000 (i.e., chronic NOAEL of 30 mg/kg/day / daily dose 0.005 mg/kg/day). The target MOE of 100 indicates no risks of concern.

Object-to-mouth

Plastics and polymers used in toys can be treated with triclosan during the manufacturing process. Therefore, children's post application incidental oral exposures to treated toys may occur. Regardless of the fact that not all plastic toys are treated with triclosan and the toys that are treated will not be used everyday, the oral endpoint selected for triclosan is based on a long-ter toxicity study and was selected for the short-, intermediate-, and long-term durations.

There is potential for incidental ingestion of triclosan residues when children play with and mouth plastic objects such as toys treated with triclosan. To determine incidental oral exposure of children mouthing objects such as triclosan-treated plastic used to manufacture toys, the following equations were used:

$$PDD = \frac{SR \times SE \times SA}{BW}$$

where:

PDD	=	potential daily dose (mg/kg/day);
SR	=	surface residue (mg/cm^2);
SE	=	saliva extraction efficiency (unitless fraction)
SA	=	surface area of toy mouthed (cm^2/day)
BW	=	body weight of an infant (kg).

And

$$SR = \frac{\% \text{ a.i} \times W \times CF \times F}{SA}$$

where:

SR	=	surface residue (mg a.i./cm^2)
% a.i.	=	fraction active ingredient in toy by total weight (unitless)
W	=	weight of toy (g/cm^2)
CF	=	conversion factor (1,000 mg/g)
F	=	fraction additive available at the surface of the toy (unitless)
SA	=	surface area (cm^2)

<u>Assumptions</u>

- It is assumed that 500 cm^2 is a representative surface area of plastic that is mouthed.
- Since chemical specific leaching data were not available, the actual amount of active ingredient at the surface of the plastic object which is available for mouthing is based on the following assumptions
    - The plastic object such as a toy is manufactured from ABS or polystyrene plastic; and
    - No more than 0.5% of the additive is available on the surface of the plastic object for each mouthing event. To put this value into perspective, this is equivalent to one-half of the total amount of triclosan in plastic products being excreted to the surface in 140 days.
- The weight of a 500 cm^2 toy is 50 g, which is based on data showing that a polyethylene highchair sample with a surface area of 12.7 cm^2 weighs 1.3072 g (i.e., 0.1 g/cm^2).
- The triclosan registered antimicrobial product contains 99% a.i. by weight and is used to treat plastic at a rate of 0.5% product by weight of the plastic material; thus, the % a.i. in treated plastic is calculated as 0.99 ai weight fraction x 0.5% = 0.5% ai in the treated plastic.
- The saliva extraction efficiency is assumed to be 50% (EPA 2001).
- The body weight of a 6 to 11 month old infant is 9 kg (average of the male and female body weights rounded to a whole number) (USEPA 2002).

Table 4.5 shows the calculations of the incidental oral exposure and MOE for infants mouthing triclosan-treated plastic objects such as toys. The MOE of 430 is above the target MOE of 100 and is not of concern.

Table 4.5. Incidental Oral Exposure and MOE for Infants Mouthing Triclosan-treated Objects such as Toys

Duration	% a.i.	Plastic Weight (g)	Fraction of triclosan available on plastic surface	Surface area mouthed (cm^2)	Residue on Surface of plastic (mg/cm^2)	Saliva extraction efficiency	Exposure [a] (mg/kg/day)	MOE (Target MOE is 100) [b]
ST	0.5%	50	0.5%	500	0.0025	50%	0.069	430

(a) Potential exposures are expressed as mg/kg/day; equations used to estimate exposure are presented above.

(b) MOE = NOAEL/exposure estimate [Where: short-, intermediate-, and long-term oral NOAEL = 30 mg/kg/day]. Target MOE = 100.

Hand-to-mouth

Children in the 6 to 12 month old age group exhibit hand-to-mouth activities that may lead to triclosan exposure that would not be accounted for in the NHANES 6-11 year old subpopulation. Residues on hands may result from touching triclosan-impregnated products or crawling on floors with triclosan-contaminated dust. An assessment is already provided for directly mouthing treated items. Therefore, hand-to-mouth activities is being assessed for an infant that may ingest dust that adheres to their hands as another potential pathway for aggregate exposure.

Canosa et al (2007) provides triclosan dust concentrations from 10 private homes in Spain. Triclosan concentrations in dust averaged 702 ng/g in the homes (range of 240 to 2,200 ng/g). The indoor dust samples were collected using a vacuum cleaner with paper dust bags. The fraction of dust with particle sizes less then 60 um were collected.

The amount of house dust that could adhere to a child's hand is not available. To estimate the amount of dust that could adhere to an infant's hand, soil adherence factors for hands from USEPA (2002) are used. The difference between the adherences of soil versus house dust is unknown. Therefore, the high end of soil adherence is used. USEPA (2002) provides in it's Table 8-8 a range of soil adherence factors from 0.0063 mg/cm^2 up to 0.15 mg/cm^2. The maximum value of 0.15 mg/cm^2 represents 1 to 6.5 year olds in a daycare facility playing indoors and outdoors (on bare earth).

To calculate incidental ingestion exposure to these chemicals due to hand-to-mouth transfer, the methodologies established in the *Standard Operating Procedures (SOPs) for Residential Exposure Assessments* (USEPA 2000 and, 2001) were used. Exposures were calculated for children contacting triclosan-contaminated house dust in residential homes and/or commercial day care centers using the following equations for hand-to-mouth transfer of pesticide residues:

$$PDD = \frac{\text{Dust (conc)} \times AF \times SA \times EF \times ET \times SE \times CF1 \times CF2}{BW}$$

where:

PDD = Potential daily dose (mg/kg/day);

Dust (conc) = Indoor dust concentration (ng/g);

AF	=	Adherence factor for soil as surrogate for house dust (mg/cm^2);
SA	=	Surface area of the hands that contact both the treated area, and the individuals mouth (cm^2/event);
FQ	=	Frequency of hand-to-mouth events (events/hr);
SE	=	Saliva extraction efficiency (unitless fraction);
ET	=	Exposure Time (4 hrs/day);
CF1	=	Unit conversion factor (0.000001 mg/ng);
CF2	=	Unit conversion factor (0.001 g/mg); and
BW	=	Body weight (9 kg)

Assumptions

- Based on USEPA/OPP/HED's Residential SOP, it was assumed that the surface area used for each hand-to-mouth event is 20 cm^2. For short-term exposures, it is assumed that there were 20 events per hour (90th percentile) and for intermediate-term exposure; it was assumed that there were 9.5 event/hour (mean value).
- The maximum soil adherence factor of 0.15 mg/cm^2 represents 1 to 6.5 year olds in a daycare facility playing indoors and outdoors (on bare earth).
- The exposure time is 4 hours a day (USEPA, 2000 and 2001).
- The saliva extraction efficiency is 50% (USEPA, 2000 and 2001).
- The body weight of a 6 to 11 month old infant is 9 kg (average of the male and female body weights rounded to a whole number) (USEPA 2002).
- Canosa et al.(2007) provides triclosan dust concentrations from 10 private homes in Spain. Triclosan concentrations in dust averaged 702 ng/g in the homes (range of 240 to 2,200 ng/g).

Results

The calculation of the short- and intermediate-term oral doses (toxicological endpoint selected is also protective of the long-term duration) and the oral MOEs are shown in Table 4.6. The oral MOEs are above the target MOE of 100.

Table 4.6. Short- and Intermediate-term (and Long-term) Incidental Oral Post-application Exposures and MOEs for Infant Hand-to-mouth from Contacting Triclosan-contaminated House Dust

Exposure Scenario	Dust Residue [a] (ng/g)	Soil Adherence Factor (mg/cm2)	Surface area mouthed (cm^2/event)	Exposure Frequency (events/hr)	Saliva Extraction Factor	Exp. Time (hrs/day)	Daily Dose[b] (mg/kg/day)	Oral MOE[c]
Dust (ST)	2200	0.15	20	20	50%	4	2.9E-5	1E+6
Dust (IT & LT)	702			9.5			4.4E-6	6.7E+6

a Dust residue: ST maximum concentration of 2200 ng/g and long-term average of 702 ng/g (Canosa et al 2007).

b Daily Dose (mg/kg/day) = [(Dust residue, ng/g)*(adherence factor, 0.15 mg/cm2)*(exposure time, 4 hrs/day)*(surface area of hands, 20 cm^2/event)*(frequency of hand-to-mouth activity, 20 events/hr, and 9.5 event for intermediate term)*(extraction by saliva, 0.5)*(conversion factor 0.000001 mg/ng)*(conversion factor 0.001 g/mg)]/(body weight, 9 kg)]

c MOE = NOAEL (mg/kg/day) / daily dose(mg/kg/day) [Where short-, intermediate-, and long-

term oral NOAEL = 30 mg/kg/day]. Target MOE = 100.

Dust Inhalation

Characteristics of children in the 6 to 12 month age group include behaviors described in USEPA (2002) as *"development of personal dust clouds"*. In other words, infants are in close proximity to carpet/floor dust. Canosa et al (2007) provides triclosan dust concentrations from 10 private homes in Spain. Triclosan concentrations in dust averaged 702 ng/g in the homes (range of 240 to 2,200 ng/g). The indoor dust samples were collected using a vacuum cleaner with paper dust bags. The fraction of dust with particle sizes less then 60 um were collected.

Typical amounts of dust inhaled in indoor environments are not available to estimate the inhalation exposure to triclosan-contaminated dust. Therefore, a range of dust standards are used to represent the high end of breathing dust. Three estimates are provided to develop an overly conservative estimate for up to a long-term duration. EPA's ambient air quality standard for dust exposure is 0.15 mg/m^3; the ACGIH-TLV level is 10 mg/m^3; and the OSHA PEL for dust is 15 mg/m^3.

The resulting route-specific inhalation MOEs are in the millions (Table 4.7). Based on this conservative approach, inhalation to triclosan-contaminated dust is considered to be negligible.

Table 4.7. Inhalation Risks to Infants Breathing Triclosan-contaminated House Dust.

Exposure Standard	Dust Exposure Level (mg/m^3)	Triclosan Concentration in Dust[A]	Triclosan Exposure Level[B] (ng/m^3)	Inhalation MOE[C] (Target MOE = 1000)
EPA Ambient Air Quality Standard - PM10	0.15	0.702 ng/mg	0.11	450,000,000
ACGIH-TLV – Inhalable Fraction	10		7.0	70,000,000
OSHA PEL – Total Dust	15		11	45,000,000

A. (702 ng/gm)/(1000 mg/gm) = 0.702 ng/mg
B. Trichlosan Exposure (ng/m^3) = Dust Exposure (mg/m^3) * Trichlosan Concentration in Dust (0.702 ng/mg)
C. Inhalation MOE = [Inhalation LOAEL (50 mg/m^3) * 1,000,000 ng/mg] / [Trichlosan Exposure (ng/m^3)]

Infant Aggregate

Aggregate risks for children less then 6 years old have also been considered separately from the results of the NHANES biological monitoring assessment. Table 4.8 presents the aggregate risks for the 6 to 12 month old age group. The aggregate risks presented represent the high-end of exposure that may co-occur from the various EPA and FDA-regulated triclosan products. The risk results of the 6-11 year old NHANES age group are used in conjunction with infant-specific exposure activities. The 6-11 year old age group represents exposures to all of the potential EPA-registered uses such as textiles and fabrics; plastic products; as well as FDA-regulated soaps and toothpaste. Clearly, including exposures to the FDA-regulated soaps and toothpaste for 6-11 year olds is a conservative assessment of exposure from these products to 6 to 12 month olds. Future refinements to the infant aggregate should focus on this portion of the total exposure.

The aggregate risks for infants 6 to 12 months old have been estimated by combining the mean NHANES distribution with the infant-specific bounding risks. The aggregate MOE from the measured mean of the 6-11 year old NHANES subjects combined with the bounding risks from nursing, object-

to-mouth, and hand-to-mouth indicate a long-term MOE of 390. The 99th percentile of the NHANES dose (when using the 95% urine volume to estimate the 99th percentile dose) is combined with the infant-specific bounding risks and indicates a long-term MOE of 290.

Table 4.8. Aggregate Exposure and Risks for Infants 6 to 12 Months.

Scenario	Risk (MOE)			Representative Products
	Mean	99th%	Bounding	
NHANES 6-11 year olds	12,000	1,100	NA	Exposures inclusive of all triclosan-treated products that co-occur in the real world for 6-11 year olds (excludes infant-specific activities)
Nursing	NA	NA	6,000	Infants nursing (contaminated breast milk) from mothers exposed to triclosan-treated products that co-occur in the real world
Object-to-mouth	NA	NA	430	Wide range of triclosan-treated products such as toys that may be mouthed by infants
Hand-to-mouth	NA	NA	6.7E+6	Infants mouthing hands that have been contaminated by triclosan residues in house dust
Aggregate [a] (Total MOE)	390[b] (mean + bounding)	290[c] (99th + bounding)	NA	Total exposure of a 6-11 year old plus infant-specific activity exposures

(a) Aggregate (Total MOE) = $1/((1/MOE_{NHANES}) + (1/MOE_{Nursing}) + (1/MOE_{Object}) + (1/MOE_{HTM}))$
(b) Mean Aggregate = Sum of the mean NHANES MOEs plus the bounding MOE estimates from nursing, object-to-mouth, and hand-to-mouth.
(c) 99th%tile Aggregate = Sum of the 99th%tile NHANES MOEs plus the bounding MOE estimates from nursing, object-to-mouth, and hand-to-mouth.

4.3.3 Dermal Irritation

The potential for dermal irritation to occur from incidental dermal exposures from products treated at low concentrations of triclosan are expected to be minimal. The lack of incident data for irritation confirms this assumption.

The localized dermal irritation effects tested at the concentrated product (i.e., 99 percent triclosan) occurs at levels lower than the NOAEL of 100 ug/cm^2. EPA applies a 10x uncertainty factor for risk assessment purposes. Plastic articles are treated at a use dilution of 0.5 percent triclosan. Only a fraction of triclosan in impregnated articles would be available on the surface. Furthermore, only a fraction of the triclosan on the surface would be transferred to a localized skin area for irritation to occur. For illustrative purposes, the film thickness of a fluid on the hands is 1.75 mg/cm^2, which was extracted from the document entitled, *"A Laboratory Method to Determine the Retention of Liquids on the Surface of Hands"* (Cinalli, 1992). The film thickness is based on a machinist immersing both hands in metalworking fluid and then partially cleaning hands with a rag. Clearly this is an exaggerated estimate of exposure compared to dermal contact of triclosan-impregnated articles. This type of a screening-level approach indicates that 1.75 mg/cm^2 x 1000 ug/mg unit conversion x 0.005 triclosan application rate is 8.75 ug/cm^2. This conservative estimate does not indicate a dermal irritation concern. Additional residue transfer assumptions for impregnated articles up to 2 percent could be determined for similar screening-level assessments but are not warranted based on the above discussions.

4.3.4 Dermal Systemic

There is the potential for dermal-specific route of exposure to adults and children contacting impregnated textiles and fabrics such as clothing items and mattresses. The contribution of dermal exposure to the aggregate exposure is represented in the NHANES data. Nonetheless, a post-application screening-level clothing assessment to represent exposure to treated textiles and fabrics is provided. The route-specific dermal toxicological endpoint for the intermediate-term exposure duration is used to represent all textile uses. Long-term duration was not assessed because transferable triclosan residues from treated textiles and fabrics are not expected to be available continuously at the levels used in this screening-level assessment.

Exposure Calculations

Potential doses are calculated as follows:

$$PDD = \frac{D \times WF1 \times TF. \times SA}{BW}$$

where:

PDD	=	potential daily dose (mg/kg/day);
D	=	Textile density (mg/cm^2);
WF1	=	weight fraction of ai product in textile (%);
TF	=	Transfer factor from clothing to skin (%);
SA	=	Surface area of body contacting treated clothing (cm^2/day); and
BW	=	body weight (kg).

Assumptions

- WF1: The product is applied at rates as high as 2% of weight of textile; the highest application rate of 2% product corresponds with the highest percent triclosan formulation (i.e., 99 percent active ingredient, EPA Reg. No. 70404-5).
- SA: The median surface area of clothing contacting skin for a 3-year-old toddler is 5,670 cm^2 (total body surface area minus the head) (USEPA, 1997). For adults, the median surface area is 16,900 cm^2 (total body surface area minus the head) (USEPA, 1997). Note: The Phase I comments suggested that triclosan in textiles is primarily limited to sports wear. However, no refinements to the assessment have been made to represent short pants and short-sleeved shirts because it is not a label restriction and some sports wear may be long pants and long-sleeved shirts (e.g., sweat pants and sweat shirts). Phase I comments also suggested that the surface area should be adjusted for inside surface area of clothing contacting skin (i.e., 50% adjustment). However, adjustments were not made to the assessment because the transfer of triclosan residues may come from both dermal contact with the suggested inside surface of clothing as well as sweat-soaked clothing which would appear to include the full fabric. Adjustments were also suggested for the fact that clothing is only worn 12 hours per day and triclosan represents less than 100% market share. These adjustments were not made for this screening-level single textile use because insufficient information on residue transfer to a person's skin over time is not available and risks are determined for those individuals wearing the treated clothing articles (i.e., not a population adjusted risk assessment). However, the aggregate assessment using the NHANES biological monitoring data for triclosan is based on real world exposures and is believed to be the best data available to regulate the uses.
- D: The textile density is 10 mg/cm^2 based on the density of mixed cotton and synthetics (HERA 2003). It is assumed that the mixed cotton/synthetic is used to cover the body for both adults and toddlers, minus the head surface area.
- TF: Potential doses were calculated using residue transfer factor of 0.55% from a leaching study developed by Sanitized, Inc, dated December 4, 2007. The leaching study provided results for cotton (0.55% leached), wool (0.06% leached), and two poly-based fabrics (0.00%

for PA and 0.34% for PES). The cotton fabric leached the highest amount over a 48 hour period at 20 degrees C. The study used an acidic sweat solution at a pH of 5.5 and the ISO 105/E04 method to extract the triclosan from the various treated fabrics.

- BW: Toddlers (3 years old) are assumed to weigh 15 kg. This is the mean of the median values for male and female toddlers (USEPA, 1997). For adults, a body weight of 70 kg has been assumed. (USEPA, 1997).

Results

The calculations of the intermediate-term dermal doses and MOEs for adults and toddlers wearing treated clothing are shown in Table 4.9. The dermal MOEs for adults and toddlers are equal to or above the target MOE of 100.

Table 4.9: Dermal Intermediate-term Post-application Exposures and MOEs for Toddlers and Adults Contacting Treated Textiles and Fabrics.

Exposure Scenario	Density of clothing (mg/cm^2)	Percent triclosan in product (%)	Percent of product applied (%)	Percent residue transferred from clothing to skin (%)	Surface Area (cm^2)	Daily dose[a] (mg a.i./ kg/day)	Dermal MOE[c] (Target MOE=100) [b]
Toddler	10	99%	2%	0.55%	5670	0.41	98
Adult	10	99%	2%	0.55%	16900	0.26	150

a. Daily Dose (mg/kg/day) = [(Density of fabric 10 mg/cm^2) * (surface area of body covered, cm^2) * 1 outfit/day * (percent a.i. in product, %) / 100 * (percent of product applied, %) / 100 * (percent residue transferred from clothing to skin, %/100) * (dermal absorption factor, 1)] / (body weight, 15 and 70 kg).

b. Dermal MOE = NOAEL (mg/kg/day) / Daily Dose [Where intermediate-term dermal NOAEL = 40 mg/kg/day]. Target MOE = 100.

5.0 OCCUPATIONAL EXPOSURE ASSESSMENT

The exposure scenarios assessed in this document for the representative uses selected by EPA are shown in Table 5.1. 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.

Potential occupational handler exposure for triclosan can occur in three use sites: commercial/institutional/industrial premises and equipment, material preservatives, and industrial processes and water systems.

Table 5.1. Representative Exposure Scenarios Associated with Occupational Exposures to Triclosan

Representative Use	Method of Application	Exposure Scenario	Example Registration #	Application Rate
Commercial/Industrial/Institutional Premises (Use Category III)				
HVAC coil applications	Airless sprayer	ST/IT Handler: Inhalation	82523-1	6.1E-4 lb ai/10 ft^2 (0.85 pints/10 ft^2 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]
Material Preservatives (Use Category VII)				
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]
Industrial processes and water systems (Use Category VIII)				
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)

5.1 Occupational Handler Exposures

The occupational handler scenarios included in Table 5.1 were assessed to determine inhalation and dermal exposures. The general assumptions and equations that were used to calculate occupational handler inhalation risks are provided in Section 1.2, Criteria for Conducting the Risk

Assessment. The majority of the scenarios were assessed using CMA data and Equations 1-3 as outlined in Section 1.2. However, for the occupational scenarios in which CMA data were insufficient, other data and methods were applied.

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. The systemic dermal assessment is based on a dermal route-specific endpoint, and therefore, dermal absorption adjustments are not necessary. The intermediate- and long-term dermal endpoints are identical (but require different target MOEs to account for the long-term duration).

Unit Exposure Values (UE): Inhalation and dermal unit exposure values were taken from the proprietary Chemical Manufacturers Association (CMA) antimicrobial exposure study (USEPA, 1999b: DP Barcode D247642) or from the Pesticide Handler Exposure Database (USEPA, 1998).

- The For the ***liquid pour*** scenarios, the unit exposure depends on the material being treated. The following CMA unit exposures were available and used for the assessment of the risk associated with the treatment of the specified materials.
    - *Paint manufacturing:* CMA preservative data. The dermal unit exposure is 0.135 mg/lb ai (gloved). The inhalation unit exposure is 0.00346 mg/lb a.i. These unit exposure values are based on 2 replicates where the test subjects were wearing a single layer of clothing and chemical resistant gloves. Although these unit exposures are based on minimal replicates, the exposure values are similar to the ones found in PHED for a similar scenario.

  The For the ***liquid pump*** scenario, the unit exposure depends on the material being treated. The following CMA unit exposures were available and used for the assessment of the risk associated with the treatment of the specified materials.

    - *Paint and pulp & paper*: CMA preservative pump data. The dermal UE is 0.00629 mg/lb ai(with gloves) and the inhalation UE is 0.000403 mg/lb ai. The values are based on two replicates where the test subjects were wearing a single layer of clothing and chemical resistant gloves.

- For ***airless sprayer*** scenarios, the occupational PHED inhalation and dermal unit exposure values for airless sprayer application (PHED scenario 23) were used. The inhalation exposure value is 0.83 mg/lb ai. The dermal unit exposure is 38 mg/lb ai for ungloved replicates. PPE are not considered for material preservatives in paint because the paint is considered a treated article and as such there is no pesticide label on the paint container to communicate PPE.
    - For ***roller/brush*** scenarios, the occupational PHED dermal and inhalation unit exposure values for paintbrush applications (PHED scenario 22) were used (single layer of clothing). The inhalation exposure value is 0.28 mg/lb a.i. The dermal unit exposure is 180 mg/lb ai for no glove replicates. PPE are not considered for material preservatives in paint because the paint is considered a treated article and as such there is no pesticide label on the paint container to communicate PPE.

Quantity handled/treated: The quantity handled/treated values were estimated based on information from various sources. The following assumptions were made:

- For the ***liquid pour*** scenarios, the quantity of the chemical that is handled depends on the material that is being treated. The following values were used for the different materials:
    - *Paint*: 20,000 lbs (approximately 2,000 gallons, weight based on a density 10 lb a.i./gal) (standard AD assumption).

For the ***liquid/metering pump*** scenarios the quantity that is handled depends on the material that is being treated. The following values were used for the different materials:

- *Pulp and Paper*: 500 tons/day.
- *Paint*: 200,000 lbs (approximately 20,000 gallons, weight based on a density of 10 lb a.i./gal) (standard AD assumption).

- For the ***roller/brush*** painting scenario, it was assumed that 50 lbs (approximately 5 gallons of paint with a density of 10 lb/gal) of treated paint are used (standard AD assumption).
- For the ***airless sprayer*** in the ***painting*** scenario, it was assumed that 500 lbs (approximately 50 gallons of paint with a density of 10 lb/gal) of treated paint are used. (standard AD assumption).
- For the ***airless sprayer*** in the ***HVAC coil*** scenario, it was assumed 1,000 ft^2 of coil surface area is treated.

Duration of Exposure: The MOEs were calculated for the short- and intermediate-term durations for occupational handlers using the appropriate endpoints in Table 3.2.

Exposure Calculations and Results

The resulting inhalation and dermal exposures and MOEs for the representative occupational handler scenarios are presented in Table 5.2. The calculated dermal MOEs were above the target MOE of 100 for all scenarios, except for the commercial painters (both by brush and airless sprayer) and the pulp & paper use. The inhalation MOEs are below the target MOE of 1000 for the airless sprayer (paint), the paint manufacturing, and the pulp and paper.

Table 5.2. Short- and Intermediate-Term Inhalation and Intermediate-Term Dermal 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)[a]		MOE[b] (Target MOEs = 1000 inhalation, 100 dermal)	
		Inhalation	Dermal			Inhalation	Dermal	Inhalation	Dermal
Commercial, Institutional and Industrial Premises and Equipment (Use Site Category III)									
HVAC	Airless sprayer	0.83	38	6.1E-4 lb ai/10ft^2	Large building 1000 ft^2	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
Material Preservatives (Use Site Category VII)									
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
Industrial Processes and Water Systems (Use Site Category VIII)									
Pulp and Paper	Metering pump	0.000403	0.00629 (gloves)	2% ai	500 tons	Require closed loading systems to mitigate the exposure/risk			

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 = LOAEL or 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 = 1000 for inhalation and 100 for dermal.

5.2 Occupational Post-application Exposures

Occupational post-application dermal and inhalation exposures are assumed to be negligible based on the use patterns.

5.3 Data Limitations/Uncertainties

There are several data limitations and uncertainties associated with the occupational handler and post application exposure assessments. These 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) (See Appendix A for summaries of these data sources). 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.

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APPENDIX A: Summary of CMA and PHED Data

Chemical Manufacturers Association (CMA) Data:
In response to an EPA Data Call-In Notice, a study was undertaken by the Institute of Agricultural Medicine and Occupational Health of The University of Iowa under contract to the Chemical Manufacturers Association. In order to meet the requirements of Subdivision U of the Pesticide Assessment Guidelines (superseded by Series 875.1000-875.1600 of the Pesticide Assessment Guidelines), handler exposure data are required from the chemical manufacturer specifically registering the antimicrobial pesticide. The applicator exposure study must comply with the assessment guidelines for Applicator Exposure Monitoring in Subdivision U and the Occupational and Residential Exposure Test Guidelines in Series 875. For this purpose, CMA submitted a study on 28 February, 1990, entitled "Antimicrobial Exposure Assessment Study (amended on December 8, 1992)" which was conducted by William Popendorf, et al. It was evaluated and accepted by Occupational and Residential Exposure Branch (OREB) of Health Effect Division (HED), Office of Pesticides Program (OPP) of EPA in 1990. The purpose of this CMA study was to characterize exposure to antimicrobial chemicals in order to support pesticide reregistrations (CMA, 1992). The unit exposures presented in the most recent EPA evaluation of the CMA database (USEPA, 1999b) were used in this assessment.

The Agency determined that the CMA study had fulfilled the basic requirements of Subdivision U - Applicator Exposure Monitoring. The advantages of CMA data over other surrogate data sets is that the chemicals and the job functions of mixer/loader/applicator were defined based on common application methods used for antimicrobial pesticides. A few of the deficiencies in the CMA data are noted below:

- The inhalation concentrations were typically below the detection limits, so the unit exposures for the inhalation exposure route could not be accurately calculated.
- QA/QC problems including lack of either/or field fortification, laboratory recoveries, and storage stability information.
- Data have an insufficient amount of replicates.

The Pesticide Handlers Exposure Database (PHED):
The Pesticide Handlers Exposure Database (PHED) has been developed by a Task Force consisting of representatives from Health Canada, the U.S. Environmental Protection Agency (EPA), and the American Crop Protection Association (ACPA). PHED provides generic pesticide worker (i.e., mixer/loader and applicator) exposure estimates. The dermal and inhalation exposure estimates generated by PHED are based on actual field monitoring data, which are reported generically (i.e., chemical specific names not reported) in PHED. It has been the Agency' policy to use surrogate or generic exposure data for pesticide applicators in certain circumstances because it is believed that the physical parameters (e.g., packaging type) or application technique (e.g., aerosol can), not the chemical properties of the pesticide, attribute to exposure levels. [Note: Vapor pressures for the chemicals in PHED are in the range of E-5 to E-7 mm Hg.] Chemical specific properties are accounted for by correcting the exposure data for study specific field and laboratory recovery values as specified by the PHED grading criteria.

PHED handler exposure data are generally provided on a normalized basis for use in exposure assessments. The most common method for normalizing exposure is by pounds of active ingredient (ai) handled per replicate (i.e., exposure in mg per replicate is divided by the amount of ai handled in that particular replicate). These unit exposures are expressed as mg/lb ai handled. This normalization method presumes that dermal and inhalation exposures are linear based on the amount of active ingredient handled.