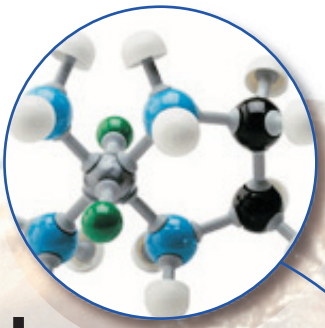
Exposure and Risk Screening Methods for Consumer Product Ingredients



SDA

The Soap and Detergent Association

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Exposure and Risk Screening Methods for Consumer Product Ingredients

The Soap and Detergent Association
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Acronyms and Abbreviations

ACA	Alliance for Chemical Awareness
AISE	Association Internationale de la Savonnerie, de la Détergence et des Produits d'Éntretien
AP	Asia Pacific
APAG	European Oleochemicals and Allied Products Group
CESIO	Comite Europeen des Agents de Surface et de Leurs Intermediaries Organiques
CTFA	Cosmetic, Toiletry, and Fragrance Association
E-FAST	Exposure & Fate Assessment Screening Tool
EFH	U.S. EPA's *Exposure Factors Handbook*
EQC	equilibrium criterion
EU	European Union
EUSES	European Union System for the Evaluation of Substances
HERA	Human & Environmental Risk Assessment project
HPV	high production volume
IC	ingredient concentration
JSDA	Japan Soap and Detergent Association
K_{ow}	octanol-water partition coefficient
LAS	linear alkylbenzene sulfonate
LOAEL	lowest-observed-adverse-effect level
MOE	margin of exposure
NA	North America (U.S. and Canada)
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
OECD	Organisation for Economic Co-operation and Development
OPPT	Office of Pollution Prevention and Toxics
PBT	persistent, bioaccumulative, and toxic
PDM	probabilistic dilution model
PE	product exposure
PEC	predicted environmental concentration
PNEC	predicted no-effect concentration
POP	persistent organic pollutant
POTW	publicly owned treatment works
QSAR	quantitative structure activity relationship
SDA	The Soap and Detergent Association
SIAR	SIDS initial assessment report
SIC	standard industrial classification
SIDS	screening information data sets
STP	sewage treatment plant
TCC	triclocarban
TGD	technical guidance document
U.S. EPA	U.S. Environmental Protection Agency
WWTP	wastewater treatment plant

1 Introduction

1.1 Purpose and Audience

The consumer products industry has exposure information and screening methods that can be of value in putting high production volume (HPV) chemical hazard data into an exposure perspective and thereby facilitate prioritization of chemicals for further evaluation if appropriate.

The main purpose of this document is to present methodologies and specific consumer exposure information that can be used for screening-level risk assessments of environmental and repeated human exposures to HPV chemicals through the manufacturing and use of consumer products, mainly laundry, cleaning, and personal care products. However, the approach can be applied to other consumer products when information on how consumers use the products is available. These methodologies allow hazard information to be put into context by using exposure information to characterize risk. Screening-level risk assessments are useful for prioritizing the need for further work.

The intended audience of this document is chemical risk assessors within governmental agencies, businesses, and stakeholder groups who have limited experience in the area of consumer product exposure and risk assessment, and have responsibility for prioritizing chemical safety reviews of numerous substances. This document would also be useful for assessors involved in chemical risk management work as a tool to improve the efficiency of resource utilization.

1.2 Background on SDA HPV Program

In support of the HPV chemicals program, The Soap and Detergent Association (SDA) is coordinating preparation of the Organisation for Economic Co-operation and Development (OECD) screening information data sets (SIDS) initial assessment reports (SIARs) for eight families of chemicals:

Aliphatic acids	Methyl esters
Amine oxides	Aliphatic alcohols
Fatty acid distillation residues	Alkyl sulfates
Hydrotropes	Glycerides

These chemicals have a wide range of uses including, for example, soaps and detergents; disinfectants, sanitizers, and household pest controls; cosmetics, fragrances, and personal care products; food and food additives; automotive care products; and polishes. The scope of the SIARs includes both human and environmental health exposure and hazard evaluations as each relates to the production and use of 300+ chemicals grouped into eight families. It is generally

recognized that during chemical manufacturing, product formulation, and the use and disposal of products, some human exposures and environmental releases can occur. Human exposure can be both direct and indirect. There can be both occupational exposure and exposure resulting from consumer products. Environmental releases to air, water, and land might occur during the manufacture, processing or formulating, and intended use of the chemical or product.

Preparing a SIAR involves multiple steps. The initial step in the SIAR process involves assembling the available hazard data (i.e., physicochemical properties, environmental fate, ecotoxicity, and mammalian toxicity) and preparing a summary document, an Assessment Plan, for each chemical family as prescribed by the U.S. Environmental Protection Agency (U.S. EPA) HPV Chemical Challenge Program (http://www.epa.gov/opptintr/chemrtk/volchall.htm). The second step is a global effort to gather and summarize available production, use and exposure information for these same families of chemicals. The information gathered includes the following:

- Annual production volumes by region (North America, Europe, Asia Pacific)
- Use categories and/or functions
- Pounds of chemical for each use category and/or function
- Physical form of the product(s)
- Likely sources of exposure including occupational (manufacturing and commercial use), consumer use, and indirect via food, water, and air
- Recommended workplace exposure limits and/or controls in place
- Sources of potential releases to the environment
- Relevant routes of human exposure by use category and/or function
- Modeling and/or monitoring data on human exposure and on releases to air, water, and land.

The hazard information along with the use and exposure information is summarized into a SIAR that includes a recommendation that either 1) the chemical (or family) is currently of low priority for follow-up work, except for periodic review, or 2) the chemical is a candidate for further work. This document describes screening-level methodologies that assist in such priority setting by integrating exposure information along with the HPV hazard data to characterize risks posed by exposures.

1.3 Background on Screening-Level Assessments for Priority Setting

Screening-level risk assessments are typically used to prioritize chemicals for future work based on their hazards and exposure potential. These assessments use readily available exposure data and simple models based on first principle equations that are generally used by the scientific and

regulatory communities. Conservative default assumptions are integrated into the assessments to compensate for uncertainties and gaps in the data. The assumptions are deliberately designed to be conservative in order to avoid risk decisions based on "false negatives."[1] Consequently, screening estimates of releases, exposure, and risks are conservative and often higher than actual values reported (Pittinger et al. 2003).

More refined assessments can be conducted if warranted. The refined assessments are designed to closely simulate a particular exposure scenario and thus require more detailed chemical, site, and receptor-specific data, and employ fewer default "conservative" assumptions.

Screening tools that prioritize chemicals for further work can include those based on readily available information on the intrinsic properties of the chemical (e.g., physicochemical properties and toxicity), amounts released into the environment (e.g., Toxic Release Inventory), and a combination of these two, as well as assessments that integrate the available hazard data with more sophisticated exposure estimates based on mathematical model predictions. In general, because screening-level risk assessments are less resource-intensive or costly, they serve as an efficient means of categorizing and prioritizing those chemicals that either warrant more tailored and detailed assessments or those that are of no concern and can be put aside.

The Alliance for Chemical Awareness (ACA) has presented an assessment framework that focuses on a screening-level approach to inform priority setting for HPV chemicals titled *Framework for Evaluation of HPV Chemicals for Potential Ecological Exposure and Risk* (March 10, 2002) (ACA 2002). This framework provides a step-wise approach for assessing potential exposure and risks posed by HPV chemicals to relevant ecological and human receptors. Figure 1-1 presents the ACA generic exposure framework, starting with a broad general evaluation and, as appropriate, proceeding to a more specific detailed evaluation. The following questions are addressed in the framework:

1. When, during commerce, could people or the environment be exposed to HPV chemicals? In manufacturing, distributing, formulating, end-use?
2. What are the plausible routes for exposure, via industrial facilities, products, and/or dispersed environmental sources?
3. What is the magnitude of exposure for key routes, either separately or in aggregate, as appropriate?
4. How does exposure compare to the relevant hazards?
5. What decisions can be recommended about further work on the chemical? Low priority, needs further evaluation, or risk management?

This document presents more specific exposure information and methodologies that can be used for doing screening-level risk assessments for environmental and human exposures to HPV chemicals resulting from the manufacturing and use of consumer products, mainly laundry, cleaning, and personal care products. For screening purposes, both environmental and human

[1] In this context, false negative means that exposure and risk estimates are lower than their actual levels.

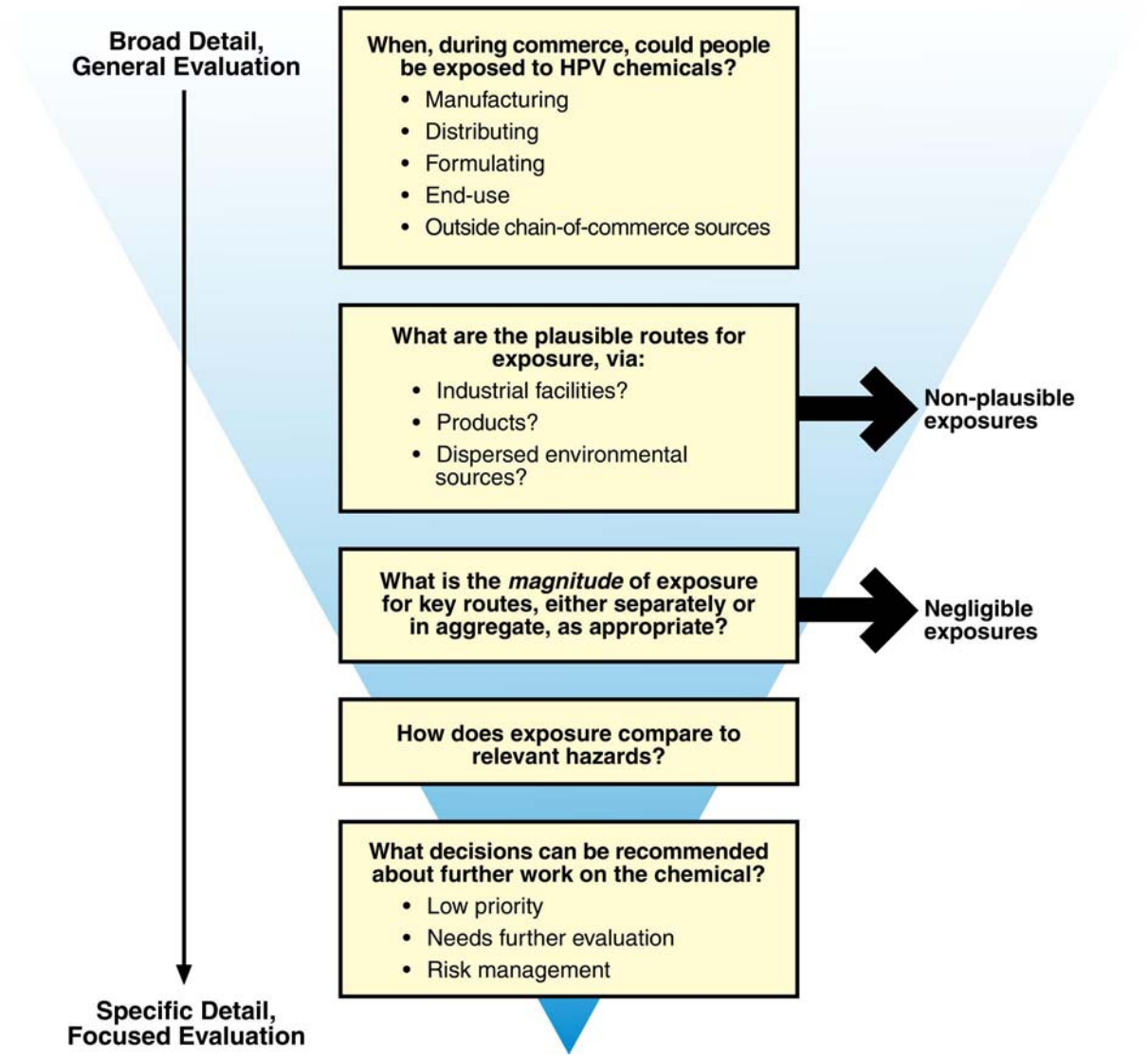

Figure 1-1. Generic exposure framework

exposures are typically established using models based on conservative assumptions and readily available information. For environmental screening assessment, conservative assumptions are usually made about characteristics of the chemical, its manufacture and use, and environmental fate. Similarly, in a screening assessment of consumer exposures via direct use of products, exposure factors such as frequency of use and amount of product use are conservatively estimated.

The screening assessment methodologies presented in this document are based on the ACA generic exposure framework. Three exposure scenarios are of primary interest as they relate to use of chemicals in consumer products discussed in this paper:

1. Human exposures (dermal, oral, and inhalation) to HPV chemicals via use of consumer products

2. Environmental releases of HPV chemicals at a manufacturing facility

3. Environmental releases of HPV chemicals following use and down-the-drain disposal of consumer products.

In the environmental releases scenarios (i.e., from manufacturing sites and down-the-drain disposal), potential exposures to both ecological (e.g., fish and wildlife) and human receptors (e.g., drinking water and eating fish) are considered. For human exposure scenarios involving the direct use of consumer products, the main objective of the risk screening methodology is to identify product categories and associated use scenarios that present the greatest potential for exposure. Based on this information and appropriate hazard information, uses that warrant detailed evaluation can be identified. For prioritization purposes, this is done by comparing the estimated human exposure to the appropriate no-observed-adverse-effect level (NOAEL)[2] for the most sensitive human toxicity endpoint. In this comparison, if a margin of exposure (MOE, the quotient of the NOAEL divided by the estimated human exposure) is adequate, no further evaluation is needed. However, as this initial evaluation process relies on conservative high-end[3] exposure assumptions, if the MOE is not adequate more refined analyses can be conducted by replacing high-end assumptions with more detailed, scenario-specific information.

For the environmental release scenarios, the main objective of the environmental exposure screening methodology is to provide reasonable estimates on predicted environmental concentrations (PECs). These PECs are specific to the chemical (or chemical category) and, by design, are intended to be representative of conditions in a given geographic region. When data are available, refined analyses are conducted by replacing standard, conservative defaults with more chemical-specific and local/regional information. PECs can be used in screening-level risk evaluations by comparing the exposure estimate to a concentration expected to have no effect on organisms in the environment (i.e., the predicted no-effect concentration [PNEC]) and determining the margin between the predicted exposure level and the level determined to not cause adverse effects.

The screening methodology to evaluate risks from exposure to HPV chemicals via direct use of consumer products is presented in Section 2 of this report. The environmental screening methodology addressing environmental release scenarios is described in Section 3. Integrated case studies based on the OECD use and exposure format (as shown in Appendix IV) are developed to illustrate how both screening methodologies are applied to produce initial exposure and risk characterization outputs.

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[2] An allowable daily intake or reference dose is typically used in traditional safety assessment. However, these exposure guidelines are not available for most HPV chemicals.

[3] High-end: a plausible estimate at the upper end of a distribution of values, conceptually above the 90th percentile.

2 Risk Screening Methodology for Exposure to High Production Volume Chemicals via Consumer Products

2.1 Background and Scope

Consumer products may have multiple forms, uses, and exposure scenarios. Their uses are often associated with a range of exposure frequencies, durations, and pathways. Given the large number of products and possible associated consumer exposure scenarios, a priority setting process is needed to identify consumer products and use scenarios for which more detailed exposure and risk assessment may be needed to adequately characterize consumers' exposures and risks, and to set aside those that represent a low level of concern. Screening-level risk assessments provide the basis for that process.

The OECD SIDS program provides the following guidance with respect to characterization of potential human exposure to HPV chemicals:

> The human population for which there is a potential exposure to the chemical should be identified with specific consideration of occupational exposure, consumer exposure and indirect exposure via the environment. These considerations should be based on readily available general information on exposure, the use pattern, and physicochemical properties of the chemical.

Consistent with these guidelines, exposure can be estimated for priority setting purposes without the need for either monitoring or sophisticated modeling data. Rather, estimates of exposures can be based on simple, first principle exposure equations that are regularly used in the scientific and regulatory communities, conservative assumptions about exposure, and readily available information about the characteristics of the HPV chemical group, the consumer product type, and the nature of product use. Although the use of conservative assumptions would clearly lead to over-estimation of exposure, conservatism is appropriate for screening-level assessments that are purposely designed to avoid making "false negative decisions."[4] This section of the paper provides a proposed screening methodology for evaluating potential human exposures and risk from HPV chemicals resulting from their use in consumer products. Indirect exposures via releases to the environment and from manufacturing facilities, and disposal of consumer products down the drain are discussed in the environmental section (Section 3) of this document.

The ACA developed a screening-level assessment as part of a framework for a step-wise approach for risk characterization that provides for the opportunity, on an as-needed basis, to replace conservative exposure assumptions with more realistic data prior to deciding whether additional toxicology information needs to be gathered or risk management actions need to be

[4] False negative decisions are based on exposure and risk estimates that are lower than their true levels. For example, a decision not to conduct further tests because risk estimates were falsely estimated to be low.

taken. By design, one only advances to the next step in the process if there is reason to believe that the refinement will likely result in a different decision about the priority for further work on the HPV chemical. The following are the key steps in the screening-level process as described in the ACA framework (ACA 2001):

1. Identify product category(ies) and product(s) where the HPV chemical is used, the concentration (percent) of the HPV chemical in the product(s), the physical and chemical properties of the HPV chemical and the product(s), available SIDS hazard data, related products that could be evaluated as a group, etc.
2. Estimate, qualitatively or quantitatively, exposure to the HPV chemical for each product category, initially by using highly conservative assumptions about the circumstances of product(s) use.
3. Identify the relevant SIDS endpoint and a NOAEL or a lowest-observed-adverse-effect level (LOAEL) from an epidemiology study or animal toxicology study.
4. Determine, for each product category, whether or not the MOE to the HPV chemical is adequate.
5. If necessary, sequentially develop more detailed and realistic exposure information.
6. Make the decision about the need for further evaluation or risk management.

In general, the risk screening methodology described in this document mirrors the key steps identified in the ACA framework. It includes an initial assessment of the products that contain a given HPV chemical group and its uses in order to identify those products that are most likely to contribute significantly to the overall exposure based on the circumstances of their use. Related chemicals may be grouped together, based on shared exposure scenarios, in order to simplify the analysis and to maximize the use of available hazard information.

The described methodology addresses non-cancer SIDS endpoints relevant to chronic exposures (i.e., repeated exposures) and is focused on a screening-level assessment. Since the SIDS program focuses on initial prioritization of chemicals for further work and non-cancer endpoints, exposure and risk assessments beyond screening approaches and cancer risk assessment are beyond the scope of this methodology. Additionally, the scope of this risk screening methodology is limited to the exposure scenarios that fall within the intended/labeled use of products. While it is recognized that there are foreseeable misuses of products, for example, washing the side of a house with dishwashing liquids, this scenario is a minor use.

2.2 Objectives

Chemical hazard information is required under OECD SIDS program. However, in order to effectively prioritize chemicals for further work, it is necessary to put the hazard information

into the context of exposure and risks. Toward this goal, the objective of the exposure and risk screening methodology outlined below is to provide relevant information regarding human exposure to consumer products and a transparent process for putting the hazard information in the context of the estimated human exposure. The process involves identifying the product category(ies) and associated use scenario(s) with the greatest exposure potential, and then integrating the potential exposures with the HPV hazard data so that uses that may warrant more detailed characterization can be identified.

It should be emphasized that this identification process is only an initial screening assessment, which relies on conservative, "worst-case" toxicity and exposure assumptions (e.g., using the most toxic chemical in the group of chemicals, and assuming maximum absorption of the chemical), which are designed to overestimate exposures and risks. When necessary, refined risk analyses can be conducted by replacing high-end assumptions with more detailed scenario and chemical-specific information.

2.3 General Framework

A general approach to screening-level risk assessment is to develop exposure and risk estimates for the chemical or group of chemicals for each product category based on default high-end exposure and conservative dose-response parameters. These screening-level risk estimates would represent reasonable worst-case estimates of exposure and risks for a given product. The following screening-level risk characterization algorithm is applied:

$$\text{Margin of exposure (MOE)} = \frac{\text{Dose-response threshold}}{[\text{exposure to product (PE)} \times \text{ingredient concentration (IC)}]}$$

or

$$\text{MOE} = \text{NOAEL}/(\text{PE} \times \text{IC})$$

For screening purposes, the selection of the appropriate NOAEL/LOAEL for non-cancer chronic exposure risks is based on the following considerations:

- The most sensitive repeated-exposure toxicity endpoints (i.e., lowest NOAEL of all the repeat dose endpoints evaluated, when a range of values is available)
- Routes of exposure relevant to the product use-exposure scenarios (i.e., dermal, oral, or inhalation)
- The quality of available experimental study data.

Based on a screening analysis, product categories with the lowest MOEs can be identified for more detailed characterization if the MOE is not adequate. In the subsequent refined assessment of these product categories, a more detailed evaluation to identify both the most appropriate NOAEL for the chemical in the product and exposure scenarios, and more realistic exposure information beyond the screening approach described above, could be pursued.

Conceptually, [PE × IC] is the surrogate high-end exposure to the chemical substance, also called the screening-level chemical exposure. The product exposure component is an estimate of exposure to the consumer product ($mg_{product}$/kg-day) and the ingredient concentration component is the concentration (percent) of the chemical ingredient in that product. More details on these components of the screening risk characterization are described in the exposure data matrix in Sections 2.4 and 2.5 below. Where applicable, examples and data for a real HPV chemical group are provided.

2.4 Screening-Level Exposure Data

As indicated above, the screening-level chemical exposure estimate is based on two components: the product exposure estimate and the ingredient concentration (percent) in that product. The product exposure estimates are based on several screening exposure equations. The equation input parameters have been derived from a number of governmental and non-governmental sources (See Appendix I-A for list of sources for Product Exposure Models and Input Parameters. See Appendix 1-B for their relevance to the exposure scenarios addressed in this document.) The ingredient concentration estimates are based on a survey of companies that produce these products, which was sponsored by SDA and the Cosmetic, Toiletry, and Fragrance Association (CTFA). The following sections provide detailed descriptions of these components of the screening chemical exposure estimate.

2.4.1 Product Exposure Estimates and Data Sources

2.4.1.1 Data Matrix

To facilitate the implementation of this risk screening methodology, a product exposure data matrix has been constructed for several categories of consumer products. The data matrix provides exposure factors (e.g., frequency of use, duration of use, amount used per occasion) and equations used to estimate oral, inhalation, and dermal exposures for the key scenarios of each consumer product category. It should be noted that the exposure estimates are provided in terms of product—not specific chemical substance. To estimate exposures to the HPV chemical, these exposures would be combined with formulation data. This matrix does not account for indirect exposures (e.g., environmental, dietary or drinking water). Estimated exposures from those routes are developed separately and integrated into the overall assessment.

Several first principle equations (models) are used to estimate exposure to consumer products. Although most are generic models based on general parameters and high-end values associated with conservative estimates of exposure, some are based on chemical- and scenario-specific parameters. Table 2-1 provides an overview of the model equations and parameters included in the data matrix.

Table 2-1. Summary of model equations used to calculate product exposure

Exposure Route	Product Exposure Scenario	Product Exposure Model	Parameters
Dermal: Indirect	**Exposure after activity/use of:**	**North American (NA) Approach**	
	Laundry detergents: wearing clothing		A: amount used (g/day)
	Fabric conditioners: wearing clothing	$\frac{A \times PR \times PT \times CF \times DA}{BW}$	PR: percent retained on clothing (percent)
			PT: percent transferred from clothing to skin
		where:	CF: conversion factor (1,000 mg/g)
		PR = 1 percent based on SDA data	BW: female body weight (60 kg EU, 65.4 kg NA)
			DA: dermal absorption (100 percent)
		European (EU) Approach	
		$\frac{A \times PR \times PT \times CF \times DA}{BW}$	PD: percent deposition (percent)
			FD: fabric density (mg/cm^2)
		where:	W: total wash weight (mg)
		PR = (PD x FD) / W) x CA	CA: body surface contact area (cm^2)
		and PD = Sw / Tw	Sw: mass of water after spin cycle (kg)
			Tw: mass of water per spin cycle (kg)
Dermal: Direct	**Exposure during the activity/use of:**	**NA and EU Approach**	
	Laundry detergent: hand-washing clothes		FQ: frequency of use (use/day)
	Laundry detergent: laundry pretreatment	$\frac{FQ \times CA \times PC \times FT \times CF \times TF \times DA}{BW}$	CA: body surface contact area (cm^2)
	Dish detergent: hand washing dishes		PC: product concentration (g/cm^3)
	Dish detergent: washing hands		FT: film thickness on skin (cm)
	Dilutable hard surface cleaners		CF: conversion factor (1,000 mg/g)
	Non-dilutable hard surface cleaners		TF: time scaling factor (unitless)
	Dilutable all-purpose cleaners		BW: female body weight (60 kg EU, 65.4 kg NA)
	Non-dilutable all-purpose cleaners		DA: dermal absorption (100 percent)

Table 2-1. (continued)

Exposure Route	Product Exposure Scenario	Product Exposure Model	Parameters
Dermal: Direct	**Exposure after the activity/use of (residual):**	**NA and EU Approach**	
	Adult rinsed-off products:	$\frac{FQ \times A \times PR \times CF \times DA}{BW}$	FQ: frequency of use (use/day)
	Body washes		A: amount used (g/use)
	Bath foam/bubble baths		PR: percent retained (percent)
	Hair conditioners		CF: conversion factor (1,000 mg/g)
	Hair rinses		DA: dermal absorption (100 percent)
	Hand/body/face soaps		BW: female body weight (60 kg EU, 65.4 kg NA)
	Shaving cream		male body weight (70kg) (shaving products)
	Shampoos		child body weight (15 kg) (baby care products)
	Adult leave-on products:		
	Antiperspirants		
	Aftershave		
	Face/eye cosmetics		
	Fragrances		
	Facial cream		
	Hand/body moisturizer		
	Hair spray		
	Styling/tonic gel		
	Styling mouse		
	Sun cream/lotions		
	Baby care rinsed-off products:		
	Baby bath liquids		
	Kid shampoos		
	Baby care leave-on products:		
	Baby lotion and cream		

Table 2-1. (continued)

Exposure Route	Product Exposure Scenario	Product Exposure Model	Parameters
Oral: Indirect	**Exposure after activity/use of:**	**NA and EU Approach**	
	Dish detergents (hand washed)	$\frac{C' \times Ta' \times Sa \times CF}{BW}$	C': product concentration (mg/cm^3) Ta': amount of water on dish after rinse (ml/cm^2) Sa: area of dish contacting food (cm^2/day) CF: conversion factor (1 cm^3 water/1 ml water) BW: female body weight (60 kg EU, 65.4 kg NA)
Oral: Direct	**Exposure during activity/use of:**	**NA and EU Approach (except additives and OTC medicine):**	
	Mouthwash Lipstick	$\frac{FQ \times A \times FI \times CF}{BW}$	FQ: frequency (use/day) A: amount used (g/day)
	Toothpaste	**NA and EU Approach (additives and OTC medicine only):**	FI: fraction ingested (percent)
	Food additives Over the counter medicine/ pharmaceuticals	$\frac{FI \times C}{BW}$	CF: conversion factor (1,000 mg/g) BW: female body weight (60 kg EU, 65.4 kg NA) child body weight (15kg) (toothpaste) C: food consumption of pharmacological dose **Note:** FI and C will vary by food types. Default screening values have not been established.
Inhalation: Direct	**Exposure during activity/use of:**	**NA and EU Approach**	FQ: frequency (use/day)
	Hair spray Antiperspirants–aerosols Fragrances Paints	$\frac{FQ \times A \times IR \times ED \times F \times CF}{V \times BW}$	A: amount used (g/use) IR: inhalation rate (m^3/hr) ED: exposure duration (hr/day) F: respirable fraction (percent) CF: conversion factor (1,000 mg/g) V: effective breathing air space (2 m^3) (**Note:** This value is not appropriate for paints.) BW: female body weight (60 kg EU, 65.4 kg NA)

Table 2-1. (continued)

Exposure Route	Product Exposure Scenario	Product Exposure Model	Parameters
	Exposure during activity/use of:	**NA and EU Approach**	FQ: frequency (use/day)
	Laundry detergent–powders	$\frac{FQ \times A \times F}{BW}$	A: amount used (g/use) (**Note:** A is the amount of dust/scoop × 1 scoop/use.)
			F: respirable fraction (percent)
			BW: female body weight (60 kg EU, 65.4 kg NA)
	Exposure during activity/use of:	**NA and EU Approach**	
	Trigger spray cleaners	$\frac{FQ \times RPC \times IR \times ED \times BA}{BW}$	FQ: frequency (use/day)
			RPC: respirable product concentration in breathing zone (mg/ m^3)
			IR: inhalation rate (m^3/hr)
			ED: exposure duration (hr/day)
			BA: bioavailability fraction (100 percent)
			BW: female body weight (60 kg EU, 65.4 kg NA)

For a screening-level assessment, high-end exposure factors (e.g., high-end frequency of product use, longer duration of product use/contact, largest amount of product use per occasion) would be used. The default high-end screening product exposure data matrix and associated references/documentation can be found in Appendix II-A. For transparency and comprehensiveness, the readily available ranges of values (minimum-maximum) and associated references/documentation are also summarized in Appendix II-B. If it is determined that further refinement is necessary as the result of a screening assessment, typical values from the data range could be utilized in a refined analysis, when exposure condition and hazard information are available to support such refinement.

In general, product exposure estimates are based on a 65.4 kg body weight for females (U.S. EPA 1997). However, for products designed for a specific target population, the representative body weights for those populations were employed. For example, if the product was developed for use by males, then the exposure estimates were based on a male body weight of 70 kg, or if the exposure estimates were being made for baby care products, the default body weight used for children was 15 kg. Also, in those instances where a product may be used by multiple subgroups (e.g., both adults and children use toothpaste) the product exposures are calculated based on the subgroup resulting in the greatest exposure. For example, for the toothpaste ingestion scenario, the default sub-population was based on children.

2.4.1.2 Product Exposure Data Sources

Exposure equations and parameters were extracted from a variety of sources including governmental agency documents, use surveys involving consumer product manufacturers, SDA companies' in-house habits and practices data obtained from product development studies, and the published literature. Since the resulting screening exposure assessments are to be submitted to OECD and/or U.S. EPA under the HPV Challenge Program, it was necessary to select model equations and parameters that are used and/or would be accepted by the appropriate regulatory authorities. Thus, the prevailing North American (NA)[5] and European Union (EU) equations and exposure factors compiled in the data matrix are based on guidance and practices previously provided by the EU, U.S. EPA, and the OECD. The sources of data were selected in the following order:

1. Governmental documents written by regulatory authorities (e.g., U.S. EPA *Exposure Factors Handbook* [EFH], EU *Technical Guidance Document* [TGD])
2. Documents written for submission to regulatory authorities (e.g., Association Internationale de la Savonnerie, de la Détergence et des Produits d'Éntretien [AISE] Human & Environmental Risk Assessment project [HERA] risk assessments, American Industrial Health Council exposure initiative assessments)
3. Survey data collected by industry associations (i.e., CTFA and European Cosmetic Toiletry and Perfumery Association cosmetic use surveys, AISE HERA Habits and Practices Survey for cleaning products)

[5] For the purposes of this survey, "North America" included only the U.S. and Canada.

4. SDA member company data

5. Data found in the published literature.

Much of the data in the published literature have been captured in the source categories 1 and 2 described above. In most cases, data were found in source categories 1–4 and exhaustive searches of the published literature were limited to exposure parameters that were not found among these sources. Generally, the selection process followed the above hierarchy; however, there were some minor exceptions. For example, in some cases, such as the cosmetic use pattern parameters, data from association surveys (e.g., CTFA's use survey for body lotion, hair spray, face cream, lipstick, perfume, and foundation) were selected over the data found in U.S. EPA's EFH. U.S. EPA's 1997 EFH refers to older CTFA data. Therefore, it was reasonable to select CTFA use data from a more recent survey (May 2000). Region-specific data were used for the NA and EU regions unless it was not available. In these cases, the references are identified by the appropriate footnotes in Appendices II-A and II-B.

Description of references, detailed mapping of documents reviewed for each exposure scenario, relevant secondary references within the primary source, and the documents that are selected as the source information for the habit and practice data presented in Appendices II-A and II-B are summarized in Appendices I-A and I-B. Each selected document may be used as source information for several parameters and equations, and Appendices II-A and II-B provide more specific source identification for each individual equation and input parameter.

2.4.2 Screening-Level Ingredient Concentration Data

In 2001, the SDA conducted a survey of manufacturers, importers, processors and formulators of HPV chemicals used in soaps, detergents and related consumer, commercial, and industrial products for up to ten families of chemicals (aliphatic acids, aliphatic alcohols, amine oxides, anionic surfactants, fatty-acid distillation residues, glycerides, hydrotropes, linear alkylbenzene sulfonate [LAS]/alkylbenzene sulfonate, methyl esters, and triclocarban [TCC]). SDA conducted the survey to provide information on chemical production, uses, and exposures for these chemical families managed by SDA at a regional level for NA, EU, and Asia Pacific (AP). The ingredient concentration data presented in this document are based on that SDA survey.

The survey was administered in two parts. The first part was directed toward collecting very general information about company activities for each of the listed chemicals, to determine if the surveyed companies were a manufacturer/importer, processor, or formulator of the respective chemicals and to determine focus areas for follow up surveys. The following definitions were used for the survey:

Manufacturer/Importer:	Produces the subject chemical, including importation and toll manufacturing, as a commodity or intermediate.
Processor:	Uses the subject chemical in the production of derivatives or other intermediates, but not end-use products.
Formulator:	Uses the subject chemical or intermediates derived from a subject chemical in formulation of end-use products.

The second part of the survey involved collection of specific data and information on:

- Chemical production and/or importation amounts
- Chemical use by product type
- Chemical releases to the environment
- Conditions under which potential worker exposures are mitigated with personal protective equipment and/or engineering controls
- Chemical concentrations in formulated products.

The information collected from the survey was compiled to develop a minimum and maximum ingredient concentration for each product category. For conducting a screening-level assessment, both minimum and maximum ingredient concentration for an entire group of HPV chemicals was generated for each product use category. Table 2-2 shows the information that was collected on one HPV group (herein HPV Chemical "A" Group). In screening-level assessments, both the minimum and maximum ingredient concentration values could be used to develop screening exposure estimates encompassing the range of ingredient concentrations.

Table 2-2. An ingredient concentration data matrix for the HPV Chemical "A" Group[a]

Product Type	Concentration in Products (percent range)
Dishwashing detergents (liquid)	0.1–10
Hard surface cleaners (liquid spray)	1–5
Hard surface cleaners (liquid)	0.1–5
Laundry detergents (liquid)	1–5
Hand/face soaps (bar)	0.1–5
Shampoos	0.09–5
Hair conditioners	0.6–0.7
Hair styling tonic/gel	0.1–2
Cleansing products	0.04–9
Skin creams/moisturizers	0.2–0.6
Aftershaves	0.5–1
Home dry cleaning products	0.1–0.5
Douches	1–2
Face/eye foundations (liquid)	<0.1
Hair coloring preparations	<0.1
Permanent waves preparations	1–2

[a] The product concentration ranges indicate active HPV Chemical A concentration in the formulated products and do not take into account any dilution prior to or during use. Many products on the market in these categories do not contain HPV Chemical A and not all the products listed are available in NA, EU, and AP regions.

2.5 Selecting No-Observed-Adverse-Effect Levels for Screening-Level Risk Characterization

The OECD guidance (OECD 2003) for the preparation of an SIAR for hazard assessment indicates that the results of the following toxicity tests and other information should be summarized and discussed in the SIAR:

- Toxicokinetic, metabolism, and mechanism of action (if known)
- Acute toxicity
- Repeated dose toxicity
- Reproduction/developmental toxicity
- Genetic toxicity
- Any other information that is available (e.g., experience with human exposure).

The guidance (OECD 2003) also indicates that a judgment on the NOAEL and LOAEL must be made and presented in the context of the adverse effects, information on the dose-response relationship, and an assessment of whether any adverse effects are considered compound-related based on the test results of repeated-dose and reproductive/developmental toxicity. In addition, the toxicological significance of breakdown products or metabolites (if any), and relevant available data on non-SIDS elements such as irritation, skin sensitization, and carcinogenicity are to be stated and the associated results, discussion, and conclusions summarized in a similar manner.

The OECD SIDS program provides the option to put the hazard information into perspective by reporting the exposure information along with the hazard data. The primary focus of the SDA methodology is to put repeated-dose studies in an exposure/risk context. Most HPV chemicals with substantial consumer product use have relatively low acute toxicity, with oral or dermal LD_{50}s greater than 2,000 mg/kg and classifiable as Category 5 (the least acutely toxic classification) under the OECD Harmonized Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures.[6] However, in less common situations where an HPV chemical has oral or dermal LD_{50} less than 50 mg/kg (Categories 1 and 2 under the OECD Harmonized Integrated Classification System), risks from acute toxicity would be evaluated. Further, if non-SIDS elements such as metabolism, irritation, and carcinogenicity are noted and described in the hazard assessment, they would also be discussed accordingly and put in an exposure context in the screening-level assessments.

Given the number of chemicals that may be grouped into an SDA HPV chemical group, the hazard data set for a chemical group is expected to consist of one or more chemicals with

[6] In light of animal welfare considerations, testing on animals using HPV chemicals in the Category 5 ranges is discouraged and should only be considered when there is a strong likelihood that results of such testing would have a direct relevance for protecting human health (OECD 2001).

NOAELs and/or LOAELs for various SIDS endpoints and routes of exposure. For the initial screening-level risk characterization, a default approach would be to select the most sensitive endpoint (i.e., the toxicity endpoint with the lowest NOAEL). Table 2-3 displays a hypothetical, but typical, hazard data matrix in which different chemicals within an HPV group have different NOAELs for different SIDS endpoints. For this hypothetical data matrix, the lowest NOAEL value would be selected as the default NOAEL for the entire group.

Table 2-3. Hypothetical hazard data matrix

	NOAEL				Selected NOAEL for Chemical Group
Toxic Endpoints	CAS #1	CAS #2	CAS #3	CAS #4	
A–Reproductive	X_{1A}	No data	No data	No data	
B–Developmental	No data	No data	No data	X_{4B}	X_{1C}
C–Repeated	$*X_{1C}$	X_{2C}	X_{3C}	X_{4C}	

Note: X - NOAEL; subscripts A, B, and C indicate the endpoints and 1, 2, 3, and 4 indicate the corresponding chemical number
* - indicates lowest NOAEL value

This default approach adds conservatism to the screening-level analysis because all products would not necessarily contain this specific chemical but may actually contain a chemical from the group that is less toxic. When applying this default strategy, additional considerations could lead to a decision to choose a NOAEL other than the lowest one:

- One consideration is experimental data quality. The default approach of selecting the lowest relevant NOAEL would be examined when the quality of the underlying study is poor. In such cases, a higher NOAEL from a better quality study would be used.
- Another consideration for deviation from the default selection of the lowest relevant NOAEL would be to consider the use of a LOAEL from a higher quality study, which could improve consistency in data quality across chemicals and family of chemicals.
- Routes of exposure should be relevant to the use of the chemicals. When a dermal NOAEL is available, it should be used for comparison with dermal exposure data. If an oral NOAEL from a gavage study is used for comparison with dermal exposure, then dermal absorption factors should be used to adjust estimates of exposure. It is important to note that if dermal absorption is taken into consideration to determine systemic exposure then oral absorption must also be considered and expressed on a systemic exposure basis. Published guidelines such as the *European Commission Guidance Document on Dermal Absorption* should be used as a reference for dermal absorption factors (European Commission 2004).

Table 2-4 presents an example of a hazard data matrix for the HPV Chemical "A" Group. For this chemical group, a NOAEL of 52.6 milligrams/kilogram body weight per day (mg/kg_{BW}-day) was selected as representative for the chemical family and used to determine the MOE. This NOAEL was chosen because of the high quality of the study from which it is derived; it is the highest NOAEL (below the lowest LOAEL) with the longest study duration (e.g., 2-year exposure), and it is consistent with the NOAELs from the other toxicity endpoints.

Table 2-4. HPV Chemical "A" group hazard data matrix

Toxic Endpoints	NOAEL (mg/kg_{BW}-day)				Representative NOAEL for Chemical A Group
	CAS #1	CAS #2	CAS #3	CAS #4	
A–Reproductive	>40[a]	No data	No data	No data	52.6
B–Developmental	25[b]	100	No data	No data	
C–Repeated	80	No data	No data	No data	
D–Chronic	52.6[c]	No data	No data	No data	

[a] Effect was not observed at any dose levels in the experiment, including the highest dose level; 40 mg/kg_{BW}-day was the lowest dose group in the experiment and no effect was observed at this lowest dose.

[b] Maternal toxicity was observed at a LOAEL = 100 mg/kg_{BW}-day. However, no effect was observed at 25 mg/kg_{BW}-day.

[c] The chronic NOAEL of 52.6 is consistent with the result in the reproductive study (i.e., NOAEL < 40 mg/kg_{BW}-day) and with the developmental study, because it falls in the range between the NOAEL (25 mg/kg_{BW}) and the LOAEL (100 mg/kg_{BW}-day).

2.6 Screening-Level Assessments

Based on the outline described above in Section 2.3, *General Framework*, screening-level assessments can be carried out for HPV chemical groups. Several approaches for applying this framework are described in this section:

- Screening based on exposures can be conducted to identify product categories and use scenarios that result in the highest exposures in the chemical group.
- Screening risk characterization can be conducted by comparing screening exposure estimates with appropriately selected hazard data. Appropriate selection of hazard data is described above in Section 2.5.

Where necessary, refinements can be made to provide more realistic estimates of exposure and risk. The initial screening assessments are described below. Section 2.7 describes the refinement process in more detail.

2.6.1 Screening Based on Exposures

The purpose of this assessment is to identify the product category(ies) with the most significant exposure potential prior to consideration of the hazard data. In this assessment, the screening-level estimate of exposures (in $mg_{chemical}/kg_{BW}$-day) is based on PE × IC. The output of this exposure assessment is a list of product-exposure scenarios and their corresponding screening-level exposure estimates for the oral, dermal, and inhalation routes for each product category where the HPV chemical is used. By sorting screening exposure estimates for each route (i.e., dermal, oral, and inhalation) from high to low, product exposure scenarios with the highest potential exposures to the HPV chemical can be identified, as well as those that would be expected to result in negligible exposure.

As an example, screening-level exposures to Chemical A from consumer uses of products were estimated using this methodology. The default high-end product exposure estimates were based on the habits and practices data provided in Appendix II-A and the ingredient concentration for Chemical A was obtained from the SDA survey work as previously described and summarized in Table 2-2. The exposure estimates for this screening-level assessment are shown in Table 2-5.

Table 2-5. Chemical A screening-level exposures by product exposure scenarios

	Screening-Level Exposure Estimates ($mg_{chemical\ A}$/kg-day) (minimum to maximum)	
Product Exposure Scenarios	Dermal	Inhalation
Cleaning Products (direct exposure)		
Laundry pre-treatment (undiluted)	1.0E-3 to 5.0E-3	
Hard surface cleaner (undiluted)	1.0E-4 to 5.0E-3	
Hand–wash laundry (diluted)	4.7E-5 to 2.3E-4	
Hand dishwashing–dishes (diluted)	9.0E-6 to 9.0E-4	
Hand dishwashing–hands (dish liquid–diluted)	3.0E-6 to 3.0E-4	
Hard surface cleaner (diluted)	9.4E-6 to 4.7E-4	
Spray cleaner		1.6E-6 to 8.2E-5
Laundry Product (residual on clothing)		
Liquid detergent	2.0E-3 to 1.0E-2	
Personal Care Product (residual after use)		
Hair conditioner	4.1E-3 to 4.7E-3	
Shampoo	2.5E-3 to 1.4E-1	
Bar soap–hand	3.6E-4 to 1.8E-2	
Cleansing products	2.3E-4 to 5.1E-2	
Bar soap–face	4.5E-5 to 2.2E-3	
Personal Care Product (leave on materials)		
Aftershave	7.0E-2 to 1.4E-1	
Hair styling tonic/gel	4.7E-3 to 9.3E-2	
Body moisturizer	1.1E-3 to 3.2E-3	

2.6.1.1 Screening Aggregate Exposures: Within Product Categories

Screening-level exposure estimates for the various product exposure scenarios could be aggregated within each product category to identify the product category with the highest potential exposure to the HPV chemical. This aggregation by product category could be simply based on adding the scenario exposures within a product category. In the case of Chemical A, for the liquid detergents product category, this could be done by simply adding the screening estimates from the three modeled scenarios—hand-washing, pre-treatment, and residual on clothing.

Table 2-6 provides a summary of the screening exposure estimates for various product categories based on aggregation within a product category. For Chemical A, neither inhalation nor indirect exposures shown above contribute significantly to the overall exposure. As indicated in the table, at maximum screening exposure level, two of the product categories—hair care (hair conditioner, shampoo, styling tonic/gel) and aftershave—are the primary drivers of the exposure, with exposures from all other product categories being one to three orders of magnitude lower.

Table 2-6. Exposures to Chemical A by product category

Product Category	Estimated Exposure ($mg_{chemical\ A}$/kg-day) (minimum to maximum)
Hair care	1.1E-2 to 2.4E-1
Aftershave	7.0E-2 to 1.4E-1
Laundry detergent–liquid	3.0E-3 to 1.5E-2
Bar soap	4.1E-4 to 2.0E-2
Cleansing products	2.3E-4 to 5.1E-2
Dish detergent–liquid	1.2E-5 to 1.2E-3
Body moisturizer	1.1E-3 to 3.2E-3
Hard surface cleaner–liquid	1.1E-4 to 5.5E-3

2.6.1.2 Screening Aggregate Exposures: Relevant Product Combination

An estimate of total aggregate exposures can be obtained by simply adding the exposures from all the individual products. In the case of Chemical A, the use of all of consumer products by a single consumer is plausible because there are no duplicate product types within a category. If there were duplicate types of product (e.g., both liquid and granular laundry detergents), as a conservative approach, the product resulting in the higher exposure would be used. It could be argued that consumers using aftershave (probably men) would be less likely to use body moisturizers and cleansing products (probably women). However, adding these exposures with other uses would be appropriate for a conservative screening approach.

In the case of Chemical A, which has fairly widespread uses across household cleaning and personal care categories, the simple addition of multiple exposures did not change the order of magnitude of the total exposure. In fact, the total aggregate exposure estimate is not significantly different from the exposures estimated for two product categories (hair care and

aftershave) because the use of these two products contributes 80–85 percent of the total aggregate exposure. Table 2-7 provides a summary of the percent of total exposure by each product type.

Table 2-7. Percent contribution of total exposure by product type

	Estimated Chemical A Exposure (mg/kg-day)	
	Minimum	Maximum
Aggregate Exposure	8.59E-02	4.76E-01
Product Type	Percent of Exposure	
Aftershave	81.5	29.4
Hair care	12.8	50.4
Laundry detergent–liquid	3.5	3.2
Body moisturizer	1.3	0.7
Bar soap	0.5	4.2
Cleansing products	0.3	10.7
Hard surface cleaner–liquid	0.1	1.2
Dish detergent–liquid	0.0	0.3

2.6.2 Screening Risk Characterization

Screening risk characterization is conducted by estimating MOEs (i.e., MOE = NOAEL/(PE × IC)). Using the screening aggregate exposure estimate for each product category and screening total aggregate exposure estimate for all relevant product category combination, as previously described, screening MOEs for each product category and combined product categories can be developed, respectively. The following sections described these steps in more detail.

2.6.2.1 Screening Risk Characterization by Product Categories

For each product category, a number of screening-level MOEs can be developed for all possible routes of exposure (dermal, oral, inhalation). The approach of selecting a default conservative NOAEL was previously described in Section 2.5. Table 2-8 illustrates a hypothetical output from the screening risk characterization.

Table 2-8. Hypothetical outputs from a screening risk characterization

Product Category	Screening Risk Characterization		
	MOE_{Dermal}	MOE_{Oral}	$MOE_{Inhalation}$
A	$NOAEL_{dermal}/PE_A \times IC_A$	$NOAEL_{oral}/PE_A \times IC_A$	$NOAEL_{inh}/PE_A \times IC_A$
B	$NOAEL_{dermal}/PE_B \times IC_B$	$NOAEL_{oral}/PE_B \times IC_B$	--
C	$NOAEL_{dermal}/PE_C \times IC_C$	--	$NOAEL_{inh}/PE_C \times IC_C$

Note: -- = not applicable

Table 2-9 provides the screening-level MOEs for various products with Chemical A as an ingredient. Chemical A exposure estimates for various product exposure scenarios described in Section 2.6.1.1 were compared to a NOAEL of 52.6 mg/kg_{BW}-day to develop the MOEs.

Table 2-9. Screening-level MOEs from Chemical A exposures by product category (NOAEL = 52.6 mg/kg_{BW}-day)

	MOEs	
Product Type	At Minimum Exposure	At Maximum Exposure
Aftershave	730	375
Hair care	4,782	219
Laundry detergent–liquid	17,533	3,506
Body moisturizer	47,818	16,438
Bar soap	128,293	2,630
Cleansing products	228,696	1,031
Hard surface cleaner–liquid	478,182	9,564
Dish detergent–liquid	4,383,333	43,833

2.6.2.2 Determination of Products and Routes of Exposure Requiring Further Evaluation Based on MOE

The purpose of the screening risk characterization is to identify product and route-specific exposures that can be set aside with high confidence as well as those that are of potential concern and warrant more in-depth evaluation. Identification of products with high or low potential risks is based on the screening-level MOEs. An initial default for the decision of "not of concern and no further refinement" based on an MOE of 1,000 or greater is considered adequate for two reasons:

1. The conservative approaches used to develop the screening-level exposure estimates.
2. The use of the lowest NOAEL of all the toxicity studies conducted has deliberately erred on the side of protection (i.e., conservative estimates).

   In general, the following "default" filtering process would be applied:

   a. For product categories with MOEs larger than 1,000 (MOE is unitless), there would be no need for further consideration or assessment.

   b. For product categories with MOEs greater than 100 but less than 1,000, a decision for refined assessment would depend on the specifics of the study conducted (e.g., a 90-day study versus a

6-month or longer study, the severity of the response, the quality and comprehensiveness of the data set) and the particular product and its uses.

c. For product categories with low screening MOE estimates (i.e., less than 100), refinement of the NOAEL and/or the exposure estimates would be warranted.

Various factors need to be taken into consideration when determining whether an initial default MOE of less than 1,000 but greater than 100 is adequate:

- The quality and comprehensiveness of the database available on the chemical/group of chemicals
- The duration of the study (28-day versus 90-day versus a 6-month study or greater)
- The quality of the study upon which the MOE is based
- The seriousness of the effect observed
- The steepness of the dose-response curve
- What is known about the toxicokinetics and toxicodynamics of the chemical in animals versus in humans.

With respect to study duration, for repeat dose-toxicity studies an initial default of 10 is generally used when extrapolating a 90-day repeat dose study to lifetime exposures. If the repeat dose study is 6 months or longer, an uncertainty factor of 10 is not necessary because a study of this duration is considered predictive of non-cancer, chronic toxicity. With respect to consideration of the seriousness of the adverse effect, if the effect that is observed is minor and/or reversible, the MOE is based on a high-quality 90-day study, and the database for the chemical group is of high quality and is comprehensive with respect to studied endpoints, then an MOE of less than 1,000 may be adequate for making the decision that no further refinement of the assessment is needed.

Numerous documents have been written about risk assessment and application of appropriate uncertainty factors to studies/data sets when deriving appropriate guidance values for exposure limits for humans. It is not the intent of this paper to list all those documents nor to discuss in-depth the various factors. However, one key document that one can consult in making a decision about the adequacy of the MOE is the International Programme on Chemical Safety's Environmental Health Criteria 170 Document, *Assessing Human Health Risks of Chemicals: Derivation of Guidance Values for Health-Based Exposure Limits* (WHO/IPCS 1994).

In the case of the Chemical A example, with the exception of the hair care and aftershave products, all products have MOEs greater than 1,000 and thus should not be subject to further assessment. Although the MOEs for hair care and aftershave use are below 1,000, refinements should not be necessary for the following reasons:

- The MOE was based on a high quality chronic toxicity study
- The Chemical A family has a comprehensive toxicity data set that includes developmental toxicity and reproductive toxicity, as well as carcinogenicity data (beyond SIDS endpoint requirements)
- The MOE is greater than 100 and thus is sufficient to account for the 10-fold uncertainty factor for interspecies variability and a 10-fold uncertainty factor for intra-species variability (Health Canada 1994; Kodell and Gaylor 1999).

2.6.2.3 Screening Aggregate Risk Characterization: Relevant Product Combination

The main purpose of developing screening-level aggregate exposure by summing exposures for the relevant combination of product uses by an individual (described in Section 2.6.1.1) is to identify product-exposure scenarios that are the drivers for total exposures and that may warrant more detailed and refined exposure assessments. Taking this a step further and comparing this screening-level aggregate exposure to the default lowest NOAEL from the hazard data set of an entire HPV chemical group to characterize risks (i.e., MOEs) would amount to a cumulative risk assessment, with an explicit assumption that there is equivalent toxicity for all chemicals within an HPV group. Clearly, this is not the case. However, if one uses this conservative approach and the resulting MOE is adequate (see discussion above on adequacy of MOE), then a conclusion of "no concern and no further work needed" for the use of the entire HPV chemical group in consumer products could be made with high degree of confidence. On the other hand, if this "no concern" conclusion cannot be made, refined assessments for the product uses that were identified as exposure/risk drivers would be carried out using more chemical-specific information. The following section describes such refinements in more detail.

2.7 Consideration for Refinements

Similar to most screening-level assessment methodology, the methodology described above is purposely designed to prevent false negative decisions by making the worst-case assumptions about toxicity and exposure, including default assumptions of high-end product-exposure estimates, ingredient concentration ranges for the group applied to all product types irrespective of the actual chemical concentration, and the use of the lowest NOAEL. As such, there is a high level of confidence in the classification of product types and use scenarios, and/or combinations thereof that are of "no concern and no further work is necessary" based on this screening-level assessment. Conversely, using this screening methodology would lead to a high likelihood for false positives.[7] Thus, refinements of exposures and risks for the product-use scenarios that have been classified as "potential concern" would be necessary.

[7] In this context, false positives are screening estimates of exposures and risks that are higher than their true estimates.

Consequently, it is important that a continual refinement process, as outlined in Figure 2-1, is implemented. This process begins with the initial screening that is based on high-end default assumptions (described in this methodology) and continues the loop of refining exposure estimates and selecting NOAELs that are more appropriate for the product use scenarios of concern.

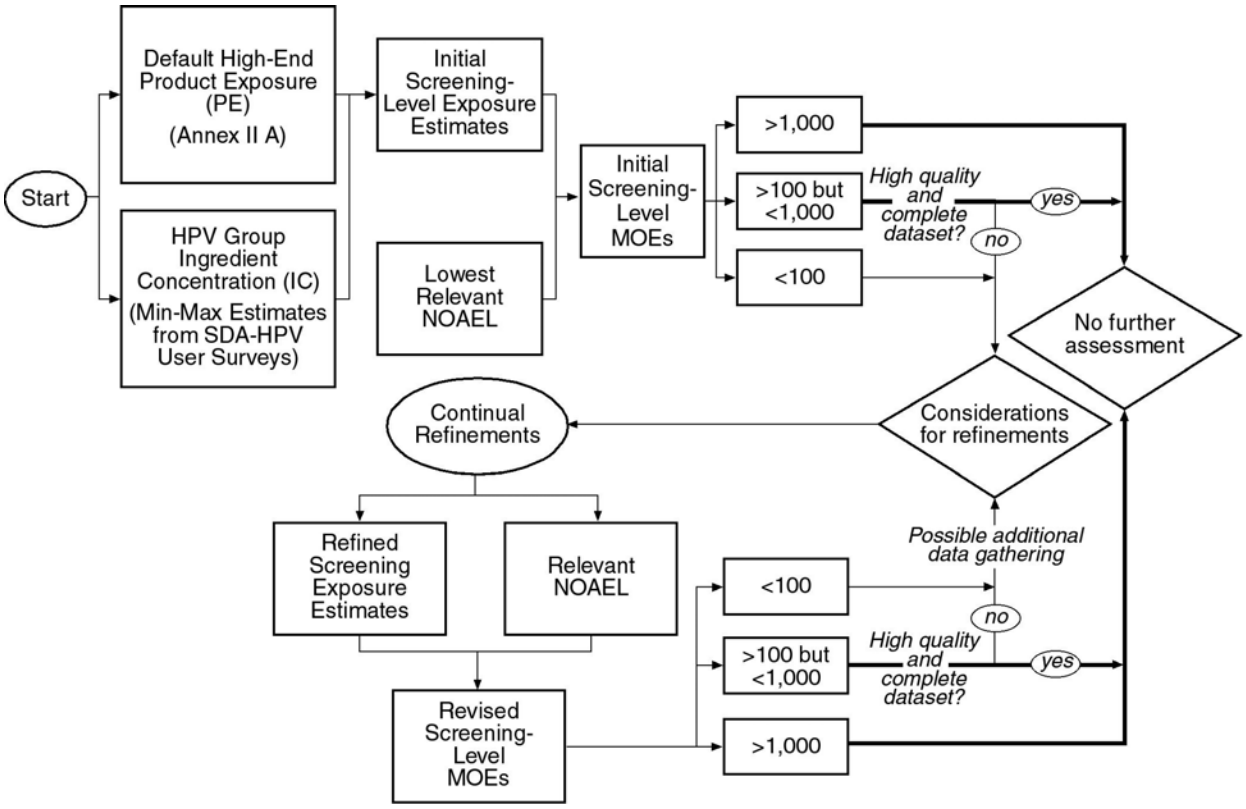

Figure 2-1. Screening-level assessment—continual refinement process

2.7.1 Refining Exposures

Conservative exposure factors were selected as defaults to yield high-end initial exposure estimates in this screening methodology. Combinations of average and high-end values for exposure model input parameters (e.g., frequency of product use, amount of product use, product retention factors, etc.) could be used to develop more realistic high-end exposure estimates rather than those based on combination of worst-case values assumed in this screening methodology (U.S. EPA 1992). Example approaches to further refine the screening exposure estimates could include the following:

- Refining the dermal penetration default value. The default value of 100 percent dermal penetration in the screening exposure assessment models can be modified based on measured dermal penetration/absorption values. If dermal exposure is modified and dermal exposure is being compared to an oral toxicity study NOAEL, actual oral absorption of the chemical must also be

taken into consideration when determining the MOE. An example of this is the HERA alcohol ethoxysulfates assessment (HERA 2003).

- Refining surface area estimates. For skin creams and other consumer products that are applied to the skin, the specific habits and practices data for these products can be used to refine exposure. For example with skin creams, total body application is assumed. However, if the HPV chemical of interest is only used in a facial cream, this surface area is not appropriate. Refinement from total body surface area to just facial surface area would significantly reduce exposure estimates.

- Refining the frequency and/or duration of product use based on more detailed product category information can also provide more realistic estimates.

2.7.2 Identifying Relevant NOAELs

Refinements of the NOAEL can be carried out through a re-examination of the appropriateness of selecting the lowest repeat dose NOAEL as the representative dose-response threshold for an entire HPV chemical group. Divisions of chemicals within each HPV chemical group based on similar toxicological potency would be more appropriate in a refined assessment. One option could be to select a NOAEL for the specific chain length(s) that is typically used in the product category. For example, if the lowest NOAEL selected in the screening assessment is based on a short chain length (e.g., C6) and the shorter chain length chemicals have been shown to be more toxic than the longer chain length chemicals, but the actual ingredient/chemical in the products that are subject to refined assessments are of the longer chain length and of lower toxicity (e.g., C14, C16 and C18), then refining the risk characterization using the higher NOAEL would be appropriate. Further, if toxicities were different for the different routes of exposure, toxicity equivalents would be considered in the aggregation. Sophisticated aggregate assessments that require more detailed specification of input parameters, including distribution and probabilistic assessment methodology similar to those required under the Food Quality Protection Act (FQPA 1996) are beyond the scope of screening-level assessment.

2.8 Minor Exposure Scenarios Not Considered in Screening Assessment

The purpose of the screening exposure assessment and screening risk characterization is to identify any products and use scenarios of potential concern. For each consumer product there may be a large number of possible exposure scenarios. However, there are usually only one or a few scenarios that are relevant in contributing the dominant exposure for each product. By comparison, the others are insignificant in the assessment of most chemicals because they do not contribute appreciably to estimated exposures and risks. For example, previous assessments have shown that human exposure to household cleaning product ingredients is very low for a number of product scenarios in which ingredients of interest comprise up to 30 percent of the product. For soaps, LAS, and alkyl sulfates, combined exposures for all household-cleaning scenarios are less than 6 micrograms per kg body weight per day (<6 $\mu g/kg_{BW}$-day)

(www.heraproject.com). Dermal exposures during hand dishwashing, household surface cleaning and from detergent residue on laundered clothes, and inhalation exposure to laundry powder dust and aerosol cleaning products contribute less than one-third of the total household cleaning product exposure (<2 $\mu g/kg_{BW}$-day). Dermal exposure during hand laundering and laundry pretreatment, and ingestion of detergent residue on dinnerware contributes to the remainder (<4 $\mu g/kg_{BW}$-day) (www.heraproject.com). In general, these minor scenario uses do not need to be included in the screening-level exposure assessment when exposures from other uses are expected to greatly exceed exposures resulting from these uses, and when the MOE is expected to be very large.

2.9 Summary

As stated in the general approach section of this document, this risk screening methodology is based on default high-end product exposure estimates and conservative dose-response data (i.e., lowest NOAEL and route-specific data when available). The main purpose of this methodology is to serve as a priority-setting tool. The screening exposure and risk characterization outputs from the application of this methodology can help focus resources to develop more refined risk assessments where such refinement is needed, and assist in deciding where exposures/risks are of minimal concern and refined assessment is not warranted.

In Appendix IV, several case studies that use this consumer exposure/risk screening method with initial exposure and risk characterization results are provided. The case studies are for LAS and hydrotropes, both of which are based on the format of the OECD use/exposure pilot project. An example of an U.S. EPA HPV assessment is also included in Appendix IV for TCC.

2.10 References

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3 Exposure, Effects, and Risk Screening Methodologies for High Production Volume Chemicals via Environmental Releases

3.1 Background and Scope

This section of the document provides a methodological approach for screening environmental exposures of SDA, European Oleochemicals and Allied Products Group (APAG), Comite Europeen des Agents de Surface et de Leurs Intermediaries Organiques (CESIO), and Japan Soap and Detergent Association (JSDA)-sponsored HPV chemicals that are used primarily in laundry, cleaning, and personal care products. Screening-level assessment is often sufficient to provide an adequate characterization of exposure and resulting risk. Conservatively high exposure estimates that are well below toxicological threshold levels support a determination that harm to the environment is unlikely.

Chemicals can be evaluated separately or as categories of related substances. Two exposure scenarios are of primary interest: 1) environmental releases of these chemicals at a manufacturing facility (including production, processing, and formulation facilities), and 2) environmental releases following product use and down-the-drain disposal.

Because of the physicochemical nature of HPV chemicals primarily used in laundry, cleaning, and personal care products, the environmental medium of most interest and the focus of this assessment is the freshwater aquatic environment. However, exposure in other media including air, soil, and biota, and in other aquatic environments such as estuarine and marine systems (see Section 3.8, *Related Compartments*) can also be considered as either part of the screening process or in subsequent assessments. It must also be recognized that some of the exposure assessment models that will be discussed later (e.g., the Exposure & Fate Assessment Screening Tool [E-FAST]) do not estimate exposure in these other media. Therefore, additional work would be required to estimate exposure in environmental media beyond the freshwater aquatic environment.

The ACA has prepared an assessment framework titled *Framework for Evaluation of HPV Chemicals for Potential Ecological Exposure and Risk* (March 10, 2002). It consists of a stepwise approach for conducting assessments of potential exposure and risk to relevant ecological and human receptors posed by HPV chemicals released to the environment. In addition to ecological receptors (e.g., fish and wildlife), environmental releases from both manufacturing sites and down-the-drain disposal can result in human exposure (e.g., drinking water and fish consumption). The ACA framework is a screening-level approach that can inform priority setting. It is a generic yet detailed framework that is well-suited to the wide range of HPV chemicals and product uses covered by the International Council of Chemical Associations Initiative, and the interests of the SDA, JSDA, APAG, and CESIO consortia. The framework and supporting documentation can be viewed in its entirety at the ACA website www.chemicalawareness.org.

The ACA exposure and risk assessment framework consists of four phases:

1. **Description of the Flow in Commerce and Resulting Emissions to the Environment:** The goal of this step is to gain an understanding of where, how, and at what gross levels the chemical is likely to reach the environment.

2. **Assessment Formulation:** The goal of this step is to determine the need for risk characterization and level of exposure based upon the available use and exposure information along with the hazard profile of the chemical. Key exposure pathways and receptors are identified as part of this step.

3. **Screening Exposure/Risk Assessment:** The goal of this step is to prepare quantitative estimates of exposure and risk based on modeled information and, where available, monitoring information.

4. **Higher Level/Refined Assessment:** This step can be deemed necessary based upon the outcome of Step 3 or the status of the substance as persistent, bioaccumulative, and toxic (PBT). Step 4 is used to refine/expand the screening-level assessment using more chemical and/or site- and situation-specific information.

This ACA guidance has established the pathways by which HPV chemicals can lead to exposure of environmental and human receptors. The guidance proposed a process for coupling environmental exposure and effects assessments into a decision-making framework. However, the ACA guidance did not specify the methods to be used to conduct the exposure and effects assessments, which is the primary objective of this document.

The ACA guidance and this document are written to estimate exposure for PBT and non-PBT chemicals. However, because of their persistence and the possibility that concentrations can build up in the environment over time, PBT chemicals may require a higher-level assessment. This document assumes that the route chemicals follow from consumer use and disposal into a municipal wastewater treatment plant (WWTP) to release into the environment occurs primarily in the form of liquid effluents. Assuming degradation, the highest environmental concentration will occur in the effluent immediately after dilution. Assuming no degradation, continued use will result in accumulation in soil, sediment, or surface waters. Hence, this accumulation may need to be considered in a higher-level assessment if the degradation rate is extremely slow. Criteria for determining if a substance is a PBT can be found in the Stockholm Convention on Persistent Organic Pollutants (POPs) (http://www.pops.int/) and in national regulations, such as the Canadian Toxic Substance Management Policy (http://www.ec.gc.ca/CEPARegistry/policies/) and the U.S. EPA PBT chemical rules (http://www.epa.gov/tri/lawsandregs/pbt/pbtrule.htm#rule). Japan's *Monitoring Report on the Persistent Organic Pollutants in Japan* can be found at http://www.env.go.jp/en/topic/pops/ and specific laws can be found at http://www.env.go.jp/en/topic/pops/Appendix/05-LawsPOPs.htm. The EU defines POPs using the *United Nations 1998 Protocol to the 1979 Convention on Long-Range Transboundary Air Pollution on Persistent Organic Pollutants* (http://www.unece.org/env/lrtap/full%20text/1998.POPs.e.pdf) with an additional commission proposal adopted in August 2004 (http://europa.eu.int/eur-lex/en/com/pdf/2004/com2004_0537en01.pdf).

The approach discussed in this document is intended to be applied to surface waters. Thus, exposure models and effects assessment procedures focus on estimated exposure and effects in this environmental compartment. This is consistent with the intent of the HPV process. Data relevant to determining exposure and effects in the terrestrial compartment or in estuarine and marine systems may be provided in HPV data summaries. Where available, these data can be used, but it should be realized that this is beyond the scope of the HPV process and the method described here.

This approach also does not directly address exposure to impurities or degradation products, although similar methods can be used if the data required for such an assessment are available or can be estimated for the impurity or degradation products of interest. Further, toxicity data are likely to help address the toxicity of impurities and degradation products to the extent that these compounds were present in tests.

3.2 Assessment Tiers versus Levels

A tiered process is typically followed in a traditional risk assessment. In the lower tiers, risks are assessed using relatively few data and conservative assumptions. If a decision can be made based on a lower tier assessment, then the assessment process is stopped. However, if a decision cannot be made and additional data are needed, the assessment proceeds to the higher tiers. Thus, the word "tier" implies an iterative process. Within the context of HPV screening-level assessments as described in this document, assessments are performed after all available data are collected and collated. Thus, most assessments will not be iterative and the concept of a tiered process does not typically apply. Hence, the term assessment "level" is used in this document to describe different amounts and types of data that are available for estimating exposure corresponding to different degrees of sophistication in the exposure and effects assessments.

With increasing assessment levels, standard, conservative defaults are replaced with more chemical-specific and local/regional information. Thus the assessment progresses from a conservative to a more realistic exposure estimate. In effect assessments, assessment factors are reduced as more ecologically relevant data are used to establish the PNEC (see Section 3.6). In screening-level risk evaluations, PECs are compared to an effect benchmark (i.e., the PNEC) to determine the margin between the predicted exposure level and the level determined to be "safe" or not to pose significant risk to the biological receptor(s) of interest.

3.3 Exposure Assessment

The following sections present a "toolbox of methodologies" for use in HPV environmental assessments. The goal is to identify those environmental exposure methods that are both widely used and accepted by regulatory agencies to place within this toolbox. Case study examples of how to take a chemical or group of chemicals through the screening process presented in the draft OECD format for HPV chemical use/exposure assessments are also provided in Appendix IV.

3.3.1 Objectives

The main objective of the environmental exposure screening methodology is to provide reasonable estimates of PECs using the best available data and widely accepted models. These PECs are specific to a chemical (or chemical group) and, by design, are intended to be representative of conditions in a given geographic region.

3.3.2 Chemical Use and Exposure Information

As part of the hazard profile developed for each of the HPV chemicals (or chemical groups), physicochemical data are provided that can be used in the exposure modeling process. These data minimally include water solubility, octanol-water partition coefficient (K_{ow}), vapor pressure, stability in water (hydrolysis), photodegradation, and biodegradability test results.

The Level 1 assessment approach assumes that these data will be available. However, for many HPV chemicals, additional data that are available and that can be used to support higher-level exposure assessments are also included in the HPV summary.

As described in the Section 2.4.2, a survey was conducted of producers and consumer product formulators to obtain information for individual chemicals (identified by CAS number). Information was collected on annual production/importation volume by geographic region and the percentage of that volume that is sold/used as a final product, exported outside the region, and/or further processed to an intermediate (and whether that intermediate is site-limited). These data can be used to obtain initial estimates of emissions to the environment, which are necessary to conduct the environmental exposure assessment. In addition, when available, region-specific information was also collected to determine the likelihood and location of manufacturing releases and offsite transfer (e.g., stack releases, discharge to wastewater treatment, landfill disposal, incineration). Requests were also made for available environmental monitoring data (e.g., wastewater treatment removal efficiency and/or surface water concentrations) and for facility classification (e.g., Standard Industrial Classification [SIC] Codes for U.S. facilities and Main and Industrial categories for EU facilities). Beyond the SIDS data collected in this survey, other information useful for the exposure assessments includes the following:

- WWTP removal
- Sorption onto soils and sediments
- Realistic degradation test results and estimates of half-lives
- Effluent/emission or environmental monitoring.

3.3.3 General Framework

Consumer product chemicals used in laundry, cleaning, and personal care products generally enter the environment during production, formulation, and after use in consumer products through water discharges (see Figure 3-1), although there are products where significant proportions of environmental releases are to air or soil as a result of use. Industrial discharges are also generally to water, although emissions can occur to the air and soil environments, depending on the process operations and the physicochemical properties of the chemical. The SDA-sponsored HPV chemicals generally have low volatility, which means that air releases are relatively limited. The sponsored chemicals range from highly water soluble to much less water soluble, with a corresponding affinity to partition to solids and/or lipids indicating that they are most likely to be in water discharges. Because most of the volume of the chemicals produced for use in consumer products is disposed to the environment after use of the product and very little during production or formulation of the product, the main focus of models that estimate the fate and exposure for consumer product chemicals is on disposal in household wastewater, which is discharged to surface waters after treatment in a WWTP.

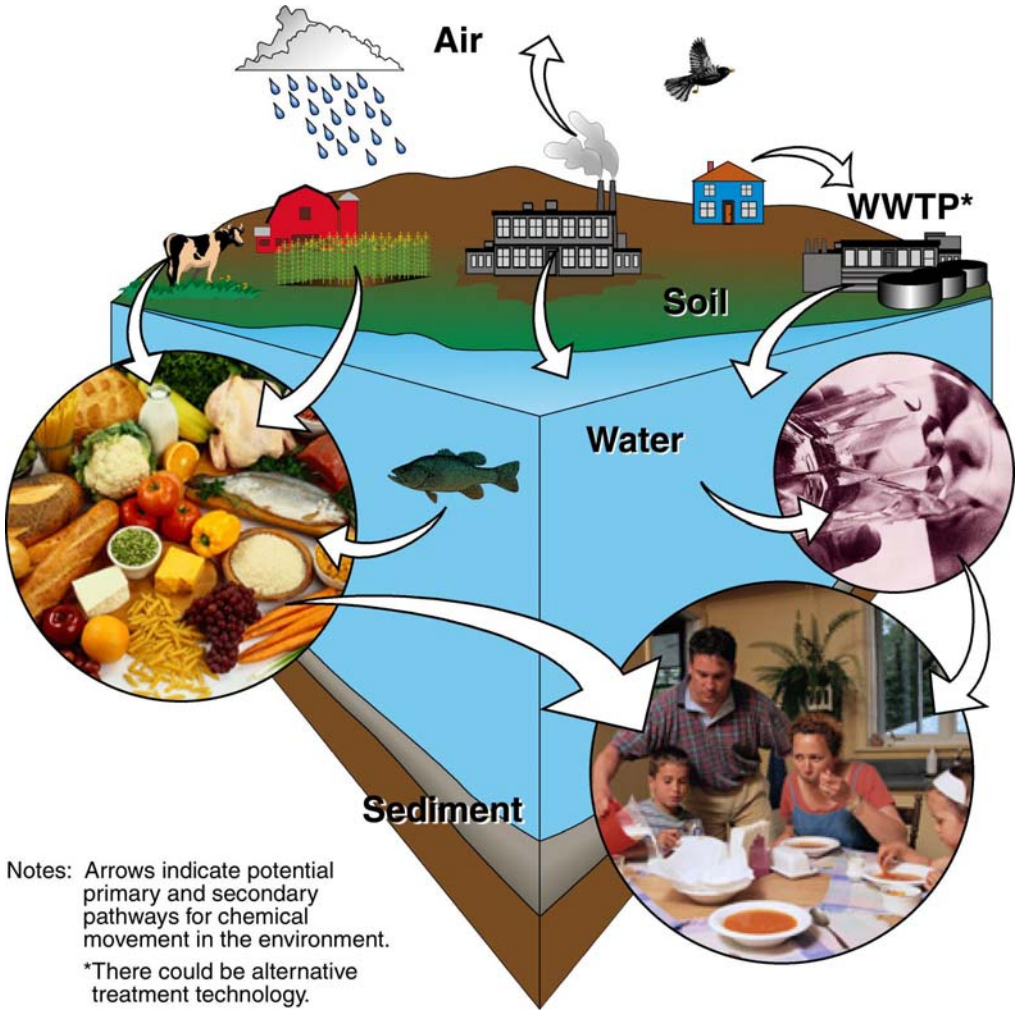


Figure 3-1. Pathways of chemicals produced and used in consumer products to the environment

3.3.4 Basic Equations

The fate model and the exposure model use very similar approaches and equations to estimate chemical concentrations in surface water resulting from chemical disposal in household wastewater. In this section, the basic approach and equations are described for clarity. The assessor should read user manuals and/or publications that describe the models to understand the specific details of the models described in this section.

The basic equation is

$$PEC = (Q \times Cf(1-R))/(365 \times WW \times POP \times DF)$$

where:

PEC	=	predicted exposure concentration (mg/L)
Q	=	quantity of the substance used in consumer products in the relevant geography (kg/year)
Cf	=	conversion factor for kg to mg
R	=	fraction of the chemical removed in wastewater treatment (percent)
365	=	conversion factor from year to days
WW	=	amount of wastewater produced by one person per day (L/day)
POP	=	population size in the relevant geography that uses the consumer product
DF	=	dilution factor for the wastewater in the surface water (unitless).

The values for these factors are generally region-specific.

3.3.5 Assessment Approach

Going the next step beyond exposure assessment, a medium-specific PEC (e.g., in surface water) can be compared with an established safe exposure threshold for a chemical (e.g., PNEC). This comparison forms the basis for an initial risk evaluation. For chemically related materials (i.e., those with similar physicochemical and toxicological properties and fates), a PEC can be derived for the chemical group or category. A conservative estimate of environmental exposure would begin with the assumption that the total production volume (e.g., metric tons per year) of the chemical, or the combined production volume for the chemical category, is released into the environment following consumer use and down-the-drain disposal. If the PEC derived in this manner is less than the PNEC for a chemical or group of chemicals, biological receptors (e.g., people, fish) are not likely to be injured. The *Effects Assessment* section of this document (Section 3.6) provides specific guidance for the derivation of a PNEC.

If it cannot be concluded with confidence that injury is unlikely, then the assessor must determine if additional work to refine the PEC value to reflect actual use conditions is possible. Refinement for the PEC value includes, for example, subtracting out that portion of the total

volume that does not go down the drain after use or, for manufacturing facilities, refining estimates of the amount of chemical released to the environment based on the total process loss amount and/or the amount removed during on-site wastewater treatment or in a municipal plant that receives wastewater from the facility. If it is not possible to refine the PEC value, the risk characterization is based on a comparison of the conservative PEC with the PNEC.

A higher-level/refined assessment would be undertaken for any of three reasons: 1) if the screening-level assessment indicates that there may be a likelihood that the chemical will cause adverse effects; 2) if the screening-level assessment indicates that the chemical is persistent and/or bioaccumulative such that longer-term exposures are likely; or 3) if the screening-level assessment indicates that environmental compartments beyond the aquatic compartment may be exposed (e.g., terrestrial biota or perhaps humans via their diet). At the discretion of the assessor, a refined assessment can also be performed to more fully and/or accurately describe environmental exposures (and risks). Higher-level exposure (and risk) assessments are tailored to a specific chemical and use scenario and the components need to be quite varied and flexible. Because there are various methodologies for conducting higher-level exposure assessments, which can be very detailed, these higher-level approaches are not covered in this document.

For the HPV screening-level assessments, the exposure assessment can be based on the approach outlined in Figure 3-2, where the assessments can be refined from screening-level assessments by using more accurate data either on the chemical's properties or the locations of likely release, and environmental exposure can be developed. For HPV chemicals, the recommended approach is to conduct the assessment at the highest level possible based on the available data.

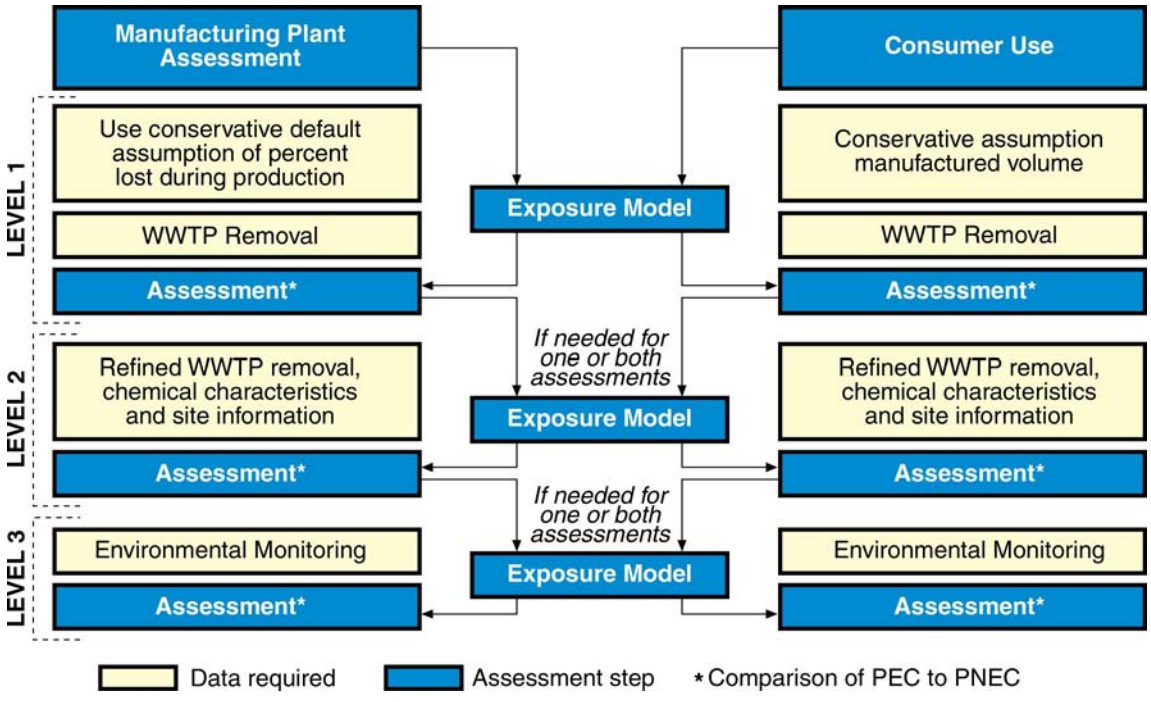


Figure 3-2. Environmental exposure assessment approach

The environmental exposure methodologies described in the previous pages and the case studies for LAS and hydrotropes provided in Appendix IV are focused at the "screening level," that is, a first approximation of exposures based on generally recognized and accepted estimation techniques. Discussion of approaches, data and model requirements, as well as case studies can also be found in published guidance documents and articles. The OECD website on environmental exposure assessment (http://www.oecd.org/document/63/0,2340,en_2649_201185_1908991_1_1_1_1,00.html), EU *Technical Guidance Documents on Risk Assessment* (http://ecb.jrc.it/php-bin/reframer.php?A=ECB&B=/DOCUMENTS/), U.S. EPA's Office of Pollution Prevention and Toxics (OPPT) exposure website (www.epa.gov/opptintr/exposure/), and the ACA website (www.chemicalawareness.org), are good starting points for identifying methods and case studies for higher-level/refined environmental exposure assessments.

3.3.6 Key Methodologies

As indicated above, different geographic regions and their regulatory agencies have established methods for estimating environmental exposures, especially at the initial screening levels of the assessment. The methods share underlying chemical fate and transport principles but contain region-specific aspects to reflect, for example, regional habits and practices, average stream flows, initial chemistry of the stream, and typical dilutions of wastewater discharges. Regional differences in product use, wastewater treatment practices and regulatory frameworks dictate which regional-specific data and modeling procedures are recommended for the U.S., EU, and AP regions.

3.3.7 Identifying Relevant Environmental Compartments and Fate Processes

A "universal" tool, often used as a first step to ensure that the subsequent exposure assessment is focused on the most relevant environmental compartments and fate processes for a given chemical, is the chemical partitioning or fugacity model that goes by numerous names (e.g., the Mackay model, the multimedia equilibrium criterion (EQC) model, or the EQC model [Mackay et al. 1996]). This model is well established and has undergone numerous refinements over the years. OPPT recommends the model and discusses its application on their website, http://www.epa.gov/opptintr/exposure. The EQC model can be viewed and downloaded from the Canadian Environmental Modeling Centre (Trent University) website, http://www.trentu.ca/cemc/welcome.html. The model allows the user to progress through a sequence of levels (I, II, and III) which have increasing data requirements, introduce greater complexity, and reveal progressively more about the distribution and fate of a chemical in the environment. At a minimum, the model requires information on the chemical's water solubility, vapor pressure, Henry's law constant (which can be calculated from the water solubility and vapor pressure) and K_{ow}. The model output includes the percent of the chemical predicted to reside in the air, water, soil, and sediment compartments under equilibrium or steady-state conditions (with or without degradation and advection occurring). The output of the EQC model identifies those environmental compartments where a chemical is most likely to reside and, therefore, where exposure is most likely to occur following the chemical's use and release. The model results

can also be used to identify which transport, exchange, and degradation processes should be included in subsequent fate and exposure modeling.

Although the EPIWIN suite of models (version 3.12 can be found at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm) contains a multi-media model, it is not recommended that the assessor use this model at this stage of the assessment because the assessor cannot view all the input parameters and output that are needed to understand the environmental distribution and processes that impact this distribution.

3.3.8 Exposure Models Used in U.S. Assessments

Numerous environmental exposure models have been developed and used in chemical assessments performed in the U.S. A partial list of these can be viewed (and in many cases downloaded) from the OPPT website at www.epa.gov/opptintr/exposure/. This site is titled *Exposure Assessment Tools and Models*.

The most relevant screening-level model for the purposes of the HPV chemicals is E-FAST. E-FAST was developed as a screening-level tool to support U.S. EPA's assessment of the potential (human and aquatic) exposures to new chemicals that are submitted to U.S. EPA for review before manufacturing (called the pre-manufacture notification). E-FAST provides screening-level estimates of the concentration of chemicals released to the environment via air, water, and land from manufacturing facilities as well as from use and down-the-drain disposal of consumer products. The model estimates environmental concentrations based on default assumptions. For example, in the down-the-drain module, the model assumes that consumer products are disposed in household wastewater and treated before being released in surface water. Surface concentrations are estimated under the assumption of average and low flow conditions. To calculate exposures using the modeled concentrations, E-FAST incorporates either a combination of upper-percentile and mean exposure parameter values (e.g., breath rates, water intake rates, etc.) or all upper-percentile parameter values as defaults. Thus, E-FAST exposure estimates are considered high-end. The following exposure scenarios are provided by E-FAST:

- **Human Exposure Scenarios—**Inhalation exposure from fugitive/vent releases from manufacturing facilities, ingestion exposure from drinking water as a result of releases to groundwater (via landfill) from manufacturing facilities, ingestion exposure from drinking water and eating contaminated fish resulting from releases to surface water by manufacturing facilities, and ingestion exposure from drinking water and eating contaminated fish because of disposal of consumer products down the drain.

- **Aquatic Exposure Scenarios—**Aquatic exposure estimates based on scenarios involving surface water releases from manufacturing facilities considers freshwater streams and rivers as well as bays, lakes, and estuaries if the industrial facility discharges to these types of environments. E-FAST also has the down-the-drain module, in which the aquatic exposure estimates are based on freshwater aquatic environments and from disposal of consumer products.

E-FAST can be viewed and downloaded at an U.S. EPA website, http://www.epa.gov/oppt/exposure/docs/efast.htm. The OPPT website as well as the U.S. EPA HPV website (http://www.epa.gov/chemrtk/volchall.htm) provide links to "case studies" for down-the-drain chemical releases as well as ecological and human exposure following environmental releases. In addition, the user manual for E-FAST (http://www.epa.gov/opptintr/exposure/docs/efast.htm) should be read before using the model, to ensure that the assessor has an adequate understanding of the equations and assumptions used in the model. There has been no formal validation or verification of the E-FAST model. However, it is based on first principles so is expected to be valid and conservative. A comparison of the E-FAST exposure predictions with those from the European Union System for the Evaluation of Substances (EUSES) is presented in Appendix III.

3.3.9 Exposure Models Used in European Assessments

Numerous environmental exposure models have been developed and used in chemical assessments performed in Europe. A partial list of these can be viewed (and in many cases, downloaded) from the European Chemicals Bureau website at http://ecb.ei.jrc.it. The most relevant screening-level model for purposes of the HPV initiative is EUSES, which is based on the EU TGDs on *Risk Assessment for New Notified Substances and Existing Substances* (see http://ecb.jrc.it/php-bin/reframer.php?A=ECB&B=/DOCUMENTS/). EUSES can be purchased online. EUSES includes a scenario to evaluate exposure and risk as a result of release of cleaning/washing agents into the environment.

EUSES can be used to carry out screening, intermediate, or refined tiers of assessment by replacing the default data, estimated parameter values, or intermediate results with more accurate estimates or measured data. It is not specifically designed to conduct site-specific assessments but it does allow evaluations for both local (i.e., in the vicinity of a large hypothetical point source) and regional (i.e., resulting from all sources in the region) exposure scenarios. The continental (i.e., the sum of all EU member states) scale is also included to provide background information for the regional scale model. For the local scale, the environment is characterized by a "standard environment" which includes a combination of average values or reasonable worst-case values, depending on the parameter in question. The generic regional environment is used to assess the release from point and diffuse sources in a larger area using the same "standard environment" characteristics. Regional concentrations are used as background concentrations in the calculation of the local exposure concentrations. Chemical concentrations are estimated for fresh surface water, freshwater sediments, soil resulting from application of sewage sludge, and releases to groundwater and air. It is anticipated that marine environments will be added to EUSES in the near future when the TGD is revised. There have been some verification/validation studies conducted for EUSES, including Jager (1995) who discussed the EUSES 1.0 validation status.

Another source of relevant environmental exposure methodologies (and case studies) for the EU can be found on the HERA project website, which addresses ingredients of European household cleaning products (www.heraproject.com). The HERA project's objective is to provide a common risk assessment framework for the European household cleaning products industry. Therefore, the focus is on conducting exposure and risk assessments for releases that occur

during and after product use, but does not include guidance on industrial facility discharges. Environmental exposure and risk assessment for the down-the-drain disposal of these type of products incorporates the use of EUSES among other exposure and risk characterization methodologies. In addition, HERA identifies the modifications to EUSES that are recommended for assessing down-the-drain ingredients such as those in detergents (Fox et al. 2002).

3.3.10 Exposure Models Used in Asia Pacific Assessments

Japan follows general OECD principles and practices for environmental exposure assessment. That is, PECs are derived using a combination of modeling and monitoring. These PEC values are then compared to their toxicology counterpart, PNEC, to provide a risk characterization. These practices and examples of their use are briefly described in a presentation by Yoshimura (2001). The JSDA has ongoing efforts regarding environmental exposure assessment. These include water quality surveys where surface waters are being monitored (analytical chemical measurements) for concentrations of high priority chemicals using chemical-specific analyses (e.g., liquid chromatography/mass spectrometry for cationic and nonionic surfactants). Recent developments published by the Environmental Committee in the JSDA *Annual Environmental Report* can be viewed at their website http://www.jsda.org/etop.html. A very good example of environmental exposure and risk characterization for HPV chemicals is presented in Yamamoto et al. (1997). This case study uses the Tamagawa River Model as a basis for establishing exposure concentrations for consumer product chemicals. The situation in Japan is unique compared to the U.S. and European environments, because there is direct discharge of grey water[8] to the environment.

3.3.11 Other International Exposure Modeling Resources

Additional international efforts aimed at harmonized methodologies for environmental exposure assessment can be viewed on the OECD website at www.oecd.org/document/63/0,2340,en_2649_34373_1908991_1_1_1_1,00.html. This site, titled *OECD Activities on Environmental Exposure Assessment*, provides links to numerous additional resources for exposure modeling as well as use of monitoring data. It also links to organizations in the U.S., Europe, and Japan that are conducting environmental exposure assessments.

A number of other countries provide their own guidance for conducting environmental exposure assessment that would be relevant to HPV chemicals. For example, Environment Canada guidance titled *Environmental Assessments of Priority Substances Under the Canadian Environmental Protection Act, Guidance Manual, Version 1.0–March 1997, Environmental Protection Series Report EPS/2/CC/3E* available from the Chemicals Evaluation Division, Commercial Chemicals Evaluation Branch. This methodology has recently been applied to a consumer product chemical in the April 2001 *Priority Substances List Assessment Report for Nonylphenol and its Ethoxylates* (CCED 2001).

[8] Any water that has been used in the home, except water from toilets, is called grey water. Dish, shower, sink, and laundry water comprise 50–80 percent of residential "waste" water. This may be reused for other purposes, especially landscape irrigation.

3.3.12 Use of Monitoring Data

Monitoring data available for a chemical should be considered in an assessment. OECD (2000) has written guidance on how to judge and use available monitoring data in the exposure assessment of industrial chemicals like HPV chemicals. In the context of the screening-level assessments, the location and characteristics of the monitoring sites should be an important consideration in whether the data can be used. Also, the monitoring data can be used to verify estimated exposures derived from models.

3.4 Instructions for Generating PECs in the U.S., EU, and Asia Pacific (Japan)

In this section, guidance is supplied for estimating surface water chemical exposure concentrations in the U.S., EU, and Japan after the EQC model has confirmed that the aquatic environment is the most likely exposure medium for a chemical of interest. For each geographical region, the guidance is split into separate approaches based on consumer use and manufacturing.

3.4.1 United States

In the U.S., the environmental exposure assessment approach is quite advanced, and has been used for many years within U.S. EPA to determine the acceptability of new and existing chemicals that are released to fresh surface waters. The overall scheme is shown graphically in Figure 3-3.

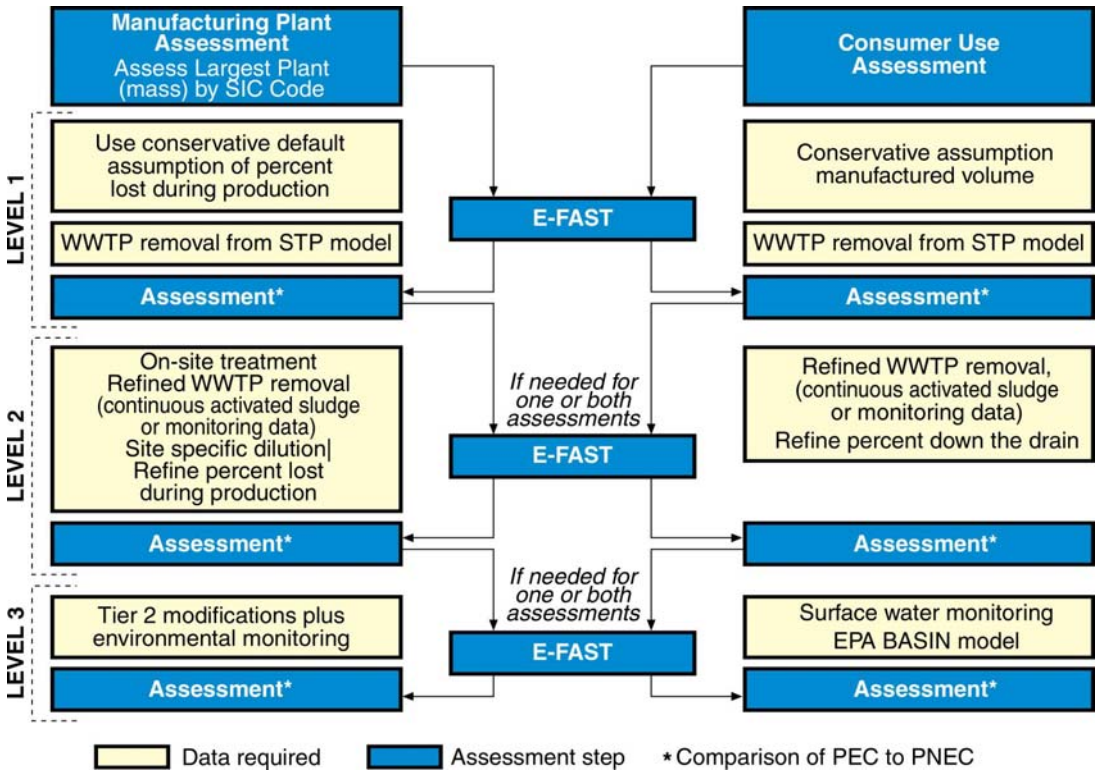


Figure 3-3. U.S. environmental exposure assessment process

3.4.1.1 Consumer Product Use and Disposal

Level 1—Use the U.S. EPA's E-FAST model to estimate surface water concentrations from consumer use and disposal after sewage treatment. Select the module *Models for Screening Level Exposure Assessments* and within that, select the *Down the Drain* module. It is necessary to select the CAS number and replace default values wherever actual physical and chemical data exist before running any module. The following input parameters are required:

- **Annual Production Volume**
- **Years of Use—**This input parameter does not affect surface water concentrations but is needed to estimate human exposures via drinking water and fish consumption.
- **Bioconcentration Factor—**This input parameter does not affect the surface water concentrations. It is used to estimate human exposures via fish consumption. If a measured value is not available, one can be estimated with the BCFWIN model in EPI Suite™. EPI Suite™ v3.11 is a series of structure activity and structure property prediction tools produced by U.S. EPA and widely accepted by the scientific community. This tool can be found at http://www.epa.gov/oppt/exposure/docs/episuitedl.htm.
- **Percent Removal—**Estimated or measured removal by sewage treatment plant (STP) with STP model which can be downloaded at http://www.trentu.ca/cemc/models/VBSTP.html. It is not recommended that the STP model results from the EPIWIN suite be used because the model allows only for the use of estimated property data and a direct link between the BIODEG model results and the degradation rates has not been developed. See Appendix III for information on how to choose default input values.

E-FAST's down-the-drain module will produce median (50th percentile) and high-end (10th percentile) surface water concentrations for various flow regimes. The 10th percentile surface water concentration indicates that 90 percent of the surface waters will have concentrations less than this value. The high-end surface water concentration should be used as the environmental exposure concentration for screening purposes.

If additional data are available to estimate the exposure in the aquatic environment or the exposure concentration exceeds the PNEC, then a Level 2 assessment should be considered.

Level 2—In the second level, there are two options for including additional or refined data:

- **Percent Removal—**Removal during sewage treatment can be further refined by continuous activated sludge[9] testing or by conducting a monitoring study to generate a WWTP removal percentage. These studies could require the use of radiolabeled compounds or development of appropriate analytical

[9] Continuous activated sludge is a bench-scale simulated sewage treatment system.

methods to analyze the concentrations of the specific chemical ingredient in influents and effluents.

- **Down-the-Drain Volume—**Volume can be better estimated to reflect the total mass going down the drain. This will require sound data on the use of an ingredient in different product categories and its disposal pathways.

With these input parameters, the assessor should run E-FAST to estimate the environmental exposure concentration. If additional data are available to better estimate exposure in the aquatic environment or if the PEC exceeds the PNEC at this level of assessment, a Level 3 assessment should be considered.

Level 3—In the third level, there are several options for including additional or refined data or using additional approaches:

- Using a river basin, or national surface water model to estimate the concentrations in relevant surface waters. These types of models include the U.S. EPA BASIN's model (http://www.epa.gov/OST/BASINS/) and the ROUT model (Wang et al., in press).

- Using WWTP removal data obtained by field monitoring of WWTPs. Chemical-specific analytical methods are needed to analyze the concentrations of the ingredient in influent and effluent.

- Using concentrations in surface waters measured during field monitoring. Chemical-specific analytical methods are needed to analyze the concentrations of the ingredient in surface water. Locations to be monitored should be selected to represent conditions downstream of a range of STP types (i.e., activated sludge, trickling filter, lagoon, oxidation ditch, rotating biological contactor) that operate properly.

The environmental exposure concentration is estimated using refined input parameters developed by these approaches.

3.4.1.2 Manufacturing Plant Releases

Level 1—U.S. EPA's E-FAST model can be used to estimate surface water concentrations from manufacturing releases from a particular industry, as identified by its SIC code, after wastewater treatment. Select the "General Population and Ecological Exposure from Industrial Releases" as the module after data on the chemical of interest has been selected. Within this module, select the "average probabilistic dilution model (PDM) analysis (SIC Code)" on the right hand side. Then go to the "select SIC Code" tab and choose the appropriate code. This will populate the data on the "General Release Info" tab. Once any data or comments have been entered, select the "Release activities completed?" button on the bottom and the exposure factors page for human exposure will appear. Finally, after the "Calculate, Save results and Display results" button is clicked, the exposure will be calculated.

The following are required input values:

- **SIC Code—**An input selected from a pick list provided by this E-FAST module. The recommendation would be soap, detergent, etc. manufacturers.
- **Release Data—**The choice of SIC code will indicate which data are needed. When choosing data to represent the emissions to the environment, facilities of different sizes should be examined to determine if there is any trend in percent releases with the size of the manufacturing or formulation facility.

E-FAST's PDM SIC code module will produce median (50th percentile) and high-end (upper 10th percentile) surface water concentrations as a result of discharges to wastewater from this type of industry across the U.S. under the "SIC Code" tab. Use the high-end surface water concentration as the environmental exposure concentration. If additional data are available to better estimate exposure in the aquatic environment or if a conclusion that the use of the chemical is unlikely to harm the environment is unsupported, then a Level 2 assessment is recommended.

Level 2—In this level, exposure is assessed at one site using the PDM and a realistic worst-case estimate of the mass produced at the largest site. To conduct this Level 2 assessment, some information from the company owning the site producing the greatest volume will need to be obtained. The best available data (continuous activated sludge unit, monitoring, etc.) should be used to estimate removal during wastewater treatment.

Chemical manufacturers, rather than formulators or processors, are the most likely to discharge large amounts to wastewater. This narrows the number of facilities considered to those manufacturers of the HPV chemical under consideration. Industry associations, whose members are sponsoring an HPV chemical, can help compile site-specific information about members' facilities.

The Permit Compliance System database, maintained by the U.S. EPA's Office of Wastewater, tracks information about facilities that are regulated by the National Pollutant Discharge Elimination System. The database can be used to identify and locate major dischargers of any particular chemical.

The following information about the worst-case manufacturing sites (those that will result in the highest surface water concentrations) will need to be obtained:

- On-site treatment (yes/no) and percent removal by on-site treatment, if any.
- Amount released (kg/day) after any type of on-site treatment but before treatment by municipalities or publicly owned treatment works (POTW). When choosing data to represent emissions to the environment, facilities of different sizes should be examined to determine if there is any trend in percent releases associated with the size of the manufacturing or formulation facility.

- Wastewater flow from the site (volume/day).
- Wastewater flow through the WWTP (volume/day) that treats the wastewater from the site.
- Information on the ratio of the sewage treated effluent versus the river flow at the point of discharge.

For each manufacturing site that is analyzed, E-FAST's site-specific PDM module will produce median (50th percentile) and high-end (10th percentile) surface water concentrations. The high-end surface water concentration should be used as the environmental exposure concentration in screening risk assessments. If additional data are available to better estimate the exposure in the aquatic environment or if a conclusion that use of a chemical is unlikely to harm the environment cannot be supported, then a Level 3 assessment is recommended.

Level 3—This third level for assessing manufacturing releases requires obtaining site-specific information from field monitoring. Manufacturing facilities to be included in the monitoring should be carefully selected to represent good operating conditions at the on-site treatment units and any public STPs, if appropriate. Great care should be taken to make sure the facilities' operations are representative of "typical" manufacturing operations at the time of sampling. Facilities classified as worst-case from the standpoint of discharge amounts, on-site treatment, number of release days per year and downstream dilution factors, should be included in the monitoring.

Three criteria are used to select sites: volume of material processed, presence of wastewater treatment of the effluent, and final dilution in the river. Using the criteria, the goal is to end up with sites that are realistic but representative of locations where environmental concentrations can reasonably be expected to be the greatest.

With the refined or additional input parameters, environmental exposure concentration can be estimated. If there are still potential concerns regarding environmental safety, additional monitoring of the surface waters downstream of the industrial facility should be considered.

3.4.2 European Union

The EU has a long history of conducting environmental exposure assessments for new and existing ingredients. As mentioned previously, they have also developed tools to use in these assessments. The EU-recommended approach uses the model EUSES and recommended refinements from the HERA project. The general procedure is similar to that described above for the U.S. However, key differences in both the consumer use and manufacturing release scenarios exist (Figure 3-4).

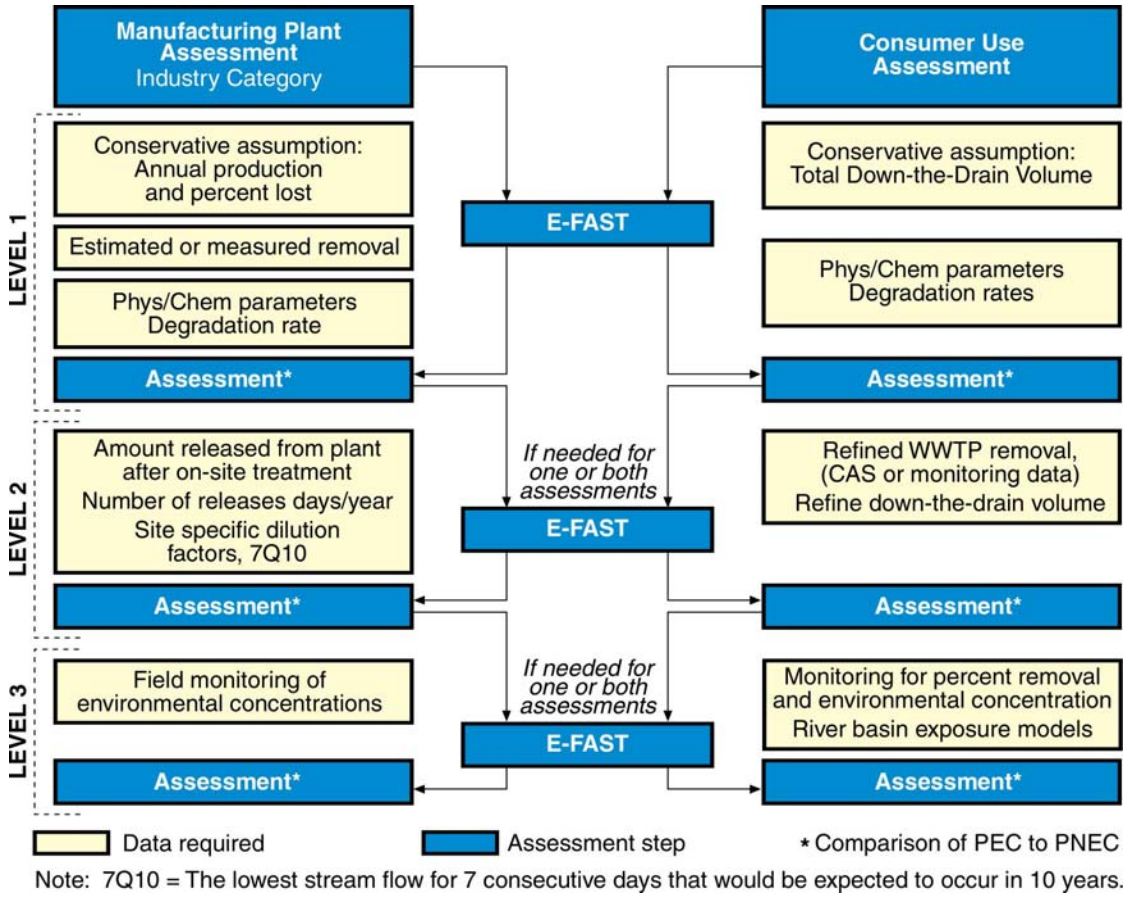


Figure 3-4. EU environmental exposure assessment process

3.4.2.1 Consumer Product Use and Disposal

Level 1—The exposure assessment is obtained by running the EUSES model, the most relevant screening-level model for purposes of assessing HPV chemicals in Europe. For the assessment of exposure resulting from widespread consumer use in densely populated areas, the regional model is used.

The following chemical-specific input parameters are needed for a Level 1 assessment using EUSES:

- Molecular weight (g/mol)
- Melting point (°C)
- Boiling point (°C)
- Vapor pressure (Pa)
- Water solubility (g/m^3)
- Octanol/water partition coefficient (no unit)

- Degradation half-life in air or photo-oxidation half-life (days)
- Degradation half-life in water (days)
- Degradation half-life in soil (days)
- Degradation half-life in sediment (days).

The degradation rates are estimated from pass/fail "ready" biodegradation test results.

In addition, the "total down-the-drain volume" or "environmental emission rate," in EUSES terminology, of the ingredient (metric tons/year) is needed. Note that for detergent product chemicals, HERA has recommended that changes be made in the default scenario parameters in EUSES (www.heraproject.com and Fox et al. 2002), which should be considered when conducting these analyses.

EUSES' local module will produce the following results:

- PEC in air (ng/m^3), usually very low for down-the-drain consumer product ingredients; typically an assessment in air is not necessary
- PEC in surface water ($\mu g/L$)
- PEC in soil (μg/kg dry weight)
- PEC in sediment (mg/kg dry weight).

The high-end surface water concentration should be used as the environmental exposure concentration in an assessment. If additional data are available to better estimate exposure in the aquatic environment or if a conclusion that using the chemical is unlikely to cause harm to the environment cannot be supported, then a Level 2 assessment is recommended.

Level 2—In a second level assessment, the following additional or refined data can be used in the assessment to override defaults:

- Percent removal in sewage treatment can be further refined by measuring it in laboratory units that mimic WWTPs (e.g., continuous activated sludge testing). Specific analytical methods or radiolabeled compounds may be needed for this testing to analyze the concentrations of a chemical ingredient in influent and effluent.
- In addition, it may be possible to refine the volume or release information.

With the refined input parameter for percent removal and/or volume or release information, EUSES regional module can be re-run using the high-end surface water concentration as the environmental exposure concentration. If additional data are available to better estimate exposure in the aquatic environment or if a conclusion that the chemical is unlikely to harm the environment cannot be supported, then a Level 3 assessment is recommended.

Level 3—In the third level, additional or refined data on the percent removal in sewage treatment and/or the concentrations in surface waters from field monitoring or from river basin exposure modeling can be used in the assessment.

- River basin models such as GREAT-ER (http://www.great-er.org/pages/home.cfm) can be used to estimate the surface water concentrations in rivers of interest.
- Field monitoring of selected WWTPs and/or river waters can be performed. The river water sites and the WWTPs to be monitored should be selected based on their operating conditions and the range of sewage treatment types (i.e., activated sludge, trickling filter, lagoon, oxidation ditch, rotating biological contactor) in the country.

These revised surface water concentrations can be used as the environmental exposure concentration in a Level 3 assessment. If additional perspective is still needed and no monitoring or limited monitoring has been conducted, then a more extensive field monitoring program should be considered.

3.4.2.2 Manufacturing Releases

Level 1—Estimates of environmental exposures from manufacturing discharges are obtained by means of the EUSES model, the most relevant screening-level model for purposes of the HPV initiative in Europe. The following input values are needed for a Level 1 assessment:

- **Industry Category—**Select the appropriate industry category in EUSES. For each of the industry categories that are represented, EUSES contains release estimates for a generic point source (before treatment) and estimates of the number of days per year that these releases are expected to occur, based on industry averages. These parameter estimates for generic point sources in EUSES are based on surveys of facilities in EU member countries.
- **Annual Production/Processing Volume or Environmental Emission Rate—**In EUSES terminology, the amount of chemical ingredient (metric ton/year) produced, processed, or emitted. When choosing data to represent the emissions to the environment, facilities of different sizes should be examined to determine if there is any trend in percent releases with the size of the manufacturing or formulation facility.
- **Percent Removal—**Estimated or measured removal by sewage treatment.
- The following chemical-specific input parameters are also required:
  - Molecular weight (g/mol)
  - Melting point (°C)
  - Boiling point (°C)

- Vapor pressure (Pa)
- Water solubility (g/m^3)
- Octanol/water partition coefficient (no unit)
- Degradation half-life in air or photo-oxidation half-life (days)
- Degradation half-life in water (days)
- Degradation half-life in soil (days)
- Degradation half-life in sediment (days).

The degradation rates are estimated from pass/fail "ready" biodegradation test results.

The EUSES local module will produce this output:

- PEC_{air} (ng/m^3) (predicted environmental concentration in air)
- $PEC_{surface\ water}$ ($\mu g/L$)
- PEC_{soil} (μg/kg dry weight)
- $PEC_{sediment}$ (mg/kg dry weight).

The high-end surface water concentration can be used as the environmental exposure concentration. If additional data are available to better estimate exposure in the aquatic environment or if a conclusion that use of a chemical is unlikely to harm the environment cannot be supported, then a Level 2 assessment is recommended.

Level 2—For a Level 2 assessment, additional or refined data for site-specific scenarios are used. The greatest challenge in conducting these site-specific assessments is selecting which available data should be used or which sites should be monitored in planned studies. Even though there is no general formula for site selection, some guidelines can be offered.

Chemical manufacturers, rather than formulators or processors, are the most likely to discharge large amounts of a chemical into municipal wastewater. This narrows the number of facilities to be considered to manufacturers of the HPV chemical under consideration. Industry associations, whose members are sponsoring an HPV chemical, can help compile site-specific information about members' facilities.

The following information will need to be obtained for the worst-case manufacturing sites (those that will result in the highest surface water concentrations):

- **Amount Released (kg/day)—**This is after any type of on-site treatment but before treatment by municipalities or POTWs. When choosing data to represent the emissions to the environment, facilities of different sizes should

be examined to determine if there is any relationship between percent releases and size of the manufacturing or formulation facility.

- **Number of Release Days per Year—**Typically this will probably be less than 365 because there will at least be a certain number of maintenance days.
- **Dilution Factors—**Of POTW effluent into receiving surface water, under median flow, low flow, and flood conditions.

With the refined input parameters, the risk assessor should run EUSES (local module) with these parameters replacing the model defaults, and using the high-end surface water concentration as the environmental exposure concentration. If additional data are available to better estimate exposure in the aquatic environment or if a conclusion that use of a chemical is unlikely to harm the environment cannot be supported, then a Level 3 assessment is recommended.

Level 3—In the third level for manufacturing releases, data from field monitoring, if available, are used to refine the concentrations immediately downstream from where industrial effluents enter surface waters. For sampling during routine production, great care should be taken to make sure that the facilities' operations are representative of "typical" manufacturing operations at the time of sampling. At the same time, reasonable worst-case considerations from the standpoint of discharge amounts, on-site treatment, number of release days per year and downstream dilution factors should be included in the monitoring.

3.4.3 Japan

In Japan, the assessment approach has not yet been clearly defined. There is no defined and accepted regulatory approach to environmental exposure assessment, either for consumer products or manufacturing releases. However, two projects on chemical exposure modeling have recently been started. One is the Virtual World Project led by the National Institute for Environmental Studies, Japan (NIES 2003). Their approach is focused on evaluation of the ambient concentration of endocrine-disrupting chemicals using a geographic information system modeling technique (http://www.nies.go.jp/edc/index-e.html). Another approach is led by the Research Center for Chemical Risk Management, National Institute for Advanced Industrial Science and Technology (CRM/AIST 2003), Japan. In this approach, the emission amounts of chemicals are estimated based on national statistics or data obtained from the Japanese Pollutant Release and Transfer Register (http://www.env.go.jp/en/topic/prtr.html). The Research Center also includes estuarine modeling with an illustration of Tokyo Bay (http://www.riskcenter.jp/RAMTB/). While both approaches can be expected to provide us with more realistic exposure scenarios, both projects are still under way.

Level 1—One approach that can be used is to conduct the exposure assessment using the river model that was developed for the Tama River and its tributaries based on the actual river flow, POTW discharge flow, and water abstraction flow data measured in 1992 (Yamamoto et al. 1997).

The following input parameters are needed:

- Consumer ingredient usage (mg/person-day)
- Untreated gray water flow (L/person-day)
- In-stream removal degradation rate (L/day)
- Fraction of ingredient removed in conveyance systems (assume 0 if no data)
- Fraction of gray water reaching the river
- Fraction of ingredient removed in sewage treatment, by type:
  - Percent $\text{removal}_{\text{primary}}$
  - Percent $\text{removal}_{\text{activated sludge}}$
  - Percent $\text{removal}_{\text{trickling filter}}$

The Tama River model will produce a range of PECs in surface water (μg/L) for each section of the Tama River and its tributaries. The high-end surface water concentration can be used as the environmental exposure concentration in an assessment. If additional data are needed to better understand exposure in the aquatic environment, continue with a Level 2 assessment.

Level 2—Level 2 can use field monitoring to further refine estimates of exposure concentrations immediately downstream of discharge points for consumer products, or where industrial effluents join surface waters. Specific analytical methods should be used to analyze concentrations of a chemical ingredient in influent, effluent, and river water. The consumer product discharge points and/or the manufacturing facilities included in the monitoring should be carefully selected to represent good operating conditions of the on-site treatment units and the public STPs. Great care should be taken to make sure the facilities' operations are representative of "typical" manufacturing operations at the time of sampling. Worst-case facilities, from the standpoint of discharge amounts, on-site treatment, number of release days per year, and downstream dilution factors, should be included in the monitoring.

3.5 Exposure Assessment Summary

The following sections of this document present a basic framework as well as widely used methods to assess the exposure (and potential risk) to ecological receptors (non-target organisms) and humans as a result of contact with consumer product HPV chemicals released into the environment. Specific screening-level models are identified and links to websites where those models can be obtained are provided. Several documents are appended that provide comparisons between the principal models (i.e., E-FAST and EUSES) as well as case study examples of environmental exposure assessments in different geographies. Finally, two examples are provided (following the draft format of the OECD use/exposure pilot project) for SDA-sponsored categories of HPV chemicals. The case studies use screening-level exposure models and present initial exposure and risk characterization results. Screening-level

assessment is often sufficient to provide an adequate characterization of exposure and risk. That is, conservative (generally high) exposure estimates are well below toxicological threshold levels. Refinements to the initial assessment, including more data-intensive models and more location-specific data, can be made as warranted. Such refinements are discussed in the ACA framework document (ACA 2002) and at most of the websites listed throughout this methodology document.

3.6 Effects Assessment

Much has been written about the development of a quantitative structure-activity relationship (QSAR)[10] (U.S. EPA 1999a) and empirical aquatic effects data on HPV chemicals (OECD 2003; U.S. EPA 1999b). Toxicity or effects data are frequently gathered in order to understand the relative toxicity of chemicals, to assess the need for hazard labeling, and to evaluate the potential for effects in the environment. Because most toxicity data are developed in the laboratory with relatively few species, these data must be extrapolated to protect the environment in general. Extrapolation is intended to address a number of uncertainties arising from the fact that structure-activity or laboratory toxicity data on a limited number of species are used to attempt to understand effects on organisms in the environment. The usual procedure is to divide the effects value by an assessment or uncertainty factor or to use a statistical extrapolation technique to generate a PNEC. Though generation of a PNEC is not required under the OECD HPV program, it "might nevertheless be useful for the interpretation of available toxicity data" (OECD 2003). The PNEC is generated once all relevant aquatic toxicity data on the HPV chemical have been collated and evaluated for quality. Because much has been written about the summary and evaluation of data (AISE 2002; EU 2003; OECD 2003) and the extrapolation process (Cowan et al. 1995; EU 2003; OECD 2003) the intent of this section is to summarize this guidance and facilitate the development of PNECs for HPV chemicals.

3.6.1 Objective

Environmental effects data may be available for different organisms tested under a variety of conditions. To be useful within the HPV process, a consistent approach to interpreting and valuing these data is needed to help reach conclusions supported by the available information. The objective of this section is to provide a uniform approach for using the variety of effects data about a compound to determine a concentration expected to have no effect on organisms in the environment (i.e., the PNEC).

3.6.2 Data Evaluation

Toxicity data are typically generated on a wide variety of aquatic organisms, and occasionally on sediment-dwelling and terrestrial organisms. However, because of the sensitivity of aquatic organisms, the likelihood of exposure, and the possibility of wide distribution of chemicals released into the environment, effects assessments are limited to assessing effects on the aquatic

[10] QSAR is a mathematical expression used to relate physical or chemical parameters to the biological or chemical activity of a molecule.

organisms within the OECD HPV program, with a minimum requirement of three acute studies—on fish, algae, and invertebrates.

The most relevant data for setting the PNEC are reliable chronic toxicity data obtained under field or mesocosm conditions (assuming that systems are well-controlled and the studies are operated and evaluated well; see Level 3 below). That said, there should be some level of consistency within the entire data set from acute data up to the highest-level data. While higher-level data are preferred and do take precedence, all toxicity data should be used to help evaluate the appropriateness of the higher-level information and to ensure data consistency. When an inconsistency exists, the inconsistency should be evaluated and explained (e.g., acute toxicity LC_{50} data at a concentration lower than chronic no-observed-effect concentration [NOEC] values for the same species).

Information may be available on a variety of organisms tested acutely and/or chronically in the laboratory, microcosm, mesocosm, or field. As these data are collated, they should be separated by their method of collection (acute, chronic, microcosm, mesocosm). When few data points exist, the assessment factor approach is used. When six or more chronic toxicity values exist on relevant organisms, a statistical or probabilistic extrapolation process may be used.

In acute and chronic toxicity tests, a variety of statistics (e.g., LC_{50}, NOEC) on a variety of endpoints (growth, survival) can be calculated. At the acute level, the LC_{50} or the EC_{50} should be used and should be based on mortality (LC_{50}) or immobility (EC_{50}). Death is readily determined in fish but can be difficult to assess in some invertebrates. Immobility is the endpoint typically used with these organisms. At the chronic level, the NOEC is conventionally determined based on growth, survival, and/or reproduction. In some cases, an EC_x value such as the EC_{20} may be available instead of the NOEC. When an EC_{10} or EC_{20} value is available, it can be used as the appropriate statistic in the risk assessment. EC_{10} and EC_{20} values are not equivalent to the NOEC, but provide an acceptable endpoint for risk assessment. As with the NOEC, the EC_{10} and EC_{20} values should be based on adverse effects on growth, survival, or reproduction. For a discussion of the relative merits of EC_x and NOEC values, please refer to Bruce and Versteeg (1992).

3.6.3 Assessment Factors Approach

The extrapolation process attempts to use existing data to protect biological community structure and function. When limited data are available, assessment or extrapolation factors (see Table 3-1) are used to account for uncertainties in extrapolating from acute to chronic, few to many species, laboratory to field, etc. These factors have a long history of use and their development and applicability to aquatic effects assessments are discussed in multiple publications (Cowan et al. 1995; EU 2003; OECD 2003).

Table 3-1. Assessment factors[11] for the derivation of PNECs from aquatic toxicity data[12]

Level	Data	Assessment Factor
1	Acute LC_{50} and EC_{50} values for fish, algae, and invertebrates	100–1,000
2	Chronic EC_{20} or NOEC values for fish, algae, and invertebrates	10–100
3	Mesocosm or field data	1–5

Level 1—Acute LC_{50} or EC_{50} values for fish, algae, and invertebrates are divided by 100 to 1,000. If only one or two species are available, the factor of 1,000 should be used. The PNEC is the lowest value. The factor of 1,000 is conservative and protective but may be reduced to 100 when all three groups are included and:

- Data from related chemicals suggest that the acute to chronic ratio will be less than 10, or
- Data suggest that the chemical acts via a non-specific or narcotic mode of action.

For compounds with a log $K_{ow} > 5$, the factor of 1,000 should be used.

Level 2—Chronic EC_{20} or NOEC values for fish, algae, and invertebrates can be divided by 10 to 100. The Level 3 PNEC is the lowest of these values. If data on all three species are available or convincing evidence is provided that the most sensitive species has been tested (i.e., Level 2 data for that species are well below 5 times the other tested species), 10 may be used. When EC_{20} or NOEC values for one or two among fish, algae, and invertebrates are available, a factor of 50 or 100 may be used. In this case, the chronic PNEC is compared with the Level 2 PNEC and the lower PNEC is used. If microcosm data exist, they should be compared with the available acute and chronic toxicity data. These data should be used qualitatively to support or refute the single species toxicity data. If the microcosm data refute the single species toxicity data, additional effects data may be required.

Level 3—Mesocosm and field data will exist for a small subset of HPV chemicals. When high quality data are available from a well-operated mesocosm or field study, an assessment factor of 1–5 can be applied to the NOEC value. Criteria used to evaluate the rigor of a mesocosm or field study are discussed in Giddings et al. (2002), Scholz et al. (1997), Hill et al. (1994), and Okkerman et al. (1993), which recognize the need for flexibility in design and interpretation by practitioners and regulators. These data should be evaluated on a case-by-case basis and should be compared with the acute and chronic toxicity data. There is presently no universal definition

[11] All toxicity values should be compared with the solubility limit prior to applying assessment factors. If the toxicity endpoint exceeds the solubility limit, the solubility limit is used as a conservative estimate of the endpoint.

[12] If multiple values are available for an individual species, and the values are of similar quality and technical merit, the geometric mean should be used as the best estimate of the toxicity value for that species.

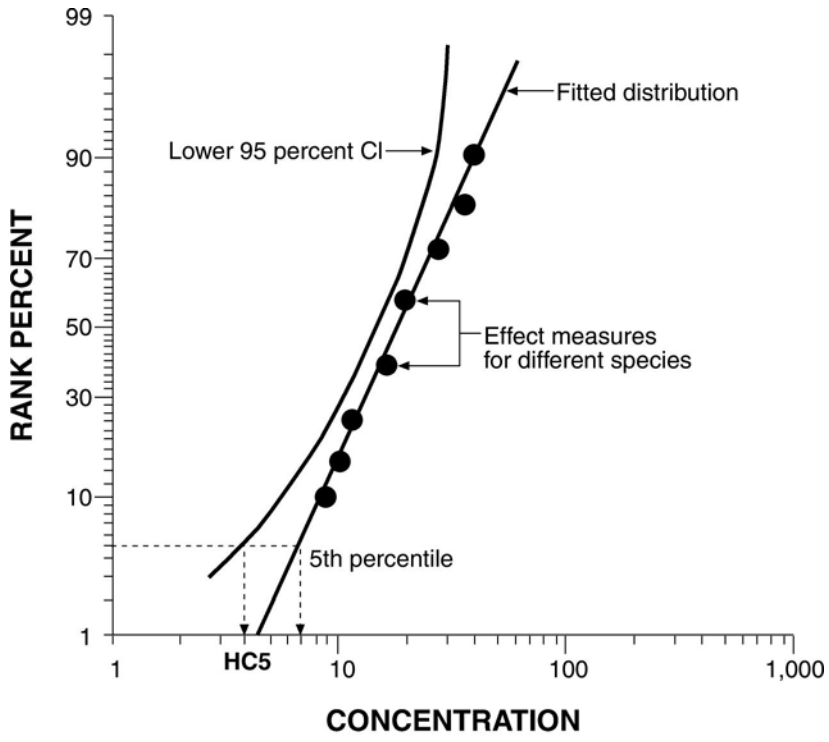
of a mesocosm (size, level of biological complexity required, experimental design details). Particular attention should be given to the type of mesocosm used and the route of exposure. After bioavailability is considered, if the mesocosm or field data refute the single-species toxicity data, additional effects data may be needed to ensure protection of appropriate species and communities. Mesocosm studies vary considerably in their ability to discern differences between biological responses in the control and treated groups. Hence, care is needed in accepting mesocosm NOECs as the sole value for use in a risk assessment. Selection of high quality studies is important, as is comparison of mesocosm NOECs with single species data.

3.6.4 Statistical Extrapolation Process

When chronic toxicity values (NOEC, EC_{10}, or EC_{20} values) from six or more species are available, the statistical or probabilistic extrapolation process may be used to establish the PNEC (Stephan et al. 1985; Aldenberg and Slob 1993; Versteeg et al. 1999; Posthuma et al. 2002). This approach, called the probabilistic approach, uses all the available chronic toxicity data to construct a species sensitivity frequency distribution. Statistical tools are then used to determine the concentration where 5 percent of the distribution is lower and 95 percent of the distribution is greater. In theory, at this concentration, only 5 percent of the species will have a lower chronic toxicity value.

The minimum number of toxicity values needed to estimate the PNEC using the statistical approach is being debated. U.S. EPA uses a minimum of eight species with at least one representative from eight different taxonomic groups. The EU (2003) recommends a minimum of 10 (preferably 15) from eight taxonomic groups while OECD (2003) appears to support eight species from among fish, crustacean, insects, algae, higher plants, and another group not previously tested. van Leeuwen (1990) and Scott-Fordsmand and Jensen (2002) suggest a minimum of five species. Versteeg et al. (1999) used as few as six and observed good agreement between the statistically derived PNEC and the mesocosm NOEC. Inclusion of toxicity data from the family Daphnidae improves the ability of limited single species toxicity data to predict the probabilistic PNEC (Host et al. 1991, as cited in Pennington 2003). Further, increasing the sample size from six to eight species results in a small change in the probabilistic PNEC (Pennington 2003). Given the practical demonstration of the utility of the statistical approach with six species and the use of five species in ecological risk methods supported by the Danish environmental authorities (Scott-Fordsman and Jensen 2002), a minimum of six species, including a daphnid species (e.g., member of the genus *Daphnia* or *Ceriodaphnia*) should be used to estimate the PNEC using the statistical extrapolation approach. Clearly, the more data available, the better. However, the statistical approach using all the available data can provide a useful perspective on the PNEC when six or more chronic single species effects values are available.

The statistically-derived concentration that is lower than 95 percent of single species toxicity values can be visualized graphically using a cumulative species sensitivity plot (see Figure 3-5).



Source: Recreated from Posthuma et al. (2002)

Figure 3-5. Extrapolation from a species sensitivity distribution

Chronic toxicity values (e.g., EC_{20}, EC_{10}, NOEC values) are ranked from low to high and a probability value is assigned to each rank according to the Van Waerde equation (Erickson and Stephan 1988):

$$P(r) = r/(n+1)$$

where:

P(r) = probability of observing values less than or equal to the rank, r

r = the rank of each species sensitivity

n = number of species in the data set.

The probability values and associated toxicity values are fit to a log-logistic, log-normal, or other distribution using maximum likelihood procedures to estimate distribution parameters (McCullagh and Nelder 1989; Aldenberg and Slob 1993). The goodness-of-fit of the distribution can be evaluated using Cramér von Mises or a related test (i.e., Kolmogorov-Smirnoff statistical test) (Stephens 1986).

From the plot of the cumulative probability distribution, it becomes relatively easy to calculate the concentration that is lower than 95 percent of the data (i.e., the value protective of 95 percent of the species from adverse chronic effects). This value is considered to be the probabilistic PNEC. As a probability value it provides a margin of safety, thus no application factor is applied in the derivation of the PNEC.

3.7 Comparison of PEC and PNEC

Voluntary HPV programs are designed to provide a level of familiarity with the fate and effects of HPV chemicals. The U.S. EPA Test Plan and the OECD SIAR are intended to communicate available environmental fate and effects data to regulators and the public, and are not intended to provide a comprehensive risk assessment for the compounds being studied. However, much of the information that might be used in a risk characterization is provided in robust study summaries. Further, the SIAR does provide guidance on the calculation of surface water PECs downstream of manufacturing plants and municipal WWTPs, as well as the PNEC, which can be used to understand the potential for effects in surface waters. While it is not the intent of these HPV programs to calculate and report a risk ratio (PEC/PNEC), an exposure annex may be included in the report, which provides reliable information on monitored and/or estimated surface water PECs. The PECs can be brought forward into the SIAR and be compared with the PNEC(s) for aquatic organisms to support insights about whether hazard levels are reached in the aquatic environment, and to assist in drawing conclusions about whether additional data are needed and the priority for further work on the compound.

The environmental HPV screening assessment process leads to one of two decisions for each chemical category: 1) no further testing or 2) priority for additional testing. The decision is based on several criteria: completeness of data relevant to deriving the PEC and PNEC, quality of data, the compounds for which data are available, and the factor separating the PEC and PNEC values.

Completeness of Data—Much of the environmental data reported in the SIAR can be used to estimate the PEC and or PNEC for an HPV chemical in the aquatic environment. However, not all endpoints must be available for all HPV chemicals. For example, data on vapor pressure and Henry's law constants are more useful than the boiling point in understanding volatility. If data are available on either vapor pressure or Henry's law constant, information on boiling point is not needed.

Data Quality—HPV chemical groups consist of several toxicologically similar compounds. Data for some compounds can be used to predict the value of end points for others. The precision of these predictions depends on the appropriateness of the prediction tool (e.g., QSAR) and the similarity between the compounds with data and those for which data are estimated. Both the number and the quality of the data predictions, and the relevance of these data in predicting the PEC and PNEC should be considered.

Factor Separating the PEC and PNEC—Safety is assured when the concentration that organisms are exposed to in the environment (PEC) is below the maximum concentration at which effects will not be observed (PNEC). The larger the factor separating the PEC and the

PNEC, the greater the confidence that there will be no effects in the environment. The process of estimating the PEC and PNEC values in the environment typically applies conservative approaches when few data are available (Levels 1 and 2) and approaches leading to more realistic values, but greater certainty at higher levels (Levels 3 and 4). The relative importance of data completeness and data quality should be balanced with the relative separation of the PEC and PNEC. Simply put, when the PNEC is orders of magnitude above the PEC, modest increases in the uncertainty in the PEC and/or PNEC will not affect conclusions regarding the potential for harm to the environment.

The following discussion helps incorporate these criteria into decisions about each HPV chemical. The key consideration is the level of comfort with the derived PEC and PNEC values and whether, after considering uncertainty, the PNEC is less than the PEC. Clearly, there are judgment calls and it is not possible to consider every situation. Therefore, the following is intended to be guidance describing conditions that support the OECD decisions.

I. No further testing decision would be implemented under the following conditions:

- Where the PEC equals zero. In this case, there is no need to investigate.
- The PEC and the PNEC are based on complete sets of environmental data such that further study of fate and effects are unlikely to cause a reduction in their uncertainty or a change in these values. In this case, if the PEC is less than the PNEC, there is no need for additional work. However, if the PNEC is less than the PEC, then risk management options need to be considered.
- Environmental fate and effects data are relatively complete for the chemicals within an HPV chemical group or the methods used to read across are likely to provide an accurate estimate of environmental properties. The available data are sufficient to establish good estimates of the PEC in the aquatic environment after consumer use and manufacturing, and there is an order of magnitude or more between the maximum PEC and the PNEC. If some of the critical fate or effects data are missing or if predictions are uncertain, no further testing would be necessary as long as these data are replaced by conservative estimates and those estimate support an order of magnitude between the PEC and PNEC.

II. Priority for further testing would be implemented under the following conditions:

- If the PEC is greater than the PNEC regardless of data uncertainty. In this case, further investigation is always necessary.
- Environmental data are incomplete, leading to inaccurate estimates of the PEC and/or PNEC, and conservative estimates of the PEC and PNEC are either impossible or result in a PEC greater than the PNEC.

3.8 Related Compartments

While the current HPV process focuses on fresh surface waters as the primary environmental compartment, exposure to organisms also occurs in the marine compartment. Because of dilution factors in freshwater systems, the highest environmental concentrations of consumer product ingredients are expected in these systems. While the marine compartment also receives effluents directly and is the ultimate sink for non-volatile, non-degradable materials via rivers and streams, dilution factors in marine systems are generally greater than in freshwater systems (EU 2003). Therefore, exposure concentrations will be less than those occurring in freshwater systems.

Available data suggest that marine and freshwater organisms are similar in sensitivity to the toxic effects of chemicals (ECETOC 2000). Hence, risk (i.e., PEC/PNEC) to marine organisms resulting from the release of a chemical into the environment is likely similar to the risk to freshwater organisms. For perspective, the TGD (EU 2003) uses a factor of 10 to account for the possibility of increased susceptibility of marine organisms, but adds another dilution factor of 10 to account for lower exposure in marine systems.

3.9 Summary

This section provides guidance on the derivation of the PEC, PNEC, and the use of fate and effects data in decision-making. The types of data considered range from information predicted from structure-activity relationships up to environmental monitoring and field testing. As with any scientific endeavor, when new methods are developed and as additional data become available these approaches can be refined and improved. That said, these approaches have a long and successful history of use in protecting the environment and are appropriate for evaluating effects of HPV chemicals.

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4 Glossary of Terms

Acute exposure: Human—one exposure or multiple exposures occurring within a short time (24 hours or less). Environmental—exposures lasting far less than a reproductive cycle of an organism, generally 24 to 96 hours, but species dependent.

Aggregate exposure: Total exposure to all individual products containing the same chemical to which a consumer is likely exposed.

AISE: Association Internationale de la Savonnerie de la Détergence et des Produits d'Éntretien, or International Association for Soaps, Detergents and Maintenance Products, represents the European soap, detergent, and maintenance product industries to European and international organizations.

Alliance for Chemical Awareness (ACA): A voluntary initiative by chemical and consumer-product manufacturers to enhance the availability of information to the public pertaining to major chemicals in commerce, with a particular focus on HPV chemicals.

Allowable daily intake (ADI): The amount of a chemical a person can be exposed to on a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects.

APAG: The European Oleochemicals and Allied Products Group.

Assessment factors: Numbers used to extrapolate available toxicity data to predict actual toxicity. Available toxicity data are divided by numbers generally ranging from 1 to 1,000 to address uncertainties in the use of the toxicity data to protect human health and the environment.

CESIO: Comite Europeen des Agents de Surface et de Leurs Intermediaries Organiques.

Chemical Abstract Service (CAS) number: A unique number for each chemical. It is used to search for a specific chemical regardless of the choice of chemical name.

Chronic effect: An effect that is manifest as a result of repeated exposure over time. See also health hazard and chronic exposure.

Chronic exposure: Multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or the individual's lifetime.

Concentration-response: A relation between the exposure concentration and the biological response (effect) to that exposure.

Dose-response: A correlation between a quantified exposure (dose) and the proportion of a population that demonstrates a specific effect (response).

EC_x: The effective concentration or concentration of the substance causing an x percent decline in the biological parameter of interest (i.e., reproduction, growth). Similar to the LC_x or concentration causing x percent mortality. Typically calculated using concentration response statistics and avoids some of the interpretation problems associated with NOECs.

Exposure: Contact between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs/gills, gut).

Exposure assessment: The process of measuring or estimating the intensity, frequency, and duration of exposures to an agent currently present in the environment, or of estimating hypothetical exposures that might arise from the release of new chemicals into the environment.

Exposure concentration: The concentration of a chemical in its transport or carrier medium to the point of contact.

Exposure pathway: The physical course a chemical or pollutant takes from the source to the organism exposed.

Exposure route: The way a chemical or pollutant enters an organism after contact (e.g., by ingestion, inhalation/respiration, or dermal exposure).

Exposure scenario: A set of facts, assumptions and/or inferences about how exposure takes place that aids the exposure assessor in evaluating, estimating, or quantifying exposures.

Fabric density (FD): A parameter used in the screening-level exposure equation for the indirect dermal laundry detergent/fabric conditioner scenario. This parameter refers to the weight of the fabric per square centimeter and is used to calculate the percent retained factor. The value used in this assessment, 10 mg/cm^2, represents a medium blend fabric. A nylon or polyester fabric has a fabric density of 1 mg/cm^2 whereas a terry cloth fabric has a fabric density of 20–30 mg/cm^2 (SDA 2003).

HERA: Human & Environmental Risk Assessment. European project that standardizes risk assessment of ingredients in household cleaning products.

High-end: A plausible estimate at the upper end of a distribution of values, conceptually above the 90th percentile.

High-end exposure (dose) estimate: A plausible estimate of individual exposure or dose for those persons at the upper end of an exposure or dose distribution, conceptually above the 90th percentile, but not higher than the individual in the population who has the highest exposure or dose.

High production volume (HPV): Chemicals produced in quantities greater than one million pounds annually.

ICCA: International Council of Chemical Associations.

JSDA: Japan Soap and Detergent Association

K_{ow}: The octanol-water partition coefficient. A measure of the potential for a molecule to occur in a non-polar phase such as a lipid membrane or a more polar phase such as water.

LC_x: The concentration of the substance that causes x percent mortality.

Lowest-observed-adverse-effect level (LOAEL): The lowest exposure level at which there is statistically significant increase in frequency or severity of adverse effects between the exposed population and its appropriate control (mammalian system).

Lowest-observed-effect concentration (LOEC): The lowest exposure concentration at which there is a statistically significant increase in frequency or severity of adverse effects between the exposed population and its appropriate control (environmental system).

Margin of exposure (MOE): The ratio of the NOAEL to the estimated exposure dose.

Mesocosm/microcosm: A subset of the natural environment contained, controlled, and manipulated for experimental purposes. Mesocosms and microcosms are used to investigate interactions among the physical, chemical, and biological components of the ecosystem in a controlled environment. Mesocosms are larger experimental systems than microcosms and thus can support more species complexity.

No-observed-adverse-effect level (NOAEL): The highest exposure level in a study or a group of studies at which there is no statistically significant increase in the frequency or severity of adverse effects between the exposed population and its appropriate control (mammalian system).

No-observed-effect concentration (NOEC): The exposure concentration below which there is no statistically significant increase in the frequency or severity of adverse effects between the exposed population and its appropriate control (environmental system).

OECD: Organisation for Economic Co-operation and Development.

Percent deposition (PD): A parameter used in the screening-level exposure equation for the indirect dermal laundry detergent/fabric conditioner scenario. This parameter refers to the percentage of product that is deposited on the fabric during the wash cycle and is based on the amount of water used during the spin cycle and the amount of water remaining on the fabric after the spin cycle. The PD parameter is used to calculate the value of the percent retained.

Percent retained (PR): A parameter used in some of the screening-level exposure equations. When used in the indirect dermal laundry detergent/fabric conditioner scenario, PR refers to the percentage of product that remains on the fabric after the fabric has been washed. When used in the direct dermal personal care product (i.e., shampoo, soap, lotions, etc.) scenarios, PR refers to the percentage of product that remains on the body after the use of the product. When used in the indirect oral dish detergent scenario, PR refers to the percentage of product that remains on the dish after the dish has been washed but not rinsed with clean water.

Percent transferred (PT): A parameter used in the screening-level exposure equation for the indirect dermal laundry detergent/fabric conditioner scenario. This parameter refers to the percentage of product remaining on the fabric that is transferred to the skin.

Predicted no-effect concentration (PNEC): The environmental concentration at which there would be no observable adverse effects on naturally occurring biological communities.

Product exposure (PE): An estimate of exposure to an end-use product typically expressed in $mg_{product}/kg_{BW}$-day.

Quantitative structure activity relationship (QSAR): A mathematical expression used to relate physical or chemical parameters to biological or chemical activity of a molecule.

R (product retained on skin): A parameter used in the screening-level exposure equation for the direct dermal baby bath liquid scenario. This parameter refers to the amount of product remaining on the baby's skin after the use of the product. This parameter is very similar to the PR parameter, however it is presented in terms of $mg_{product\ remaining}/cm^2_{body\ surface\ area}$.

Reasonable worst case: A semi-quantitative term referring to the lower portion of the high end of the exposure, dose, or risk distribution. The reasonable worst case has historically been loosely defined, including synonymously with maximum exposure or worst case. As a semi-quantitative term, it is sometimes useful to refer to individual exposures, doses, or risks that, while in the high end of the distribution, are not in the extreme tail.

Reference dose (RfD): An estimate of the daily exposure to the human population that is likely to be without appreciable risk of deleterious non-cancer effects during a lifetime.

Screening Information Data Set (SIDS): A data set consisting of general information on a chemical's production, use patterns, physical and chemical characteristics (particularly those that might suggest how and to what extent people might become exposed), and its fate in the environment. A basic set of toxicology data is included: acute (single) dose toxicity, repeated dose toxicity, genetic toxicity, reproductive toxicity, and developmental toxicity. Similar testing requirements exist for harmful (non-human) effects in the environment.

SDA: The Soap and Detergent Association (USA)

SIAR: SIDS Initial Assessment Report

SIC: Standard Industrial Classification Code

Threshold dose: The dose or exposure below which no deleterious effect is expected to occur.

Time scaling factor (TF): A parameter used in the direct dermal scenario exposure equations. This factor refers to the amount of time actually spent performing an activity (i.e., hand-washing clothes, hand-washing dishes, using cleaning products, etc.). The values used for these factors are based on the number of minutes performing the specific activity divided by the total number of minutes in one day.

Tolerable daily intake (TDI): The total intake by ingestion (expressed in $mg_{chemical\ agent}/kg_{BW}$-day) to which it is believed that a person can be exposed daily over a lifetime without deleterious effects.

Worst case: A semi-quantitative term referring to the maximum possible exposure, dose, or risk, that can conceivably occur, whether or not this exposure, dose, or risk actually occurs in a specific population.

Appendix I-A

Sources of Product Exposure (PE) Models and Model Input Parameters

Appendix I-A. Sources of Product Exposure (PE) Models and Model Input Parameters

Numerous documents were reviewed in compiling the exposure equations and input parameters provided in the product exposure factor data matrix. The emphasis in this effort was on identifying screening-level factors and calculation approaches. The identified sources include the following:

1. AISE Human & Environmental Risk Assessment (2002) *Table of Habits and Practices for Consumer Products in Western Europe*. Developed within the HERA project using consolidated company data.

2. AISE Human & Environmental Risk Assessment on Ingredients of European Household Cleaning Products. (April 22, 2002) *Guidance Document Methodology*. http://www.heraproject.com/files/Guidancedocument.pdf

3. AISE Human & Environmental Risk Assessment (HERA). *Risk Assessments.* http://www.heraproject.com/RiskAssessment.cfm
   - -(June 2001) Ingredients of European household cleaning products: zeolite A represented by CAS number 1344-00-9 (sodium aluminum silicate) and CAS No. 1318-02-1 (zeolites).
   - -(June 2001) Ingredients of European household cleaning products: fluorescent brightener FWA-5 (CAS 27344-41-8).
   - -(March 2002) Ingredients of European household cleaning products: sodium carbonate CAS No. 497-19-8.
   - -(June 2002) Ingredients of European household cleaning products: fatty acid salts human health risk assessment.
   - -(July 2002) Linear alkylbenzene sulphonate: LAS. CAS No. 68411-30-3.
   - -(December 2002) Ingredients of European household cleaning products: alcohol sulphates human health risk assessment.
   - -(January 2003) Ingredients of European household cleaning products: alcohol ethoxysulphates human health risk assessment.

4. Alliance for Chemical Awareness. (October 2001) *Reporting of Hazard, Exposure and Initial Safety Assessment Information of HPV Chemicals to Technical Audiences.*

5. Alliance for Chemical Awareness. (May 2001) *Generic Technical Evaluation Framework for Screening-Level Evaluations of Human Exposures to HPV Chemicals.*

6. Alliance for Chemical Awareness. (February 2002) *A Product-Related (Consumer, Commercial/Institutional) Human Exposure and Hazard Evaluation Framework for an HPV Chemical.* http://www.chemicalawareness.org/toolkit/consumer.html

7. Alliance for Chemical Awareness. (January 31, 2002) *Generic Technical Evaluation Framework for Screening-Level Evaluations of Human Exposures to HPV Chemicals.*

8. American Industrial Health Council (AIHC).
   - (March 15, 2000) *Exposure Assessment Program Team Exposure Initiative.* Appendix 1: Glucose amides case study aggregate human exposure assessment case example – glucose amides.
   - (March 15, 2000) *Exposure Assessment Program Team Exposure Initiative.* Appendix 2: Amine oxides case study aggregate human exposure assessment case example – alkyldimethylamine oxides.
   - (March 15, 2000) *Exposure Assessment Program Team Exposure Initiative.* Appendix 3: Dimethyl ether case study aggregate human exposure assessment case example – dimethyl ether (DME).
   - (March 15, 2000) *Exposure Assessment Program Team Exposure Initiative.* Appendix 4: Dipropylene glycol n-butyl (DPnB)ether case study.
   - (August 29, 2001) *Initial Human Health and Environmental Screening Assessment for Dimethyl Ether (DME).* Technical summary. Prepared by DuPont Company.
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17. Comite Europeen Des Agents De Surface et de Leurs Intermediaires Organiques; European (CESIO) Newsletters, May and Nov 2000

18. Consumer Specialty Products Association (CSPA), (2002) Personal communication, E-mail from Bob_Hamilton@access businessgroup.com to Dfratz, July 17, 2002, Subject: Exposure Assessment Scenarios, ACC-CSPA Joint Project.

19. Cosmetic, Toiletry, & Fragrance Association. (August 15, 1983) *Final Review and Analysis of Scientific Studies and Risk Assessment Supporting the Safety of D&C Red No. 9 for Use in (1) External Cosmetic and Drug Products that Are Not Subject to Incidental Ingestion at Levels Consistent with Good Manufacturing Practices and in (2) External Cosmetic and Drug Products, Lipstick and Other Lip Products that Are Subject to Incidental Ingestion Levels Up to Two Percent.*

20. Cosmetic, Toiletry, & Fragrance Association. (May 2000) *Habits and Practices Studies (for Body Lotion, Hairspray, Face Cream, Lipstick, Perfume, and Foundation).*

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28. Everest Consulting Associates. (January, 1997) D4, D5, and D6 Exposure in the Manufacture and Use of Personal Care Products. Cranbury, NJ: for USEPA, Washington DC, on behalf of Dow Corning Corporation, Midland, MI.

29. International Programme on Chemical Safety. *INCHEM Concise International Chemical Assessment Documents (CICADS).* http://www.inchem.org/pages/cicads.html:
    - (1998) *CICADS 1.* 1,2-Dichloroethane.
    - (1998) *CICADS 2.* 3,3-Dichlorobenzidine.
    - (1998) *CICADS 3.* 1,1,2,2-Tetrachloroethane.
    - (1998) *CICADS 4.* Methyl methacrylate.
    - (1998) *CICADS 5.* Limonene.
    - (1998) *CICADS 7.* o-Toluidine.
    - (1998) *CICADS 8.* Triglycidyl isocyanurate.
    - (1998) *CICADS 9.* n-Phenyl-1-naphthylamine.
    - (1998) *CICADS 10.* 2-Butoxyethanol.
    - (1998) *CICADS 11.* 1,1,1,2-Tetrafluoroethane.
    - (1999) *CICADS 6.* Biphenyl.
    - (1999) *CICADS 12.* Manganese and its compounds.
    - (1999) *CICADS 13.* Triphenyltin compounds.
    - (1999) *CICADS 14.* Tributyltin oxide.
    - (1999) *CICADS 15.* Ethylenediamine.
    - (1999) *CICADS 16.* Azodicarbonamide.
    - (1999) *CICADS 17.* Butyl benzyl phthalate.
    - (1999) *CICADS 18.* Cumene.
    - (2000) *CICADS 19.* Phenylhydrazine.
    - (2000) *CICADS 20.* Mononitrophenols.
    - (2000) *CICADS 21.* 2-Furaldehyde.
    - (2000) *CICADS 22.* Ethylene glycol: environmental aspects.
    - (2000) *CICADS 23.* 2,2-Dichloro-1,1,1-trifluoroethane (HCFC-123).
    - (2000) *CICADS 24.* Crystalline silica, quartz.
    - (2000) *CICADS 25.* Chloral hydrate.
    - (2000) *CICADS 26.* Benzoic acid and sodium benzoate.
    - (2001) *CICADS 27.* Diphenylmethane diisocyanate (MDI).
    - (2001) *CICADS 28.* Methyl chloride.
    - (2001) *CICADS 29.* Vanadium pentoxide and other inorganic vanadium compounds.
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- Dimethyldicotandecylammomonium chloride (CAS No. 107-64-2)
- Dodecanedioic acid (CAS No. 693-23-2)
- N,N-dimethyl-2-aminoethanol (CAS No. 108-01-0)
- L-Ascorbic acid (CAS No. 50-81-7)
- Nicotinic acid (CAS No. 59-67-6)
- Sodium dodecyl sulfate (SDS) (CAS No. 151-21-3)
- Stearyl alcohol (CAS No. 112-92-5)

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Appendix I-B

Primary, Secondary, and Selected References for Exposure Models and Factors

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
NA Dermal: laundry detergent Pretreatment Hand washing clothes Wearing clothes	ACA, Oct 2001		• AIHC glucose amides SDA data • U.S. EPA (1997, 2001) • AISE/HERA, 2002 Habits and Practices Table • AIHC alkyldimethylamine oxides
	ACA, Jan 2002		
	ACA, Feb 2002		
	AISE/HERA, 2002 Habits and Practices Table		
	AIHC glucose amides	U.S. EPA, 1997 Soap and Detergent Association (SDA) data, 2002-2003	
	AIHC alkyldimethylamine oxides	U.S. EPA, 1997 SDA data,2002-2003	
	U.S. EPA, 1997		
	U.S. EPA (1997, 2001)		
	Multiple OECD SIDS/SIARS		
	SDA data		
NA Dermal: Dish detergent: washing hands Dish detergent: washing dishes Hard surface and all purpose cleaner	ACA, Oct 2001		• AIHC alkyldimethylamine oxides • SDA data, 2002-2003 • U.S. EPA (1997, 2001) • AISE/HERA, 2002 Habits and Practices
	ACA, Jan 2002		
	ACA, Feb 2002		
	AISE/HERA 2002 Habits and Practices Table		
	AIHC glucose amides	U.S. EPA, 1997 SDA data	
	AIHC alkyldimethylamine oxides	U.S. EPA, 1997 SDA data	
	AIHC Dipropylene glycol n-butyl (DPnB)ether	U.S. EPA, 1997 U.S. EPA EFAST model	
	CSPA		
	U.S. EPA, 1997		
	U.S. EPA (1997, 2001)		
	Multiple OECD SIDS/SIARS		
	SDA data		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
NA Dermal: Personal care (hair care, skin care, antiperspirants/deodorants) Cosmetics Baby products Fragrances	ACA, Oct 2001		• K.S. Crump Group, 1999 [ECA, 1997] • K.S. Crump Group, 1999 [CTFA, 1983; COLIPA, 1981] • CTFA, 2002 • CTFA, 2003 • SDA data, 2002-2003 • TGD (2003) • U.S. EPA (1997, 2001)
	ACA, Jan 2002		
	ACA, Feb 2002		
	AIHC alkyldimethylamine oxides	U.S. EPA, 1997 SDA data, 2002-2003	
	CTFA, 2002		
	CTFA, 2003		
	K.S. Crump Group, 1999	ECA, 1997 MRI, 1995 MRI, 1996 U.S. EPA, 1997 U.S. EPA, 1989 CTFA, 1983 COLIPA, 1981	
	Multiple OECD SIDS, SIARS		
	Sciences International, 2001		
	SDA data		
	EU TGD, 2003		
	U.S. EPA, 1997		
	U.S. EPA (1997, 2001)		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
EU Dermal: Laundry detergent Pretreatment Hand wash clothes Wearing clothes	AISE/HERA 2002 Habits and Practices Table		• AISE/HERA Zeolite A, 2001 [Lally, 2001; EU TGD] • AISE/HERA Sodium Carbonate, 2002 • AISE/HERA Fluorescent Brightener, 2001 [U.S. EPA] • AISE/HERA, 2002 Habits and Practices Table • SDA data, 2002-2003 • TGD (2003)
	AISE/HERA, April 2002		
	AISE/HERA LAS, 2002	P&G unpublished data Vermeire, 1993 HERA, 2002 EU TGD	
	AISE/HERA Alcohol sulphates, 2002	EU TGD, 2003 HERA, 2002	
	AISE/HERA Sodium Carbonate, 2002	Lally, 2001 HERA, 2002 U.S. EPA, 1997	
	AISE/HERA Fluorescent Brightener, 2001	TGD (2003) HERA, 2002 U.S. EPA, 1997	
	AISE/HERA Zeolite, 2001	Lally, 2001 U.S. EPA, 1989 HERA, 2002 EU TGD,2003	
	AISE/HERA Fatty acid salts, 2002	EU TGD, 2003 HERA, 2002 Vermeire, 1993	
	AISE/HERA Alcohol ethoxysulphates, 2003	HERA, 2002 EU TGD, 2003	
	EU TGD, 2003		
	IPCS, 1994		
	Multiple IPCS CICADS (see appendix I-A)		
	Multiple OECD SIDS/SIARS (see appendix I-A)		
	SDA data, 2002-2003		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
EU Dermal: Dish detergent: washing hands Dish detergent: washing dishes Hard surface and all purpose cleaner	AISE/HERA, 2002 Habits and Practices Table		• AIHC alkyldimethylamine oxides • AISE/HERA Sodium Carbonate, 2002 • AISE/HERA, 2002 Habits and Practices Table • AISE/HERA Fluorescent Brightener, 2001 [U.S. EPA] • AISE/HERA Zeolite A, 2001 [Lally, 2001; EU TGD] • SDA data, 2002-2003 • TGD (2003)
	AISE/HERA, April 2002		
	AIHC alkyldimethylamine oxides	U.S. EPA, 1997 SDA data, 2002-2003	
	AISE/HERA LAS, 2002	HERA, 2002 EU TGD	
	AISE/HERA Alcohol sulphates, 2002	EU TGD HERA, 2002	
	AISE/HERA Alcohol ethoxysulphates, 2003	HERA, 2002 EU TGD	
	AISE/HERA Fluorescent Brightener, 2001	EU TGD HERA, 2002 U.S. EPA, 1997	
	AISE/HERA Zeolite, 2001	Lally, 2001 HERA, 2002 EU TGD	
	EU TGD, 2003		
	IPCS, 1994		
	Multiple IPCS CICADS		
	Multiple OECD SIDS/SIARS (see appendix I-A)		
	SDA data		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
EU Dermal: Personal care (hair care, skin care, antiperspirants, deodorants) Cosmetics Baby products Fragrances	AISE/HERA, April 2002		• TGD (2003) • COLIPA, 2002 • K.S. Crump Group, 1999 [ECA, 1997] • SDA data, 2002-2003 • CTFA, 2003 • U.S. EPA, 1997
	K.S. Crump Group, 1999	ECA, 1997 MRI, 1995 MRI, 1996 U.S. EPA, 1997 U.S. EPA, 1989 CTFA, 1983 COLIPA, 1981	
	Cadby, 2002	COLIPA, 1987	
	COLIPA, 2002		
	CTFA, 2003		
	EU SCCNFP, 2000	COLIPA, 1997	
	IPCS, 1994		
	Multiple IPCS CICADS (see Appendix I-A)		
	Multiple OECD SIDS, SIARS (see Appendix I-A)		
	SDA data, 2002-2003		
	EU TGD, 2003		
	U.S. EPA, 1997		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
NA Oral: Dishwashing liquid deposition Personal care products (toothpaste, mouthwash, lipstick)	ACA, Oct 2001		• AISE/HERA LAS, 2002 [Schmitz, 1973; Official French legislation 1990]) • EU SCCNFP, 2003 • EU TGD, 2003 • K.S. Crump Group, 1999 [ECA, 1997] • Barnhart, 1974 • CTFA, 2002 and 2003 • SDA data, 2002-2003 • U.S. EPA (1997, 2001)
	ACA, Jan 2002		
	ACA, Feb 2002		
	AIHC glucose amides	U.S. EPA, 1997 SDA data, 2002-2003	
	AIHC alkyldimethylamine oxides	U.S. EPA, 1997 SDA data, 2002-2003	
	AISE/HERA LAS, 2002	Schmitz, 1973 Official French legislation, 1990 HERA, 2002 EU TGD	
	Barnhart, 1974		
	CTFA, 2002		
	CTFA, 2003		
	EU SCCNFP, 2000		
	EU SCCNFP, 2003	Beltran, 1998; Bently, 1999 Barnhart, 1974; Baxter, 1980 Bently, 1997; Brunn, 1988 Dowel, 1981; Ericcson, 1969 Levy, 1993; Naccache, 1992 Naccache, 1990; Simard, 1989 Simard, 1991	
	K.S. Crump Group, 1999	ECA, 1997; MRI, 1996 U.S. EPA, 1997; CTFA, 1983 COLIPA, 1981	
	Multiple OECD SIDS, SIARs (see Appendix I-A)		
	OECD SDS SIAR	Ekstrand, 1980	
	Sciences International, 2001		
	SDA data, 2002-2003		
	EU TGD, 2003		
	U.S. EPA, 1997		
	U.S. EPA (1997, 2001)		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
EU Oral: Dishwashing liquid deposition Personal care products (toothpaste, mouthwash, lipstick)	AISE/HERA, April 2002		• AISE/HERA LAS, 2002 [Schmitz, 1973; Official French legislation, 1990]) • EU SCCNFP, 2003 • EU TGD, 2003 • Barnhart, 1974 • SDA data, 2002-2003
	AISE/HERA LAS, 2002	Schmitz, 1973 Official French legislation, 1990 HERA, 2002 EU TGD, 2003	
	Barnhart, 1974		
	EU SCCNFP, 2000		
	EU SCCNFP, 2003	Beltran, 1998; Bently, 1999 Barnhart, 1974; Baxter, 1980 Bently, 1997; Brunn, 1988 Dowel, 1981; Ericcson, 1969 Levy, 1993; Naccache, 1992 Naccache, 1990; Simard, 1989 Simard, 1991	
	Multiple OECD SIDS, SIARs (see Appendix I-A)	Ekstrand, 1980	
	IPCS, 1994		
	Multiple IPCS CICADS (see Appendix I-A)		
	SDA data, 2002-2003		
	EU TGD, 2003		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
NA Inhalation: Laundry detergent dust Spray cleaners Paints	ACA, Oct 2001		• AISE/HERA LAS, 2002 [Van de Plassche, 1998]) • CSPA, 2002 • SDA data, 2002-2003 • Battelle, 1999 • EU TGD, 2003 • U.S. EPA, 1997 • U.S. EPA (1997, 2001)
	ACA, Jan 2002		
	ACA, Feb 2002		
	AIHC DPnB	EPA CHEMSTEER	
	Battelle, 1999		
	CSPA, 2002		
	AISE/HERA LAS, 2002	Van de Plassche, 1998 HERA, 2002 EU TGD, 2003	
	U.S. EPA, 1997		
	U.S. EPA (1997, 2001)		
	EU TGD, 2003		
	Multiple OECD SIDS/SIARS (see Appendix I-A)		
	SDA data, 2002-2003		
NA Inhalation: Personal care products (hair sprays, fragrances, antiperspirants/deodorants)	ACA, Oct 2001		• AIHC DME • K.S. Crump Group, 1999 [ECA, 1997] [MRI, 1995]) • CTFA, 2002 • CTFA, 2003 • SDA data, 2002-2003 • U.S. EPA (1997, 2001) • TGD (2003)
	ACA, Jan 2002		
	ACA, Feb 2002		
	K.S. Crump Group, 1999	ECA, 1997 MRI, 1995 and 1996 U.S. EPA, 1989 and 1997 CTFA, 1983 COLIPA, 1981	
	AIHC DME		
	CTFA, 2000		
	CTFA, 2003		
	U.S. EPA, 1997		
	U.S. EPA (1997, 2001)		
	Multiple OECD SIDS/SIARS (see Appendix I-A)		
	EU TGD, 2003		
	SDA data, 2002-2003		

Appendix I-B. Primary, Secondary and Selected References for Exposure Models and Factors (cont'd)

Exposure Scenario	Documents Reviewed	Secondary References (Documents referenced within reviewed document)	Documents Selected [Secondary Reference]
EU Inhalation: Laundry detergent dust Spray cleaners Paints	AISE/HERA, April 2002		• AISE/HERA LAS, 2002 [Van de Plassche, 1998] • CSPA, 2002 • SDA data, 2002-2003 • Battelle, 1999 • TGD (2003) • U.S. EPA, 1997
	AISE/HERA LAS, 2002	Van de Plassche, 1998 HERA, 2002 EU TGD, 2003	
	Battelle, 1999		
	CSPA, 2002		
	IPCS, 1994		
	Multiple IPCS CICADS (see Appendix I-A)		
	U.S. EPA, 1997		
	EU TGD, 2003		
	Multiple OECD SIDS/SIARS (see Appendix I-A)		
	SDA data, 2002-2003		
EU Inhalation: Personal care products (hair sprays, antiperspirants, deodorants, fragrances)	AISE/HERA, April 2002		• K.S. Crump Group, 1999 [ECA, 1997 • COLIPA, 2002 • SDA data, 2002-2003 • EU TGD, 2003
	K.S. Crump Group, 1999	ECA, 1997 MRI, 1995 and 1996 U.S. EPA, 1989 and 1997 CTFA, 1983 COLIPA, 1981	
	COLIPA, 2002		
	IPCS, 1994		
	Multiple IPCS CICADS (see Appendix I-A)		
	Multiple OECD SIDS/SIARS (see Appendix I-A)		
	EU TGD, 2003		
	SDA data		

Appendix II-A

Screening Product Exposure Data Matrix: Default High-End Values

Appendix II-A
Screening Product Exposure Data Matrix: Default High-End Values

Appendix II-A presents the default high-end input values for the exposure parameters and the associated references/documentation. In cases where the maximum value was not selected as the "high-end" default value, an explanation is provided in the numeric footnotes.

Table II-A-1. Dermal Exposure Parameters to Estimate Screening Exposures to Consumer Products—North America
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Freq. [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A'] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Film Thickness [FT] (cm)[a]	Product Retained [PR] (%)	Percent Transfer [PT] (%)	Dermal Abs. [DA] (%)	Body Weight[b] [BW] (kg)	Scaling: Duration of Exposure [TF]	Product Exposure (mg/kg-day)	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1,000 mg/g; assumed 100% dermal absorption)
Soaps and Detergents																
Laundry detergent–wearing clothes		121[c]							1.00[c]	1[c]	100	65.4		0.2017	SDA data; AIHC exposure initiative: glucose amides	A×PR×PT×DA×CF/BW
Laundry detergent (tablets) – wearing clothes		135[d]							1.00[c]	1[c]	100	65.4		0.2250	SDA data; AIHC exposure initiative: glucose amides	A×PR×PT×DA×CF/BW
Fabric conditioners, rinse added – wearing clothes		112[c]							1.00[c]	1[c]	100	65.4		0.1867	SDA data; AIHC exposure initiative: glucose amides	A×PR×PT×DA×CF/BW
Fabric conditioners, dryer sheets – wearing clothes		3[c]							10.0[c]	1[c]	100	65.4		0.0500	SDA data; AIHC exposure initiative: glucose amides	A×PR×PT×DA×CF/BW
Laundry detergent/ fabric conditioner handwash	1[c]			1[c]	0.01[e]	1680[f]		0.0024			100	65.4	0.007[d]	0.0047	AIHC exposure initiative: glucose amides	FQ×PC×CA×FT×DA×TF×CF/BW
Laundry detergent pretreatment (powder paste)	1[c]			60[d]	0.6[e]	360[g]		0.0024			100	65.4	0.007[d]	0.0600	AIHC exposure initiative: glucose amides	FQ×PC×CA×FT×DA×TF×CF/BW
Laundry detergent pretreatment (liquid neat/non-dilutable)	1[c]			100[h]	1.0[e]	360[g]		0.0024			100	65.4	0.007[d]	0.1000	AIHC exposure initiative: glucose amides	FQ×PC×CA×FT×DA×TF×CF/BW
Dishwashing liquids-handwash (hands)	0.14[a]				0.9[a]	1680[f]		0.0024			100	65.4	0.00035[c]	0.0030	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×DA×TF×CF/BW
Dishwashing liquids-handwash (dishes)	3[c]			0.15[c]	0.0015[e]	1680[f]		0.0024			100	65.4	0.03[d]	0.0095	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×DA×TF×CF/BW
Hard surface cleaner-powder	1[c]	51[c]		1[i]	0.01[e]	1680[f]		0.0024		100[j]	100	65.4	0.014[d]	0.0095	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×PT×DA×TF×CF/BW
APC liquid	1[c]	76[c]		1.5[i]	0.015[e]	1680[f]		0.0024		100[j]	100	65.4	0.014[d]	0.0143	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×PT×DA×TF×CF/BW
APC gel (neat/non-dilutable)	1[d]			100[h]	1.0[e]	180[g]		0.0024		100[j]	100	65.4	0.014[d]	0.1000	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×PT×DA×TF×CF/BW
APC spray (neat/non-dilutable)	1[d]			100[h]	1.0[e]	180[k]		0.0024		100[j]	100	65.4	0.0104[l, m1]	0.0504	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×PT×DA×TF×CF/BW
Personal Care and Cosmetics																
Shampoos	1[l]	16.4[l]							1[n]		100	65.4		2.73	AIHC/D4	FQ×A×PR×DA×CF/BW
Hair rinses	1[l]	12.7[l]							1[n]		100	65.4		2.12	AIHC/D4	FQ×A×PR×DA×CF/BW
Styling tonic/gel	1[b]	5.6[n]							5[n]		100	65.4		4.67	AIHC/D4	FQ×A×PR×DA×CF/BW
Hair sprays – aerosol	2[m2, o]	5.33[m2, o]							5[n]		100	65.4		8.88	AIHC/D4	FQ×A×PR×DA×CF/BW

	Product Use Freq. [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A'] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Film Thickness [FT] (cm)[a]	Product Retained [PR] (%)	Percent Transfer [PT] (%)	Dermal Abs. [DA] (%)	Body Weight[b] [BW] (kg)	Scaling: Duration of Exposure [TF]	Product Exposure (mg/kg-day)	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1,000 mg/g; assumed 100% dermal absorption)
Hair spray (pump)	2[m2, o]	7.81[m2, o]							5[n]		100	65.4		13.02	AIHC/D4	
F&H liquid soap – hand	8[c]	1.7[c]							1.0[j]		100	65.4		2.27	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
F&H bar soap – hand	6[c]	0.36[c]							1.0[j]		100	65.4		0.36	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Liquid soap – body	0.57[l]	11.8[l, m3]							1.0[j]		100	65.4		1.12	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
F&H bar soap – body	3[l]	8.6[c]							1.0[j]		100	65.4		4.30	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Cleansing products	2[l]	1.7[l, m3]							1.0[j]		100	65.4		0.57	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Body wash	1[c]	12[c]							1.0[j]		100	65.4		2.00	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Bath foam/bubble bath	0.29[p]	17[c]							1.0[j]		100	65.4		0.82	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
F&H bar soap – face	1.00[c]	0.27[c]							1.0[j]		100	65.4		0.05	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Shave cream	1.00[c]	4[j, m4]							1[c]		100	70		0.57	AIHC/D4 (skin care);	FQ×A×PR×DA×CF/BW
Body moisturizer			16.1[m2, o]						100[q]		100	65.4		268.33	AIHC/D4 (skin care);	FQ×A×PR×DA×CF/BW
Antiperspirants – roll-ons	1[c, m5]	1.22[n]							100[q]		100	70		17.43	AIHC/D4 (male data)	FQ×A×PR×DA×CF/BW
Antiperspirant aerosols	1[c, m5]	2.2[c]							75[j]		100	65.4		27.50	AIHC/D4	FQ×A×PR×DA×CF/BW
Antiperspirant solid/bar	1[c, m5]	1.2[c]							100[q]		100	65.4		20.00	AIHC/D4	FQ×A×PR×DA×CF/BW
Lipstick	3[m2, o]	0.024[m2, o]							100[q]		100	65.4		1.20	AIHC/D4	FQ×A×PR×DA×CF/BW
Face/eye cosmetics foundation liquid	2[o]	1.2[m2, o]							100[q]		100	65.4		40.00	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Other – makeup remover	2[p]	2.5[p]							5[r]		100	65.4		4.17	AIHC/D4	FQ×A×PR×DA×CF/BW
Baby Care Products																
Baby/bath liquid	1[c]	0.873[s]				9000[c]	0.097[c]		100		100	15		58		FQ×A×PR×DA×CF/BW
Baby lotions and creams	2[l]	2[l]							100[q]		100	15		267	AIHC/D4	FQ×A×PR×DA×CF/BW
Kids' shampoos	0.43[l]	10[c]							1[n]		100	15		3	AIHC/D4	FQ×A×PR×DA×CF/BW
Fragrances																
Fine fragrances	1.67[m6, o]	0.68[m2, o]							100[q]		100	65.4		18.93	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Aftershave	1[c]	1[c]							100[q]		100	70		14.29	AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
APC	all purpose cleaners
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
F&H	face and hand
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
SRTC	CTFA's Safety and Regulatory Toxicology Committee
TGD	EU Technical Guidance Document (2003)

References:

[a] AIHC alkyldimethylamine oxide assessment.

[b] U.S. EPA (1997, 2001) (OPP Residential SOPs).

[c] SDA data.

[d] AISE/HERA (2002) (Table of Habit and Practices for consumer products in Western Europe) (no NA specific data identified).

[e] PC (%) was converted to PC (g/cm^3); where (X g product/ 100 g water) × (1g water/$1cm^3$ water).

[f] AIHC alkyldimethylamine oxide assessment: hands and forearms.

[g] EFH: both palms (average female)-- SDA 2/03 resolution.

[h] Non-diluted products use 100 percent product concentration.

[i] PC (percent) was calculated by assuming product will be diluted in 5 L of water; PC (%) = (X g/use) / (5L/use) × (1,000 g/L).

[j] CTFA's SRTC comments on SDA Exposure Assessment Methodology, April 2003.

[k] EFH & SDA 2/03 and 4/03 resolutions -- one palm, average females.

[l] U.S. EPA 1997.

[m] Value other than maximum selected, see additional numbered notes below:

1. Selected value based on mean estimate of 15 minute a day, which was based on the sum of EFH estimates for cleaning bathroom sinks/tubs (average 44 hours/year) and cleaning kitchen sinks (average 41 hours/yr)
2. Selected value at 90th percentile of data range
3. Full data range not provided; only averages were available
4. Selected reasonable average value as recommended by CTFA's SRTC
5. Selected reasonable value based on outcome of discussions among SDA member companies
6. Selected average value from CTFA (2002) which is in the upper range of data provided in EFH

[n] AIHC/K.S. Crump Group (1999) (D4 assessment).

[o] CTFA (2002).

[p] EU TGD (2003) (no NA-specific data identified).

[q] Leave-on product; assumed 100 percent.

[r] Data on percent product retained (PR) was not available for make-up remover scenario; 5 percent was assumed to be a reasonable high-end estimate.

[s] Derived based on CA × R/1000 (recommended by SDA-HPV consortium for consistency with adult dermal scenarios at February 2003 meeting).

Table II-A-2. Dermal Exposure Parameters to Estimate Screening Exposures to Consumer Products—Europe
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Freq. [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A'] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Product Retained [PR] (%)	Film Thickness [FT] (cm)	Transfer to Skin [PT] (%)	Dermal Abs. [DA] (%)	Body Weight[a] [BW] (kg)	Scaling: Duration of Exposure [TF]	Product Exposure (mg/kg-day)	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1,000 mg/g; assumed 100% dermal absorption)
Soaps and Detergents																
Laundry detergents – indirect: powder		290[b]						0.95[c]		10[d]	100	60		4.59	HERA RA for sodium aluminum silicate	A×PR×PT×DA×CF/BW
Laundry detergents – indirect: liquid		230[b]						0.95[c]		10[d]	100	60		3.64	HERA RA for sodium aluminum silicate	A×PR×PT×DA×CF/BW
Laundry detergent – indirect: tablet		135[b]						0.95[c]		10[d]	100	60		2.14	HERA RA for sodium aluminum silicate	A×PR×PT×DA×CF/BW
Fabric conditioners indirect: liquid regular		140[b]						0.95[c]		10[d]	100	60		2.22	HERA RA for sodium aluminum silicate	A×PR×PT×DA×CF/BW
Fabric conditioners indirect: liquid concentrate		90[b]						0.95[c]		10[d]	100	60		1.43	HERA RA for sodium aluminum silicate	A×PR×PT×DA×CF/BW
Handwashing: powder	2.57[b]			1[b]	0.01[e]	1980[f]			0.01[d]		100	60	0.007[b]	0.06	HERA RA for sodium carbonate	FQ×PC×CA×FT×DA×TF×CF/BW
Handwashing: liquid laundry and fabric conditioners	1.43[b]			1[b]	0.01[e]	1980[f]			0.01[d]		100	60	0.007[b]	0.03	HERA RA for sodium carbonate	FQ×PC×CA×FT×DA×TF×CF/BW
Pretreatment (powder paste)	1.00[g]			60[b]	0.6[e]	840[a]			0.01[d]		100	60	0.007[b]	0.58	HERA RA for sodium carbonate	FQ×PC×CA×FT×DA×TF×CF/BW
Pretreatment (liquid neat)	1.00[g]			100[h]	1[e]	840[a]			0.01[d]		100	60	0.007[b]	0.97	HERA RA for sodium carbonate	FQ×PC×CA×FT×DA×TF×CF/BW
Dishwashing liquids – handwash (hands)	0.14[i]				0.9[i]	1680[i]			0.01[d]		100	60	0.00035[g]	0.01	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×DA×TF×CF/BW
Dishwashing liquids – handwash (dishes)	3.0[b]	28[a]		0.93[j]	0.009[e]	1980[f]			0.01[d]		100	60	0.03[b]	0.29	AIHC exposure initiative: amine oxides	FQ×PC×CA×FT×DA×TF×CF/BW
APC liquid	1.0[b]	110[b]		2.20[k]	0.022[e]	1980[f]			0.01[d]		100	60	0.014[b]	0.10	HERA RA for sodium carbonate (detergents)	FQ×PC×CA×FT×DA×TF×CF/BW
APC powder	1.0[b]	40[b]		0.80[k]	0.008[e]	1980[f]			0.01[d]		100	60	0.014[b]	0.04	HERA RA for sodium carbonate (detergents)	FQ×PC×CA×FT×DA×TF×CF/BW
APC spray (neat) diluted	1.0[b]	30[b]		0.60[k]	0.006[e]	1980[f]			0.01[d]		100	60	0.007[b]	0.01	HERA RA for sodium carbonate (detergents)	FQ×PC×CA×FT×DA×TF×CF/BW
APC gel (neat) diluted	1.0[b]	40[b]		0.80[k]	0.008[e]	1980[f]			0.01[d]		100	60	0.014[b]	0.04	HERA RA for sodium carbonate (detergents)	FQ×PC×CA×FT×DA×TF×CF/BW
APC spray (neat) undiluted	1.0[b]			100[h]	1[e]	1980[f]			0.01[d]		100	60	0.007[b]	2.29	HERA RA for sodium carbonate (detergents)	FQ×PC×CA×FT×DA×TF×CF/BW
APC gel (neat) undiluted	1.0[b]			100[h]	1[e]	1980[f]			0.01[d]		100	60	0.014[b]	4.58	HERA RA for sodium carbonate (detergents)	FQ×PC×CA×FT×DA×TF×CF/BW

	Product Use Freq. [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A'] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Product Retained [PR] (%)	Film Thickness [FT] (cm)	Transfer to Skin [PT] (%)	Dermal Abs. [DA] (%)	Body Weight[a] [BW] (kg)	Scaling: Duration of Exposure [TF]	Product Exposure (mg/kg-day)	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1,000 mg/g; assumed 100% dermal absorption)
Personal Care and Cosmetics																
Shampoos	1[l]	8[l,m]						1[i]			100	60		1.33	TGD	FQ×A×PR×DA×CF/BW
Hair conditioners	0.29[d]	14[d]						1[i]			100	60		0.68	TGD	FQ×A×PR×DA×CF/BW
Styling mousse	2[d]	5[d]						5[i]			100	60		8.33	TGD	FQ×A×PR×DA×CF/BW
Hair sprays – aerosol	2[l]	5[l]						10[l]			100	60		16.67	No EU data; AIHC/D4	FQ×A×PR×DA×CF/BW
F&H liquid soap – hand	7[g]	1.6[g]						0.5[g]			100	60		0.93	TGD	FQ×A×PR×DA×CF/BW
F&H bar soap – hand (toilet soap)	6[l]	0.8[l]						10.0[l]			100	60		8.00	TGD	FQ×A×PR×DA×CF/BW
Liquid soap – body (shower gel)	1.07[l]	5[l]						10.0[l]			100	60		8.92	TGD	FQ×A×PR×DA×CF/BW
F&H bar soap – body	1[g]	10[g]						0.5[g]			100	60		0.83	TGD	FQ×A×PR×DA×CF/BW
F &H bar soap – face	1[g]	0.27[g]						0.5[g]			100	60		0.02	No EU data: AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Body wash	1[g]	9.2[g]						0.5[g]			100	60		0.77	TGD	FQ×A×PR×DA×CF/BW
Bath foam/bubble bath	0.29[d]	17[g]						0.5[g]			100	60		0.41	TGD	FQ×A×PR×DA×CF/BW
Shaving lubricant	1[d]	2[d]						1[g]			100	70		0.29	TGD	FQ×A×PR×DA×CF/BW
Skin lotions and creams (body lotion)	0.71[l,m]	8[l]						100[l]			100	60		94.67	TGD	FQ×A×PR×DA×CF/BW
Hand moisturizer	7[g]	0.8[g]						100[n]			100	60		93.33	TGD	FQ×A×PR×DA×CF/BW
Fragrance cream (include makeup and foundation)	0.29[l]	5[l]						100[l]			100	60		24.17	TGD	FQ×A×PR×DA×CF/BW
Facial moisturizer	2[l]	0.8[l]						100[l]			100	60		26.67	TGD	FQ×A×PR×DA×CF/BW
Antiperspirants – aerosols	3[a]	3[a]						100[n]			100	60		150.00	TGD	FQ×A×PR×DA×CF/BW
Antiperspirant – roll-ons	1[l]	0.5[l,m]						100[l]			100	60		8.33	TGD	FQ×A×PR×DA×CF/BW
Antiperspirant solid/bar	1[l]	0.5[l,m]						100[l]			100	60		8.33	TGD	FQ×A×PR×DA×CF/BW
Lipstick	6[a]	0.01[a]						100[n]			100	60		1.00	TGD	FQ×A×PR×DA×CF/BW
Face/eye cosmetics	3[a]	0.025[a]						100[n]			100	60		1.25	TGD	FQ×A×PR×DA×CF/BW
Other – makeup remover	2[a]	2.5[a]						5[o]			100	60		4.17	TGD	FQ×A×PR×DA×CF/BW
Baby Care Products																
Baby shampoo			5[g]					1[i]			100	15		3.33	SDA data	A'×PR×DA×CF/BW
Baby/bath liquid	1[g]	0.873[p]				9000[g]	0.097[g]				100	15		58.20	SDA data	FQ×R×CA×DA×CF/BW
Baby lotions and creams	2[q]	2[r]						100[n]			100	15		266.67	No EU data: AIHC/D4	FQ×A×PR×DA×CF/BW
Skin wipes																
Fragrances																
Fine fragrances – pour form	5[g]	1.2[g]						100[n]			100	60		100.00	TGD	FQ×A×PR×DA×CF/BW
Aftershave	1[g]	1[g]						100[n]			100	70		14.29	No EU data; AIHC/D4 (skin care)	FQ×A×PR×DA×CF/BW
Eau de toilette (including perfume and aftershave)	1[l]	0.75[l]						100[l]			100	60		12.50	TGD	FQ×A×PR×DA×CF/BW

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products, (Association Internationale de la Savonnerie, de la Détergence et des Produits d'Entretien)
APC	all purpose cleaners
COLIPA	European Cosmetic, Toiletry, and Perfumery Association
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment, K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
F&H	face and hand
SRTC	CTFA-Safety Regulatory Toxicology Subcommittee
TGD	EU Technical Guidance Document

References:

[a] EU TGD (2003).

[b] AISE HERA Habits and Practices, 2002 (developed by AISE within the HERA project).

[c] AISE HERA RA Sodium Aluminum Silicate where PR = (PD × FD1)/WI × CA; product deposition (5 percent); FD1 = fabric density (10 mg/cm^2); WI = total wash weight (1kg); CA = body contact area (cm^2)

[d] AISE HERA RA Sodium Aluminum Silicate.

[e] PC (%) was converted to PC (g/cm3); where (X g product/100 g water) × (1g water/1cm^3 water).

[f] AISE HERA fluorescent brightener FWA-5.

[g] SDA data.

[h] Non-diluted products use 100 percent product concentration.

[i] AIHC/D4, K.S. Crump Group (1999).

[j] SIAR triethanolamine: dilute in 3,000 cm^3 water.

[k] AISE HERA Habits and Practices (diluted in 5 L of water).

[l] COLIPA (2002).

[m] Value other than maximum selected; selected value based on COLIPA (2002) data.

[n] Leave-on product; assumed 100 percent.

[o] No available data.

[p] Derived based on CA × R/1,000 (SDA-HPV consortium's recommendation for consistency with adult dermal scenarios, February 2003).

[q] U.S. EPA (1997) (no EU-specific data).

[r] Based on CTFA-SRTC comments on SDA Exposure Assessment Methodology April 2003 (no EU-specific data).

Table II-A-3. Oral Exposure Parameters to Estimate Screening Exposures to Consumer Products—North America
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Use Conc. [C'] (g/cm^3)	Product Retained [Ta'] (ml/cm^2)	Dish Area Contacting Food [Sa] (cm^2)	Fraction Ingested [FI] (%)	Body Weight[a] [BW] (kg)	Product Exposure (mg/kg-day)	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1,000 mg/g; assumed 100% dermal absorption)
Soaps and Detergents										
Dishwashing liquids – hand wash (dishware deposition)		5[b]	0.001[c]	5.50E-05[d]	5400[e]		65.4	0.0050	HERA-LAS	C'×Ta'×Sa×CF/BW
Personal Care and Cosmetics										
Toothpaste	3[e, f1]	0.8[f2, g]				35[f3, g]	15	56.0	SCNNFP, 2003	FQ×A×FI×CF/BW
Mouthwash adult	2[e]	30[e]				8.5[e]	65.4	85.0	TGD	FQ×A×FI×CF/BW
Lipstick	2.6[f4, h]	0.024[f4, h]				100[i]	65.4	1.0	AIHC/D4	FQ×A×FI×CF/BW

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
TGD	EU Technical Guidance Document (2003)
SCCNFP	The Scientific Committee on Cosmetic Products and Non-food Products Intended for Consumers
SRTC	CTFA-Safety Regulatory Toxicology Subcommittee

References:

[a] U.S. EPA (1997, 2001) (OPP Residential SOPs).

[b] AISE HERA-LAS.

[c] AISE HERA-LAS: based on 5 g product per task divided by 5 L (5,000 cm^3) water = 1 mg/cm^3 = 0.001 g/cm^3.

[d] AISE HERA-LAS: amount of water on dishes after rinsing = 10 percent water left on non-rinsed dish × 5.5×10^{-4} mL/cm^2 = 5.5×10^{-5} mL/cm^2.

[e] SDA data.

[f] Value other than maximum selected, see additional numbered notes below:

1 Selected value is at 95th percentile of range in EFH data.

2 Selected 0.8 g/use value because it is the high end value from SCCNP (2003) and agrees with the 0.86 g/use average value presented in Barnhart (1974).

3 Selected 35% as an upper estimate based on Barnhart (1974).

4 Selected value based on CTFA-SRTC comments and at the 90th percentile of the CTFA (2002) survey data range.

[g] Barnhart (1974).

[h] Based on SRTC comments, April 2003 and CTFA (2002).

[i] No data; assumed 100 percent.

Table II-A-4. Oral Exposure Parameters to Estimate Screening Exposures to Consumer Products—Europe
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Use Conc. [C'] (g/cm^3)	Product Retained [Ta'] (ml/cm^2)	Dish Area Contacting Food [Sa] (cm^2)	Fraction Ingested [FI] (%)	Body Weight[a] [BW] (kg)	Product Exposure (mg/kg-day)	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1,000 mg/g; assumed 100% dermal absorption)
Soaps and Detergents										
Dishwashing liquids – hand wash dishware deposition		5[b]	0.001[c]	5.50E-05[d]	5400[e]		60	0.0050	HERA-LAS	C'×Ta'×CD×CF/BW
Personal Care and Cosmetics										
Toothpaste	3[e]	0.8[f]				35[g,h]	15	56.0	SIAR for Na dodecyl sulfate; SCCNFP (2003)	FQ×A×FI×CF/BW
Mouthwash adult	5[a]	10[a]				8.5[e]	60	70.8	TGD	FQ×A×FI×CF/BW
Lipstick	6[a]	0.01[a]				100[i]	60	1.0	TGD; AIHC/D4 Assessment	FQ×A×FI×CF/BW

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
TGD	EU Technical Guidance Document 2003
SCCNFP	The Scientific Committee on Cosmetic Products and Non-food Products Intended for Consumers

References:

[a] TGD (2003).

[b] AISE HERA-LAS.

[c] AISE HERA-LAS: based on 5 g product per task divided by 5 L (5,000 cm^3) water = 1 mg/cm^3 = 0.001 g/cm^3.

[d] AISE HERA-LAS: amount of water on dishes after rinsing = 10 percent water left on non-rinsed dish × 5.5×10^{-4} mL/cm^2=5.5×10^{-5} mL/cm^2.

[e] SDA data.

[f] SCCNFP: The Safety of Fluorine Compounds in Oral Hygiene Products for Children Under the Age of 6 Years (2003).

[g] Barnhart (1974).

[h] Value other than maximum selected; selected 35 percent as an upper estimate based on Barnhart (1974).

[i] Assumed 100 percent.

Table II-A-5. Inhalation Exposure Parameters to Estimate Screening Exposures to Consumer Products—North America
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Airspace Volume[a] [V] (m^3)	Respirable Product Conc. in Breathing Zone [RPC] (mg/m^3)	Inhalation Rate[b] [IR] (m^3/hr)	Exposure Duration [ED] (hr)	Respirable Fraction [RF] (%)	Bioavailable Fraction [BA] (%)	Body Weight[c] [BW] (kg)	Product Exposure	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1, 000 mg/g; assumed 100 percent dermal absorption)
Soaps and Detergents												
Laundry detergent – powder	1[d]	2.70E-07[e]					100[d]		65.4	4.50E-09	HERA LAS	FQ×A×F×CF/BW
Triggers – spray cleaners	1[d]			0.72[f]	1.0	0.25[b, g1]		100[d]	65.4	0.0032	CSPA	FQ×RPC×IR×ED×BA/BW
Personal Care and Cosmetics												
Hair spray (aerosol)	2[g2, h]	5.33[g2, h]	2		1.0	0.25[a]	50[d]		65.4	8.88	AIHC exposure initiative: DME	FQ×A×IR×ED×F×CF/V×BW
Hair spray (pump)	2[g2, h]	7.81[g2, h]	2		1.0	0.25[a]	50[d]		65.4	13.0	AIHC exposure initiative: DME	FQ×A×IR×ED×F×CF/V×BW
Antiperspirants – aerosols	2[i]	2.2[d]	2		1.0	0.78[i]	25[j]		65.4	5.7	AIHC/D4 assessment	FQ×A×IR×ED×F×CF/V×BW
Fine fragrances	1.67[g3, h]	0.68[g2, h]	2		1.0	0.78[i]	50[d]		65.4	2.95	AIHC/D4 assessment	FQ×A×IR×ED×F×CF/V×BW
Miscellaneous Products												
Paints	0.0116[b, g4]	206.6[b, g4]	2		1.0	1.52[b, g4]	1[k]		65.4	0.24	SDA; assumes exposure to 1 percent of spray	FQ×A×IR×ED×F×CF/V×BW

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997).
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
SRTC	CTFA-Safety Regulatory Toxicology Subcommittee
TGD	EU Technical Guidance Document (003)

References:

[a] TGD (2003).

[b] U.S. EPA (1997).

[c] U.S. EPA (1997, 2001) (OPP Residential SOPs).

[d] SDA data.

[e] AISE HERA LAS assessment: 0.27 μg dust/scoop × 1 scoop/load.

[f] Battelle (1999).

[g] Value other than maximum selected, see additional numbered notes below:

1 Selected value based on mean estimate of 15 minutes per day, which was based on the sum of EFH estimates for cleaning bathroom sinks/tubs (average 44 hours/year) and cleaning kitchen sinks (average 41 hours/yr)

2 Selected value at the 90th percentile of range

3 Selected CTFA value is in the upper range of EFH data source

4 Selected mean value

[h] CTFA (2002).

[i] D4 assessment.

[j] SRTC Comments on the SDA HPV Exposure Assessment Methodology April 2003.

[k] No available data, SDA.

Table II-A-6. Inhalation Exposure Parameters to Estimate Screening Exposures to Consumer Products—Europe
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Airspace Volume[a] [V] (m^3)	Respirable Product Conc. in Breathing Zone [RPC] (mg/m^3)	Inhalation Rate[a] [IR] (m^3/hr)	Exposure Duration [ED] (hr)	Bioavailable Fraction [BA] (%)	Respirable Fraction [RF] (%)	Body Weight[a] [BW] (kg)	Product Exposure	Model/Equation Reference	Model/Equation Formula (CF refers to conversion factor of 1, 000 mg/g; assumed 100 percent dermal absorption)
Soaps and Detergents												
Laundry detergent-powder	1[b]	2.70E-07[c]						100[b]	60	4.50E-09	HERA LAS	FQ×A×F×CF/BW
Trigger spray cleaners	1[b]			0.72[d]	0.8	0.33[b]	100[b]		60	0.0032	CSPA	FQ×RPC×IR×ED×BA /BW
Personal Care and Cosmetics												
Hair sprays – aerosol	2[e]	5[e]	2		0.8	0.25[a]		50[b]	60	8.33	TGD/D4 assessment	FQ×A×IR×ED×F×CF/V×BW
Antiperspirants – aerosols	3[a]	3[a]	2		0.8	0.78[f]		50[b]	60	23.4	TGD/D4 assessment	FQ×A×IR×ED×F×CF/V×BW
Fragrances												
Fine fragrances	5[a]	1.2[a]	2		0.8	0.78[f]		50[b]	60	15.6	D4 assessment	FQ×A×IR×ED×F×CF/V×BW
Miscellaneous Products												
Paints	0.012[a]	206.6[g,h]	2		0.8	1.52[g,h]		1[i]	60	0.251	No EU data; SDA assumes exposure to 1 percent of spray	FQ×A×IR×ED×F×CF/V×BW

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
COLIPA	European Cosmetic, Toiletry, and Perfumery Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
TGD	EU Technical Guidance Document (2003)

References:

[a] TGD (2003).

[b] SDA data.

[c] AISE HERA LAS assessment: 0.27 μg dust/scoop × 1 scoop/load.

[d] Battelle (1999).

[e] COLIPA (2002).

[f] D4 assessment.

[g] U.S. EPA (1997).

[h] Value other than maximum selected; selected mean value.

[i] No available data.

Appendix II-B

Screening Product Exposure Data Matrix: Minimum-Maximum Values

Appendix II-B
Screening Product Exposure Data Matrix: Minimum-Maximum Values

Appendix II-B presents the range of data input values. The range includes the minimum and maximum values identified in various sources. In some cases, the minimum and maximum values came from two different sources. In these situations, the associated sources are identified in the footnotes. It should be noted that although there are several sources of data for a particular value, only the sources that contain the minimum and maximum are reported in Appendix II-B.

Table II-B-1. Data Ranges (Minimum-Maximum) of Dermal Exposure Parameters to Estimate Screening Exposures to Consumer Products—North America
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A′] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Film Thickness [FT] (cm)[a]	Product Retained [PR] (%)	Percent Transfer [PT] (%)	Dermal Absorption [DA] (%)	Body Weight[b] [BW] (kg)	Scaling: Duration of Exposure [TF]
Soaps and Detergents													
Laundry detergent – Wearing clothes		76–121[c]							0.1–1[c]	1[c]	100	65.4	
Laundry detergent (tablets) – wearing clothes		45–135[d]							0.1–1[c]	1[c]	100	65.4	
Fabric conditioners, rinse added – wearing clothes		56–112[c]							0.1–1[c]	1[c]	100	65.4	
Fabric conditioners, dryer sheets – wearing clothes		3[c]							10.00[c]	1[c]	100	65.4	
Laundry detergent/fabric conditioner handwash	1[c]			0.1–1[c]	0.001–.01[e]	1,680[f]		0.0024			100	65.4	0.007[d]
Laundry detergent pretreatment (powder paste)	1[c]			50–60[d]	0.5–0.6[e]	360[g]		0.0024			100	65.4	0.007[d]
Laundry detergent pretreatment (liquid neat/non-dilutable)	1[c]			100[h]	1.0[e]	360[g]		0.0024			100	65.4	0.003–0.007[d]
Dishwashing liquids-handwash (hands)	0.1–0.14[a]				0.9[a]	1,680[f]		0.0024			100	65.4	0.00035[c]
Dishwashing liquids-handwash (dishes)	1.0[c]–3.0[a]			0.03–0.15[c]	0.0003–0.0015[e]	1,680[f]		0.0024			100	65.4	0.007–0.03[d]
Hard surface cleaner-powder	0.14–1[c]	20–51[c]		0.4–1[i]	0.004–0.01[e]	1,680[f]		0.0024		100[j]	100	65.4	0.007–0.014[d]
APC liquid	0.14–1[c]	41–76[c]		0.8–1.5[i]	0.008–0.015[e]	1,680[f]		0.0024		100[j]	100	65.4	0.007–0.014[d]
APC gel (neat/non-dilutable)	0.14–1[d]			100[h]	1.0[e]	180[k]		0.0024		100[j]	100	65.4	0.007–0.014[d]
APC spray (neat/non-dilutable)	0.14–1[d]			100[h]	1.0[e]	180[k]		0.0024		100[j]	100	65.4	0.0014–0.014[c,d]
Personal Care and Cosmetics													
Shampoos	0.48–1[l]	5–16.4[a,l]							0.5–1[c,m]		100	65.4	
Hair rinses	0.064–1[l]	7–12.7[c,l]							0.5–1[c,m]		100	65.4	
Styling tonic/gel	0.5–1[c]	1.5–5.6[c,m]							0.5–5[c,m]		100	65.4	
Hair sprays – aerosol	1–5.36[n1, o]	0.05–14.08[n1, o]							0.5–5[c,m]		100	65.4	
Hair spray (pump)	1–4.22[n1, o]	0–21.4[n1, o]							0.5–5[c,m]		100	65.4	
F&H liquid soap – hand	5.0–8.0[c]	1.6–1.7[c]							0.5–1[c,j]		100	65.4	
F&H bar soap – hand	1.0–6.0[c]	0.36[c]							0.5–1[c,j]		100	65.4	
Liquid soap – body	0.088–0.57[l]	11.8[l, n2]							0.5–1[c,j]		100	65.4	

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A′] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Film Thickness [FT] (cm)[a]	Product Retained [PR] (%)	Percent Transfer [PT] (%)	Dermal Absorption [DA] (%)	Body Weight[b] [BW] (kg)	Scaling: Duration of Exposure [TF]
F&H bar soap – body	0.95–3[l]	2.6–8.6[c,l]							0.5–1[c,j]		100	65.4	
Cleansing products	0.54–2[l]	1.7[l, n2]							0.5–1[c,j]		100	65.4	
Body wash	1[c]	8.0–12.0[c]							0.5–1[c,j]		100	65.4	
Bath foam/bubble bath	0.14–0.29[p]	14–17[c]							0.5–1[c,j]		100	65.4	
F&H bar soap – face	1.00[c]	0.27[c]							0.5–1[c,j]		100	65.4	
Shave cream	0.3–1[c]	1.0–9.0[j, n3]							1[c]		100	70	
Body moisturizer			0.05–36.3[n1, o]						100[q]		100	65.4	
Antiperspirants – roll-ons	0.8–2.0[l, n4]	0.52–1.22[l,m]							100[q]		100	70	
Antiperspirant aerosols	0.8–2.0[l, n4]	0.52–2.2[c,l]							75[j]		100	65.4	
Antiperspirant solid/bar	0.8–2.0[l, n4]	0.5–1.2[c]							100[q]		100	65.4	
Lipstick	1.0–4.0[l, n5]	0–0.2[n1, o]							100[q]		100	65.4	
Face/eye cosmetics foundation liquid	1.0–2.0[o]	0–2.65[n1, o]							100[q]		100	65.4	
Other – makeup remover	1.0–2.0[p]	2.5[p]							5[r]		100	65.4	
Baby Care Products													
Baby/bath liquid	1[c]	0.873[s]				9,000[c]	0.097[c]		100		100	15	
Baby lotions and creams	0.38–2[l]	1.4–2[j,l]							100[r]		100	15	
Kids shampoos	0.11–0.43[l]	0.5–10[b,l]							0.5–1[c,m]		100	15	
Fragrances													
Fine fragrances	1.0–11.6[l, n5, o]	0.1–5.08[n1, o]							100[q]		100	65.4	
Aftershave	0.66–1[c]	0.65–1[c]							100[q]		100	70	

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
APC	all purpose cleaners
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment, K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
F&H	face and hand
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
SRTC	CTFA-Safety Regulatory Toxicology Subcommittee
TGD	EU Technical Guidance Document (2003)

References:

[a] AIHC alkyldimethylamine oxide assessment.

[b] U.S. EPA (1997, 2001) (OPP Residential SOPs).

[c] SDA data.

[d] AISE/HERA (2002) (Table of Habit and Practices for consumer products in Western Europe) (No NA-specific data identified).

[e] PC (%) was converted to PC (g/cm^3); where (X g product/ 100 g water) x (1 g water/1 cm^3 water).

[f] AIHC alkyldimethylamine oxide assessment: hands and forearms.
[g] EFH: both palms (average female)-- SDA 2/03 resolution.
[h] Non-diluted products use 100 percent product concentration.
[i] PC (%) was calculated by assuming product will be diluted in 5 L of water; PC (%) = (X g/use) / (5 L/use) × (1,000 g/L).
[j] Based on CTFA-SRTC comments on SDA Exposure Assessment Methodology April 2003.
[k] EFH & SDA 2/03 and 4/03 resolutions -- one palm average females.
[l] U.S. EPA (1997).
[m] AIHC/K.S. Crump Group, 1999 (D4 assessment).
[n] Value other than maximum selected; see additional numbered notes below:

1 Selected 90th percentile from data range.
2 Full data range not provided; only averages were available.
3 Selected reasonable average value as recommended by CTFA-SRTC.
4 Selected reasonable value based on outcome of discussions among SDA member companies.
5 Selected value based on CTFA-STRC comment and at the 90th percentile of the CTFA 2002 survey data range.
6 Selected average value from CTFA 2002 which is in the upper range of data provided in U.S. EPA (1997).

[o] CTFA (2002).
[p] TGD (2003) (No NA specific data identified).
[q] Leave-on product; assumed 100 percent.
[r] No available data.
[s] Derived based on CA x R/1000.

Table II-B-2: Data Ranges (Minimum-Maximum) of Dermal Exposure Parameters to Estimate Screening Exposures to Consumer Products—Europe
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A′] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Product Retained [PR] (%)	Film Thickness[a] [FT] (cm)	Transfer to Skin[a] [PT] (%)	Dermal Absorption [DA] (%)	Body Weight[b] [BW] (kg)	Scaling: Duration of Exposure [TF]
Soaps and Detergents													
Laundry detergents-indirect: powder		55–290[c]						0.95[d]		10	100	60	
Laundry detergents-indirect: liquid		78–230[c]						0.95[d]		10	100	60	
Laundry detergent-indirect: tablet		45–135[c]						0.95[d]		10	100	60	
Fabric conditioners indirect: liquid regular		50–140[c]						0.95[d]		10	100	60	
Fabric conditioners indirect: liquid concentrate		11.0–90[c]						0.95[d]		10	100	60	
Hand-washing: powder	0.14–2.57[c]			0.1–1[c]	[e]	1,980[f]			0.01		100	60	0.007[c]
Hand-washing: liquid laundry and fabric conditioners	0.26–1.43[c]			0.1–1[c]	[e]	1,980[f]			0.01		100	60	0.007[c]
Pretreatment (powder paste)	1.00[g]			50–60[c]	[e]	840[b]			0.01		100	60	0.007[c]
Pretreatment (liquid neat)	1.00[g]			100[h]	[e]	840[b]			0.01		100	60	0.007[c]
Dishwashing liquids-hand wash (hands)	0.14[i]				0.9[i]	1,680[i]			0.01		100	60	0.00035[g]
Dishwashing liquids-hand wash (dishes)	0.43–3.0[c]	3.0–28[b,c]		0.1–0.9[j]	0.001–0.009[e]	1,980[f]			0.01		100	60	0.007–0.03[c]
APC liquid	0.14–1[c]	30–110[c]		[k]	[e]	1,980[f]			0.01		100	60	0.007–0.014[c]
APC powder	0.14–1[c]	20–40[c]		[k]	[e]	1,980[f]			0.01		100	60	0.007–0.014[c]
APC spray (neat) diluted	0.14–1[c]	5.0–30[c]		[k]	[e]	1,980[f]			0.01		100	60	0.0014–0.007[c]
APC gel (neat) diluted	0.14–1[c]	20–40[c]		[k]	[e]	1,980[f]			0.01		100	60	0.007–0.014[c]
APC spray (neat) undiluted	0.14–1[c]			100[h]	1[e]	1,980[f]			0.01		100	60	0.0014–0.007[c]
APC gel (neat) undiluted	0.14–1[c]			100[h]	1[e]	1,980[f]			0.01		100	60	0.007–0.014[c]
Personal Care and Cosmetics													
Shampoos	0.29–1[b,l]	8.0–12[b,l,m]						0.5–1[g,i]			100	60	
Hair conditioners	0.14–0.29[b]	14[b]						0.5–1[g,i]			100	60	
Styling mousse	1.0–2.0[b]	4.0–5.0[b,g]						0.5–5[g,i]			100	60	
Hair sprays – aerosol	2[l]	5[l]						0.5–10[g,l]			100	60	
F&H liquid soap – hand	5.0–7.0[g]	1.6[g]						0.5[g]			100	60	
F&H bar soap – hand (toilet soap)	6[l]	0.8[l]						10.0[l]			100	60	
Liquid soap-body (shower gel)	1.07[l]	5[l]						10.0[l]			100	60	
F&H bar soap – body	1[g]	5.0–10[g]						0.5[g]			100	60	

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Product Amount Used per Day [A'] (g/day)	Product Use Conc. (%)	Product Use Conc. [PC] (g/cm^3)	Contact Area [CA] (cm^2)	Product Retained [R] (mg/cm^2)	Product Retained [PR] (%)	Film Thickness[a] [FT] (cm)	Transfer to Skin[a] [PT] (%)	Dermal Absorption [DA] (%)	Body Weight[b] [BW] (kg)	Scaling: Duration of Exposure [TF]
F &H bar soap – face	1[g]	0.27[g]						0.5[g]			100	60	
Body wash	1[g]	9.2[g]						0.5[g]			100	60	
Bath foam/bubble bath	0.14–0.29[b]	14–17[g]						0.5[g]			100	60	
Shaving lubricant	1[b]	2[b]						1[g]			100	70	
Skin lotions and creams (body lotion)	0.71–2[b,l,m]	7.5–8[b,l]						100[l]			100	60	
Hand moisturizer	1.0–7.0[g]	0.5–0.8[g]						100[n]			100	60	
Fragrance cream (including makeup and foundation)	0.29[l]	5[l]						100[l]			100	60	
Facial moisturizer	1.0–2.0[g,l]	0.8[l]						100[l]			100	60	
Antiperspirants – aerosols	1.0–3.0[b]	0.5–3.0[b,g]						100[n]			100	60	
Antiperspirant – roll-ons	1[l]	0.5–1.0[g,l,m]						100[l]			100	60	
Antiperspirant – solid/bar	1[l]	0.5–1.0[g,l,m]						100[l]			100	60	
Lipstick	2.0–6.0[b]	0.01[b]						100[n]			100	60	
Face/eye cosmetics	0.5–3[b]	0.005–0.025[b]						100[n]			100	60	
Other – makeup remover	1.0–2.0[b]	0.5–2.5[b]						5[o]			100	60	
Baby Care Products													
Baby shampoo			5[g]					1[i]			100	15	
Baby/bath liquid	1[g]	0.873[p]				9,000[g]	0.097[g]				100	15	
Baby lotions and creams	0.38–2[q]	1.4–2[q,r]						100[n]			100	15	
Skin wipes													
Fragrances													
Fine fragrances – pour form	0.66–5[g]	0.1–1.2[g]						100[n]			100	60	
Aftershave	0.66–1[g]	0.65–1[g]						100[n]			100	70	
Eau de toilette (including perfume and aftershave)	1[l]	0.75[l]						100[l]			100	60	

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
APC	all purpose cleaners
COLIPA	European Cosmetic, Toiletry, and Perfumery Association
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment, K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
F&H	face and hand
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
TGD	EU Technical Guidance Document (2003)

References:

[a] AISE HERA RA sodium aluminum silicate.

[b] TGD (2003).

[c] AISE HERA Habits and Practices (developed by AISE within the HERA project in 2002).

[d] AISE HERA RA sodium aluminum silicate where PR = (PD × FD1) / WI × CA; product deposition (5%); FD1 = fabric density (10 mg/cm^2); WI = total wash weight (1 kg); CA = body contact area (cm^2).

[e] PC (%) was converted to PC (g/cm^3); where (X g product /100 g water) × (1 g water / 1 cm^3 water).

[f] AISE HERA fluorescent brightener FWA-5.

[g] SDA data.

[h] Non-diluted products use 100 percent product concentration.

[i] AIHC/D4, K.S. Crump Group (1999).

[j] SIAR triethanolamine: dilute in 3,000 cm^3 water.

[k] AISE HERA Habits and Practices (diluted in 5 L of water).

[l] COLIPA (2002).

[m] Value other than maximum selected; selected value based on COLIPA (2002) data.

[n] Leave on product; assumed 100 percent.

[o] No available data.

[p] Derived based on CA × R/1000 (recommended by SDA-HPV consortium for consistency with adult dermal scenarios at Feb 2003 meeting).

[q] U.S. EPA (1997) (no EU-specific data).

[r] Based on SRTC comments on SDA Exposure Assessment Methodology April 2003 (no EU-specific data).

Table II-B-3. Data Ranges (Minimum-Maximum) of Oral Exposure Parameters to Estimate Screening Exposures to Consumer Products—North America
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used Per Use [A] (g/use)	Product Use Conc. [C] (g/cm^3)	Product Retained [Ta′] (mL/cm^2)	Dish Area Contacting Food [Sa] (cm^2)	Fraction Ingested [FI} (%)	Body Weight[a] [BW] (kg)
Soaps and Detergents							
Dishwashing liquids – hand wash (dishware deposition)		2.0–5.0[b]	0.0004–0.001[c]	5.50E-05[d]	697–5,400[e]		65.4
Personal Care and Cosmetics							
Toothpaste	0.67–4.0[f, g1]	0.05–2.4[e, g2, h]				3–40[e, g3, h]	15
Mouthwash (adult)	0.4–2[e]	30[e]				8.5[e]	65.4
Lipstick	1.0–4.0[f, g4]	0–0.2[g5, i]				100[j]	65.4

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
TGD	EU Technical Guidance Document (2003)
SCCNFP	The Scientific Committee on Cosmetic Products and Non-food Products Intended for Consumers
SRTC	CTFA-Safety Regulatory Toxicology Subcommittee

References:

[a] U.S. EPA (1997, 2001) (OPP Residential SOPs).
[b] AISE HERA-LAS.
[c] AISE HERA-LAS: product amount per use divided by 5 L (5,000 cm^3) water.
[d] AISE HERA-LAS: amount of water on dishes after rinsing = 10 percent water left on non-rinsed dish $\times$ 5.5×10^{-4} mL/cm^2=$5.5\times10^{-5}$$ml/cm^2$.
[e] SDA data.
[f] U.S. EPA (1997).
[g] Selected value other than maximum; see additional notes below:

1 Selected value at the 95th percentile of range
2 Selected 0.8 g/use value because it is the high end value from SCCNP and agrees with the 0.86 g/use (average) value presented in Barnhart (1974).
3 Selected 35% as an upper estimate based on Barnhart, 1974
4 Selected value based on CTFA-SRTC comments and at the 90th percentile of CTFA 2002 survey data range
5 Selected value at the 90th percentile of range

[h] SCCNFP: The Safety of Fluorine Compounds in Oral Hygiene Products for Children Under the Age of 6 Years (2003).
[i] Based on CTFA-SRTC comments and CTFA (2002) survey data.
[j] No data; assumed 100 percent.

Table II-B-4: Data Ranges (Minimum-Maximum) of Oral Exposure Parameters to Estimate Screening Exposures to Consumer Products–Europe
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used Per Use [A] (g/use)	Product Use Conc. [C′] (g/cm^3)	Product Retained [Ta′] (mL/cm^2)	Dish Area Contacting Food [Sa] (cm^2)	Fraction Ingested [FI] (%)	Body Weight[a] [BW] (kg)
Soaps and Detergents							
Dishwashing liquids – hand wash (dishware deposition)		2.0–5.0[b]	0.0004–0.001[c]	5.50E-05[d]	697–5,400[e]		60
Personal Care and Cosmetics							
Toothpaste	1.0–3.0[a,e]	0.05–0.8[f]				3–40[e,f,g]	15
Mouthwash adult	1.0–5.0[a]	10[a]				8.5[e]	60
Lipstick	2.0–6.0[a]	0.01[a]				100[h]	60

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
TGD	EU Technical Guidance Document (2003)
SCCNFP	The Scientific Committee on Cosmetic Products and Non-food Products Intended for Consumers

References:

[a] TGD (2003).

[b] AISE HERA-LAS.

[c] AISE HERA-LAS: product amount per use divided by 5 L (5,000 cm^3) water.

[d] AISE HERA-LAS: amount of water on dishes after rinsing = 10 percent water left on non-rinsed dish $\times$ 5.5×10^{-4} mL/cm^2 = 5.5×10^{-5} mL/cm^2.

[e] SDA data.

[f] SCCNFP: The Safety of Fluorine Compounds in Oral Hygiene Products for Children Under the Age of 6 Years (2003).

[g] Selected value other than maximum; selected 35% as an upper estimate based on Barnhart (1974).

[h] Assume 100 percent.

Table II-B-5. Data Ranges (Minimum-Maximum) of Inhalation Exposure Parameters to Estimate Screening Exposures to Consumer Products—North America
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Airspace Volume[a] [V] (m^3)	Respirable Product Conc. in Breathing Zone [RPC] (mg/m^3)	Inhalation Rate[b] [IR] (m^3/hr)	Exposure Duration [ED] (hr)	Respirable Fraction [F] (%)	Bioavailable Fraction [BA] (%)	Body Weight[c] [BW] (kg)
Soaps and Detergents									
Laundry detergent – powder	1[d]	2.7E-07[e]					100[d]		65.4
Triggers spray cleaners	0.14–1[d,f]			0.13–0.72[g]	1.0	0.03–0.33[d,f]		100[d]	65.4
Personal Care and Cosmetics									
Hair spray (aerosol)	1–5.36[h, i1]	0.05–14.08[h, i1]	2		1.0	0.25[a]	50[d]		65.4
Hair spray (pump)	1–4.22[h, i1]	0–21.4[h, i1]	2		1.0	0.25[a]	50[d]		65.4
Antiperspirants – aerosols	0.8–2[b,j]	0.52–2.2[b,d]	2		1.0	0.78[j]	25[k]		65.4
Fine fragrances	1–11.6[b,f, i2]	0.1–5.08[h, i1]	2		1.0	0.78[j]	50[d]		65.4
Miscellaneous Products									
Paints	0.003–1[b, i3]	0.13–1,612[b, i3]	2		1.0	0.0003–5[b, i3]	1[l]		65.4

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
CTFA	Cosmetic, Toiletry and Fragrance Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment, K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments (subcommittee within AISE)
SRTC	CTFA's toxicology subcommittee
TGD	EU Technical Guidance Document (2003)

References:

[a] TGD (2003).

[b] U.S. EPA (1997).

[c] U.S. EPA (1997, 2001) (OPP Residential SOPs)

[d] SDA data.

[e] AISE HERA LAS assessment: 0.27 μg dust/scoop $\times$ 1 scoop/load.

[f] Table of Habit and Practices for consumer products in Western Europe, Developed by AISE within the HERA project in 2002.

[g] Battelle (1999).

[h] CTFA (2002).

[i] Selected value other than maximum; see additional notes below:
1 Selected value at the 90th percentile of range
2 Selected CTFA value is in the upper range of EFH data source
3 Selected mean value.

[j] D4 assessment.

[k] SRTC Comments on the SDA HPV Exposure Assessment Methodology April 2003.

[l] No available data.

Table II-B-6. Data Ranges (Minimum-Maximum) of Inhalation Exposure Parameters to Estimate Screening Exposures to Consumer Products—Europe
(References, abbreviations and special notes are described in footnotes at end of table)

	Product Use Frequency [FQ] (use/day)	Product Amount Used per Use [A] (g/use)	Airspace Volume[a] [V] (m^3)	Respirable Product Conc. in Breathing Zone [RPC] (mg/m^3)	Inhalation Rate[a] [IR] (m^3/hr)	Exposure Duration [ED] (hr)	Bioavailable Fraction [BA] (%)	Respirable Fraction [F] (%)	Body Weight[a] [BW] (kg)
Soaps and Detergents									
Laundry detergent – powder	1[b]	2.7E-07[c]						100[b]	60
Trigger spray cleaners	0.14–1[b,d]			0.13–0.72[e]	0.8	0.03–0.33[b,d]	100[b]		60
Personal Care and Cosmetics									
Hair sprays – aerosol	2[f]	5[f]	2		0.8	0.25[a]		50[b]	60
Antiperspirants – aerosols	1.0–3.0[a]	0.5–3[a,b]	2		0.8	0.78[g]		50[b]	60
Fragrances									
Fine fragrances	0.66–5[a,b]	0.1–1.2[a,b]	2		0.8	0.78[g]		50[b]	60
Miscellaneous Products									
Paints	0.012[a]	0.13–1,612[h,i]	2		0.8	0.0003–5[h,i]		1[j]	60

Abbreviations:

AIHC	American Industrial Health Council
AISE	International Association for Soaps, Detergents and Maintenance Products
COLIPA	European Cosmetic, Toiletry, and Perfumery Association
D4	Octamethylcyclotetrasiloxane Exposure Assessment prepared by K.S. Crump Group (1999)
EFH	EPA's exposure factors handbook (U.S. EPA 1997)
EPA	U.S. Environmental Protection Agency
HERA	Human & Environmental Risk Assessments
TGD	EU Technical Guidance Document (2003)

References:

[a] TGD (2003).

[b] SDA data.

[c] AISE HERA LAS assessment; 0.27 μg dust/scoop $\times$ 1 scoop/load.

[d] Table of Habit and Practices for consumer products in Western Europe, Developed by AISE within the HERA project in 2002.

[e] Battelle (1999).

[f] COLIPA (2002).

[g] D4 assessment.

[h] U.S. EPA (1997).

[i] Selected value other than maximum; selected mean value.

[j] No available data.

Appendix III

Comparison of E-FAST and EUSES Exposure Assessments

Appendix III. Comparison of E-FAST and EUSES Exposure Assessments

Because many chemicals are used globally, it is important to understand the differences between assessments conducted for a given geography and assessments conducted in other geographies. Industry experiences over the last few years for chemicals that have been assessed in both the U.S. and European Union (EU) have suggested that there are substantial differences in the resulting exposures and risk assessments conducted in these two regions. Because these are the two major regions where exposure and risk assessment work is more fully developed and these regions have standard assessment methods and models, it is important to understand the bases for these differences and their relative magnitudes.

Approach for Comparing E-FAST and EUSES

To start to address these questions, exposure and risk assessments for a hypothetical HPV chemical were conducted using the default scenarios in EUSES 2.0 for the cleaning/washing agents scenario (i.e., EU assessment approach) and E-FAST with the down-the-drain scenario (i.e., U.S. assessment approach). To minimize differences between the assessments, a common set of physical, chemical, degradation, and toxicity data was used to represent the chemical and per capita use of the chemical, normalized between the geographies. A chemical was assumed low to moderately sorptive (log K_{ow} = 1.69) and readily biodegradable based on standard OECD tests, which is typical of most of the SDA-sponsored HPV chemicals. Therefore, any differences in the exposure values and risk assessment outcome would be as a result of differences in either environmental infrastructure characteristics or inherent assumptions and default values in the assessment approach.

Two comparisons are made of the resulting exposure estimates. First, the local exposure estimates (i.e., the EUSES local exposure concentration and the E-FAST 10th percentile exposure concentration) were compared. Because the local exposure concentration reported in EUSES includes addition of the regional exposure concentration, the comparison was done both with the regional exposure and without it. Second, the regional exposure estimates (i.e., the EUSES regional exposure concentration and the E-FAST 50th percentile exposure concentration) were compared. These exposure predictions are not strictly equivalent, but because they are the standard output of the assessment approaches, assessors would logically compare them.

For the risk assessment comparison, the assessment factors that allow for extrapolation from acute toxicity data to the predicted no-effect concentration (PNEC) for the chemical were compared.

Conclusions

This analysis, although limited to one chemical, illustrates that there are indeed differences in the resulting exposure and risk assessments using the standard EUSES cleaning/washing agents scenario and the E-FAST down-the-drain scenario. In fact, these results (Table 1) show that the EU exposure and risk assessments based on the local scenario will be approximately 1 to 2 orders of magnitude more conservative than the corresponding local scenario for the U.S. Furthermore, most of the differences (Tables 2 and 3) are not the result of environmental and infrastructure differences but rather of inherent assumptions and defaults in the exposure and risk assessment approaches. For example, for the local exposure concentration predictions, it is differences in the assessment approach (i.e., the extra loading factor for per capita use in the EU, and the defaults for half-lives of readily biodegradable chemicals in wastewater treatment plant models) that drive the exposure differences. In addition, the EU assumes that on a regional scale 30 percent of the wastewater is untreated before discharge. This 30 percent is related to the lack of penetration of treatment plant infrastructure within the EU.

The risk assessment involves the comparison of exposure to the predicted no-effect concentration (PNEC) for the aquatic ecosystem. Because the HPV chemical data set (i.e., the SIDS data set) is limited to acute aquatic toxicity data, differences in the extrapolation of these acute data to the PNEC affect the results of the risk assessment. The EU approach uses a factor of 1,000 to extrapolate from acute toxicity data to PNEC, whereas the U.S. EPA approach uses a factor of 100. Therefore, the PNEC using the same data will be a factor of 10 lower in the EU risk assessment than in the U.S. EPA assessment.

Consequences to HPV Chemical Assessments and Next Steps

The resulting differences between the exposure and risk assessment approaches used in the EU and U.S. illustrate that it is possible that a chemical that is determined to be “safe” using the U.S. assessment approach (i.e., E-FAST and U.S. extrapolation factors) might not be deemed acceptable using the EU approach. Furthermore, the differences are primarily the result of choices made in the EU to incorporate extra precaution into their assessments. Many HPV chemicals will require additional data beyond the SIDS data set to reach similar exposure and risk assessment results. These data are 1) chronic toxicity data, and 2) wastewater treatment plant removal data (laboratory-simulated or directly collected).

Table 1: Comparison of the predicted exposure concentrations from EUSES and E-FAST

Scenario	EUSES 2.0	E-FAST	EUSES/E-FAST ratio
Local	437 µg/L (388 µg/L without regional contribution)	46.9 µg/L	9 (8 without regional contribution)
Regional	48.4 µg/L	2.8 µg/L	17

Table 2: Contributions of various factors influencing local exposure prediction

	Factor	EUSES	E-FAST	EUSES/ E-FAST ratio
Environmental and Infrastructure Differences	Wastewater Volume	200 L/capita/day	364 L/capita/day	0.55
	Dilution Factor in Surface Water	10	3.86	2.6
Assessment Scheme Differences	Wastewater Treatment Plant Removal[1]	87 percent	94 percent	2.2[2]
	Local Loading of Chemical[3]	8	1	8
	Untreated Discharge	Contribution of regional background		1.1

[1] Some of this variation is because of different models but mostly the variation is a result of different default half-lives used in these models for readily biodegradable substances.
[2] Ratios of 13 percent (EUSES) and 6 percent (E-FAST) released.
[3] EUSES assumes that 10 percent of EU detergent usage for 5.4 percent of population and adds an additional local factor of 4 times the average per capita use/release, whereas E-FAST uses average per capita use of chemical.

Table 3: Contributions of various factors influencing regional exposure prediction

	Factor	EUSES	E-FAST	Ratio of Percent Remaining After Treatment[1]
Environmental and Infrastructure Differences	Wastewater Volume	200 L/capita/day	364 L/capita/day	
	Untreated Discharge[2]	70 percent of wastewater is treated	100 percent of wastewater is treated	6.5
Assessment Scheme Differences	Wastewater Treatment Plant Removal	87 percent	97 percent	2.2
	Multi-Media vs. Dilution Factor Approach[3]	multi-media model	dilution factor = 49	1.5

[1] Ratios in this column represent the PEC from EUSES divided by the PEC from EFAST. To isolate the contribution of each factor (e.g., removal, dilution), all common model parameters were set to the same value.
[2] The ratio actually represents the ratio of the percent remaining after discharge and thus incorporates both the percent of untreated discharge and the differences in wastewater treatment plant removal. The untreated discharge scenario in EUSES results in 39 percent discharge of chemical or effective removal of 61 percent removal.
[3] There is a difference in concentrations that cannot be otherwise accounted for and therefore is assumed to be a result of the multi-media modeling versus dilution factor approaches.

Appendix IV

Case Studies

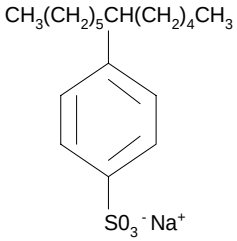
Appendix IV. Case Studies

The OECD has adopted "formats" (or templates) for reporting use and exposure information for the HPV chemicals initiative. The OECD exposure information template provides a standardized way to summarize and present exposure data in much the same way as the OECD IUCLID template provides a standardized and accepted way to summarize and present physicochemical, environmental fate, and toxicological data for HPV chemicals. The template is presented as chapters covering general information, exposure modeling, and exposure monitoring.

SDA, APAG, and CESIO participated in the OECD Use/Exposure Pilot Project. As part of this initiative, the OECD draft template procedure was applied to the linear alkylbenzene sulfonate (LAS) and hydrotrope chemical groups for U.S. use and exposure scenarios. LAS chemicals are surfactants, used as the primary cleaning agent in a variety of laundry and cleaning products. The production volume and uses in laundry and cleaning products are evaluated in the LAS case study. Hydrotropes are used as coupling agents to solubilize water insolubles and incompatible functional ingredients. Virtually all of the hydrotrope production volume is used in personal care and cleaning products. The production volume and uses in both cleaning and personal care products are considered in the hydrotropes case study. As another case study, the data availability and screening-level assessment for triclocarban (TCC), prepared for the HPV Use/Exposure Pilot Project, is also provided in this appendix. TCC is used in personal cleansing products as an antimicrobial ingredient. Worker and consumer exposure to TCC from these uses are considered in this case study.

While the OECD reporting formats would be comparable, some additional effort would be required to provide relevant use and exposure estimates for other geographies (e.g., Europe or Japan) taking into account their production volumes, local habits and practices, and exposure models. Through the case studies, the following sections describe the elements of the OECD reporting template and provide examples of the type of information expected, models used, and results produced for an environmental and consumer exposure assessment.

CASE STUDY: LINEAR ALKYLBENZENE SULFONATE (LAS)
January 24, 2005
SIDS INITIAL ASSESSMENT PROFILE

CAS No.s	1322-98-1 Decylbenzene sulfonic acid, sodium salt 25155-30-0 Dodecylbenzene sulfonic acid, sodium salt 26248-24-8 Tridecylbenzene sulfonic acid, sodium salt 27636-75-5 Undecylbenzene sulfonic acid, sodium salt 68081-81-2 C_{10-16} Monoalkylbenzene sulfonic acid, sodium salt 68411-30-3 C_{10-13} Alkylbenzene sulfonic acid, sodium salt 69669-44-9 C_{10-14} Alkyl deriv benzene sulfonic acid, sodium salt 85117-50-6 C_{10-14} Monoalkylbenzene sulfonic acid, sodium salt 90194-45-9 C_{10-13} Alkyl deriv benzene sulfonic acid, sodium salt 127184-52-5 4-C_{10-13}-sec Alkyl deriv. benzene sulfonic acid, sodium salt
CHEMICAL NAME	Linear Alkylbenzene Sulfonate (LAS)
STRUCTURAL FORMULA	This structure of a C_{12}-LAS is representative of the category. 

SUMMARY CONCLUSIONS OF THE SIAR

Category Identification/ Justification - Agreed at SIAM 17

The LAS molecule contains an aromatic ring sulfonated at the *para* position and attached to a linear alkyl chain at any position except the terminal carbons. The alkyl carbon chain typically has 10 to 14 carbon atoms and the linearity of the alkyl chains ranges from 87 to 98%. While commercial LAS consists of more than 20 individual components, the ratio of the various homologs and isomers, representing different alkyl chain lengths and aromatic ring positions along the linear alkyl chain, is relatively constant in currently produced products, with the weighted average carbon number of the alkyl chain based on production volume per region between 11.7-11.8. LAS are supported as a category because of the close consistency of the mixtures, their commercial uses, fate, and health and environmental effects. LAS is the primary cleaning agent used in many laundry detergents and cleaners at concentrations up to 25 percent in consumer products, and up to 30 percent in commercial products, with the exception of one reported product at 45% percent in concentrated solid form that is mechanically dispensed into diluted solution for dishwashing.

Human Health - Agreed at SIAM 17

Substantial data exist for mammalian toxicity. The available data indicate that LAS exhibits slight acute toxicity. Oral LD_{50} values for rats range from 1,080 to 1,980 mg/kg bw. Oral LD_{50} values for mice are 2,160 and 2,250 mg/kg bw for males and females, respectively. The rat dermal LD_{50} value was greater than 2,000 mg/kg bw. The oral and dermal acute toxicity data for LAS generally indicate low hazard potential when all studies are considered together. Acute inhalation toxicity data indicate that LAS is moderately toxic, with mortality occurring at respirable particle concentrations of 310 mg/m^3 (MMAD = 2.5 microns).

In a series of studies on rabbits, LAS was not irritating to the skin or eyes at low concentrations (0.5–2.5%), moderately irritating at 5%, and more severely irritating at higher (about 50%) concentrations. In studies that

included rinsing, eye irritation effects diminished with rinsing after 30 seconds of exposure and were slight with rinsing after 4 seconds of exposure. In a low volume eye test (LVET) using a 35% LAS solution, rabbits experienced moderate irritation that was completely reversible by day 35. (Note that the maximum concentration of LAS is 25 percent in consumer products and normally less than 30 percent in commercial products.) Accidental eye exposure in 231 manufacturing employee incidents and 284 consumer incidents established that eye irritation effects of exposure during manufacturing and use of products containing LAS and other surfactants are moderate, transient and reversible.

In 15 repeated dose studies, with rats, mice, and monkeys exposed to LAS via oral and dermal routes, LOAELs ranged from 115 to 750 mg/kg bw/day. The corresponding NOAELs ranged from 40 to 250 mg/kg bw/day. Effects commonly observed included suppressed body weight gain, diarrhea, increases in relative liver weight, differences in enzymatic and serum-biochemical parameters, and mild degeneration and desquamation of the tubular epithelium in the kidneys.

In four well designed *in vitro* bacterial (*Salmonella*) mutagenicity studies, LAS shows no evidence of mutagenicity either with or without S9 metabolic activation. LAS showed no evidence of causing increased cell transformation in an *in vitro* cell transformation assay. In *in vivo* studies, no significant differences in chromosome aberrations were seen when mice were given either oral doses up to 800 mg/kg bw/day or dietary doses up to 1170 mg/kg bw/day. In a mouse micronucleus study, LAS did not induce a clastogenic effect. Rats given dietary doses up to 450 mg/kg bw/day also showed no significant differences in chromosome aberrations. Collectively, these data support that LAS is not genotoxic.

The highest dose tested in four carcinogenicity studies with rats was 300 mg/kg bw/day. In the most documented study, rats were administered up to 250 mg LAS/kg body weight/day in the diet for two years. Results of this study indicate no gross or histopathological evidence of a carcinogenic effect. No evidence of tumorigenesis was observed in any of the carcinogenicity studies. While the quality and focus of the studies precludes a definitive assessment, the results of the genetic toxicology and rodent bioassay studies collectively provide strong weight-of-evidence support that LAS is not genotoxic and is not a rodent carcinogen.

Similarly, no evidence of reproductive or fertility effects was observed in any of the three available reproductive toxicity studies in which rats were given dietary doses over three to four generations. NOAELs from these reproductive studies ranged from 70 to 350 mg/kg bw/day, which were the highest doses tested. In 17 developmental toxicity studies, effects such as embryo death or deformities, and litter loss were most often observed only at maternally toxic doses and were associated with the irritation effects of LAS on skin or the gastrointestinal tract. No decreases in litter size, no changes in litter parameters, no malformations or significant differences in skeletal defects were observed at oral doses up to 780 mg/kg bw/day in rats and at dermal doses of 500 mg/kg bw/day in mice and 90 mg/kg bw/day in rabbits.

All of the studies included in the dossier are considered reliable, but all with limitations. The results are consistent with each other and these data are used in a weight-of-evidence approach. Based on these considerations, the highest NOAEL value below the lowest LOAEL from all of the mammalian toxicity studies is the most appropriate. Therefore, the NOAEL is 85 mg/kg bw/day. This value comes from a rat drinking water, 9-month repeated dose toxicity study. The lowest LOAEL (115 mg/kg/day) was associated with increased weight of the cecum and slight degeneration of the renal tubules.

Environment – To be discussed at SIAM 20

Pure LAS is a solid at ambient temperatures with a melting point of 198.5°C. The boiling point for LAS could not be determined experimentally due to decomposition beginning at 444°C. LAS has a low vapor pressure (3-5 x 10^{-13} Pa). LAS is water soluble, with a critical micelle concentration (CMC) value of 0.1 g/L

and forms a clear solution in water at concentrations up to 250 g/L. Although it is impossible to accurately measure an octanol-water partition coefficient for surface-active agents like LAS, an octanol-water partition coefficient of log 3.32 has been calculated for $C_{11.6}$ LAS. Based on two Fugacity III modeling studies, LAS transport between environmental compartments is primarily determined by inputs to the various compartments, biodegradation rates in water and soil, and water-sediment transfer. LAS does not undergo significant degradation by abiotic mechanisms under environmentally relevant conditions as photolyzable and hydrolyzable groups are absent from the chemical structure.

An extensive database of studies demonstrates rapid and complete biodegradation of LAS under aerobic conditions, including soil and the aqueous environment. In several tests, LAS has been shown to be readily biodegradable, and has passed the 10-day biodegradation window in mineralization tests. LAS are effectively removed in biological wastewater treatment (from 77-82% for trickling filters up to 99%+ for activated sludge). The biodegradation kinetics of the longer alkyl chain lengths are generally faster, and their sorption coefficients larger. The primary degradation intermediates are sulfophenyl carboxylates (SPCs), which further degrade to CO_2, SO_4^{2-}, and water. LAS does not generally degrade under anaerobic conditions. The bioconcentration factor decreases with decreasing average alkyl chain lengths (from almost 1000 for 2-phenyl-C_{13} LAS to 2 for 6-phenyl-C_{10} LAS). The BCF for currently produced $C_{11.6}$ LAS is 87, with rapid clearance and was 22 for filtered Mississippi River water (average alkyl chain length of surface water fingerprint = $C_{10.8}$).

Ecotoxicity data are extensively available for LAS, with several comprehensive reviews having been completed. The lowest reliable acute LC_{50}/EC_{50}/ErC_{50} values based on a review of the aquatic toxicity data on commercially representative LAS ($C_{11.6}$-$C_{11.8}$) were 1.67, 1.62 and 29.0 mg/L for fish, *Daphnia magna*, and algae, respectively. Acute toxicity is greater for individual LAS homologues with longer alkyl chain lengths. LAS biodegradation intermediates are significantly less toxic than the parent LAS with LC_{50} values >1,000 mg/L for fish and *D. magna*. Chronic single species aquatic toxicity data have been evaluated for five freshwater species in which multiple studies were reported and nine freshwater species for which single studies were reported. Available NOEC values range from 0.25 to 3.4 mg/L for freshwater species. Geometric mean NOEC values for marine species ranged from 0.025 to 5.0 mg/L. Based on the model ecosystem studies, a NOEC of 0.27 mg/L (0.37 if normalized to C11.6 LAS) was determined for the freshwater ecosystem. This value is based on model stream ecosystem studies of over 250 species, and is consistent with the single species chronic freshwater data, and the resultant HC_5 values (0.36-0.43 mg/L for $C_{11.6}$ LAS).

NOEC values for sediment exposures were greater than or equal to 81 mg/kg dry matter. Field studies indicate no adverse effects of LAS in sludge-amended soil from LAS levels of 15 mg/kg dry matter in the soil or 31,300 mg/kg dry matter in sludge.

Exposure

Agreed at SIAM 17:
Current LAS production is approximately 390,000 metric tons in the North America, 400,000 metric tons in Europe, and 85,000 metric tons in Japan. Global production was 2.6 million metric tons in 1995. In the production phase, manufacturing processes have been designed to maximize production yield and minimize potential releases. Worker exposure is possible during the detergent formulation stage by inhalation of powders or dermal contact of powders and liquids. Good manufacturing design practices (e.g., enclosed production in agglomeration processes, exhaust ventilation, dust collection) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) in place at facilities that manufacture liquid and dry (granular/powder) materials are anticipated to mitigate worker exposure to LAS. Any LAS that is not incorporated into a product is captured by dust-handling equipment for recycling back into the production

process. A limited amount of LAS in aqueous solution may be released as a dilute solution from washing and rinsing operations in the manufacturing process and is discharged to wastewater treatment. Incidental quantities of the dry (granular/powder) product (e.g., from floor sweepings) may be disposed in landfills.

Labeling of consumer products containing LAS and other surfactants include warnings of the potential for eye irritation and first aid instructions to rinse with water.

Data suggests that inhalation of LAS products during use will be low. Spray products containing LAS are designed to produce the large particle sizes needed for efficient delivery of the spray to the surface being cleaned. In laboratory simulations with six spray nozzles representing those used in spray cleaning products, less than 0.1% of the total volume sprayed consists of respirable particles (particles under 10 microns in diameter) and air concentrations in the breathing zone are in the 0.13-0.72 mg/m^3 range. Inhalation of detergent dusts during washing processes, modeled by HERA (2002), was 10-fold lower exposure than inhalation of aerosols from cleaning product sprays. This estimate is based on a published study reporting an average of 0.27 µg dust per cup of product used for machine laundering. This is a conservative (protective) estimate as exposure from modern compact/granular detergent formulations produced in agglomeration processes, which produce larger particle sizes, would be expected to be much less. Based on these data, it is expected that exposures to respirable particles from inhalation are low.

To be discussed at SIAM 20:
Results of extensive environmental monitoring evaluations in the United States indicate that measured surface water concentrations were generally below 50 µg/L for river water samples collected under low dilution (worst case) conditions below treatment plant mixing zones. Values in the 2800 km reach of the Mississippi River from Minneapolis to New Orleans range from non-detect (<0.1 µg/L) to 28 µg/L (362 samples). LAS river water concentrations similar to those in the US were observed in monitoring studies conducted in Europe and Japan.

Measured LAS concentrations in river sediments were generally less than 1-2 mg/kg dry weight. Mississippi River sediments were <1 mg/kg dry matter with one exception. LAS levels in sediments of the receiving waters of the Tiber River (Italy) were 1.8 mg/kg dry matter. Higher LAS concentrations have been observed near untreated or poorly treated wastewater discharges, e.g. LAS in sediments of a small river (Rapid Creek, USA) below a trickling filter treatment plant averaged 190 mg/kg just below the outfall, 11.2 mg/kg less than 5 miles downstream and 5.3 mg/kg greater than 5 miles downstream

RECOMMENDATIONS OF THE SPONSOR COUNTRY

The chemicals in the LAS category are currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: **AGREED AT SIAM 17** The chemicals in the LAS category are currently of low priority for further work because of their low hazard potential except for skin and eye irritation and acute inhalation. Based on data presented by the Sponsor Country, exposure to respirable particles is anticipated to be low. Other countries may desire to investigate any exposure scenarios that were not presented by the Sponsor Country.

Environmental: To be discussed at SIAM 20: The chemicals in the LAS category possess properties indicating a hazard for aquatic species (vertebrate, invertebrate and algae). However, they are of low priority for further work due to ready and/or rapid biodegradation and limited potential for bioaccumulation. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.

COVER PAGE

SIDS Initial Assessment Report

For

SIAM 19

19-22 October 2004, Berlin, Germany

1.	**Chemical Name:**	Hydrotropes Category
2.	**CAS Number:**	1300-72-7, 12068-03-0, 26447-10-9, 28348-53-0, 32073-22-6, 37475-88-0
3.	**Sponsor Country:**	Australia
4.	**Shared Partnership with:**	Hydrotropes Consortium
5.	**Roles/Responsibilities of the Partners:**	Industry Consortia prepared the initial documents. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Department of Health and Ageing was the main reviewer. The environmental sections were reviewed by the Australian Government Department of the Environment and Heritage (ADEH).
•	Name of industry sponsor /consortium	Hydrotropes Consortium
•	Process used	Consortium member companies contributed in-house studies of physical-chemical properties, environmental fate and transport, ecotoxicity and mammalian toxicity for the chemicals in the category. To supplement the industry data, literature searches were conducted of on-line databases available from the U.S. Chemical Information Systems, the European International Uniform Chemical Information Database [IUCLID], the Institute for Systems, Informatics and Safety, and Environmental Chemicals Data Information Network (e.g., Hazardous Substances Databank [HSDB], Registry of Toxic Effects of Chemical Substances [RTECS], Toxic Substances Control Act Test Submissions [TSCATS], Integrated Risk Information System [IRIS], Chemical Carcinogenesis Research Information [CCRIS], GENETOX, The Environmental Mutagen Information Center [EMIC], The Environmental Teratology Information Center [ETIC], The Developmental and Reproduction Toxicology Database [DART], The Catalog of Teratogenic Agents [CTA], ENVIROFATE, DATALOG, PHYTOTOX, TERRATOX and Aquatic Toxicity Information Retrieval [AQUIRE]), and standard scientific data compendia (e.g., CRC Handbook of Chemistry and Physics, and The Merck Index). The sum total of the in-house studies, reference books, and

	literature searches of on-line databases was the identification of a substantial amount of available data. All data/reports identified were subject to a reliability evaluation using the Klimisch Criteria to assign data adequacy for the HPV/SIDS profile. NICNAS conducted an independent literature search to ensure all available studies were included. The Consortium prepared first drafts and NICNAS and ADEH reviewed and edited drafts to achieve the final document.
6. Sponsorship History	
• How was the chemical or category brought into the SIDS Program?	The industry coalition agreed to sponsor hydrotropes in the SIDS-International Council of Chemical Associations (ICCA) Program, with Australia being the sponsor country.
7. Review Process Prior to the SIAM:	Prepared by industry. Reviewed and edited by NICNAS and ADEH to reach a consensus document.
8. Quality check process:	Industry coalition members developed the draft documents, which were then reviewed by the sponsor country.
9. Date of Submission:	2005.
10. Comments:	(Pending.)

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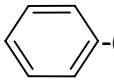
1 IDENTITY

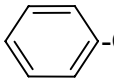
Compounds known as hydrotropes are amphiphilic substances composed of both a hydrophilic and a hydrophobic functional group. The hydrophobic part of the molecule is a benzene substituted (i.e., methyl [common name: toluene], dimethyl [common name: xylene] or methylethyl [common name: cumene] apolar segment. The hydrophilic, polar segment is an anionic sulfonate group accompanied by a counter ion (e.g., sodium and ammonium). This segment is a comparatively short side-chain as seen in the diagrams below. There are 6 sponsored hydrotropes.

Hydrotropes are produced by sulfonation of an aromatic hydrocarbon solvent (i.e., tolune, xylene or cumene). The resulting aromatic sulfonic acid is neutralized using an appropriate base (e.g., sodium hydroxide) to produce the sulfonate or hydrotrope. Commercial toluene (and cumene) sulfonates consist of mixtures of 3 isomers (ortho-, meta- and para-). Commercial xylene sulfonic acid consists of mixtures of 6 isomers. Diagrams of sodium salts for each of the three hydrotropes (without isomer orientation) are depicted below. An ortho-isomer would have adjacent attachment points to the benzene ring; a para-isomer would have attachments at opposite ends of the benzene ring; and a meta-isomer would have one open carbon between attachments on the benzene ring.

toluene sulfonic acid, sodium salt



xylene sulfonic acid, sodium salt



cumene sulfonic acid, sodium salt

The hydrotropes are used as coupling agents to solubilize the water insoluble and often incompatible functional ingredients of household and institutional cleaning products and personal care products. These hydrotropes are not surfactants but are used to solubilize complex formulas in water. They function to stabilize solutions, modify viscosity and cloud-point, limit low temperature phase separation and reduce foam. Manufactured products are used as aqueous solutions (30-60% active substance) or as granular solids containing 90-95% active substance.

1.1 Identification of the Substance Category

Chemical Abstracts Service (CAS) Numbers:	1300-72-7, 12068-03-0, 26447-10-9, 28348-53-0, 32073-22-6 and 37475-88-0. In addition to the six sponsored chemicals listed above, the following four additional substances provide supporting data and are supported by the data in this SIAR: 827-21-4, 28088-63-3, 30346-73-7, 16106-44-8.
International Union of Pure and Applied Chemistry (IUPAC) Name:	(1300-72-7 and 827-21-4) Xylenesulfonic acid, sodium salt; (12068-03-0) Toluenesulfonic acid, sodium salt; (26447-10-9) Xylenesulfonic acid, ammonium salt; (28348-53-0 and 32073-22-6) Cumenesulfonic acid, sodium salt; (37475-88-0) Cumenesulfonic acid, ammonium salt; (28088-63-3) Xylenesulfonic acid, calcium salt; (30346-73-7) Xylenesulfonic

	acid, potassium salt; and (16106-44-8) Toluenesulfonic acid, potassium salt.
Description:	The category is represented by six sponsored (and four additional supporting) hydrotropes that are amphiphilic substances composed of a hydrophobic, benzene substituted, apolar segment and a hydrophilic, anionic sulfonate, polar segment. The commercial substances can be sodium, ammonium, potassium or calcium salts. The category describes these hydrotropes that are amphiphilic coupling agents used in a wide range of cleaning and personal care products.
Molecular Formula:	$C_7H_8O_3S$[Na or NH_4 or Ca or K] *to* $C_9H_{12}O_3S$[Na or NH_4or Ca or K]
Structural Formula:	C_6H_3 . CH_3 . SO_3[Na or etc.] *to* C_6H_3 . $(CH_3)_3$. SO_3[Na or etc.]
Molecular Weight:	194 to 226
Synonyms:	1300-72-7 and 827-21-4: Xylenesulfonic acid, sodium salt; xylenesulfonate, sodium salt; sodium xylene sulfonate; Benzenesulfonic acid (1-dimentyl) sodium salt; dimethylbenzenesulfonate, sodium salt 12068-03-0: Toluenesulfonic acid, sodium salt; toluene sulfonate, sodium salt; sodium toluene sulfonate; benzenesulfonic acid (1-methyl) sodium salt; methylbenzenesulfonate, sodium salt 26447-10-9: Xylenesulfonic acid, ammonium salt; xylenesulfonate, ammonium salt; ammonium xylene sulfonate; Benzenesulfonic acid (1-dimentyl) ammonium salt; dimethylbenzenesulfonate, ammonium salt 28348-53-0 and 32073-22-6: Cumenesulfonic acid, sodium salt; cumenesulfonate, sodium salt; sodium cumene sulfonate; Benzenesulfonic acid (1 methylethyl) sodium salt; methylethylbenzenesulfonate, sodium salt 37475-88-0: Cumenesulfonic acid, ammonium salt; cumenesulfonate, ammonium salt; ammonium cumene sulfonate; Benzenesulfonic acid (1 methylethyl) ammonium salt; methylethylbenzenesulfonate, ammonium salt 28088-63-3: Xylenesulfonic acid, calcium salt; xylenesulfonate, calcium salt; calcium xylene sulfonate; Benzenesulfonic acid (1-dimentyl) calcium salt; dimethylbenzenesulfonate, calcium salt 30346-73-7: Xylenesulfonic acid, potassium salt; xylenesulfonate, potassium salt; potassium xylene sulfonate; Benzenesulfonic acid (1-dimentyl) potassium salt; dimethylbenzenesulfonate, potassium salt 16106-44-8: Toluenesulfonic acid, potassium salt; toluene sulfonate, potassium salt; potassium toluene sulfonate; benzenesulfonic acid (1-methyl) potassium salt; methylbenzenesulfonate, potassium salt

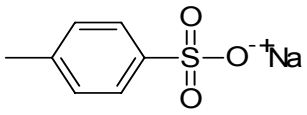
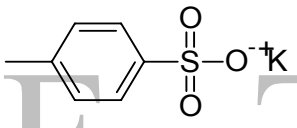
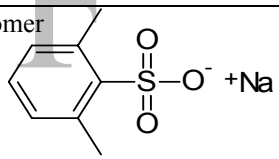
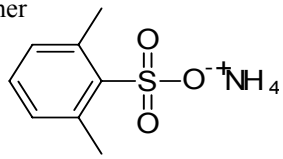
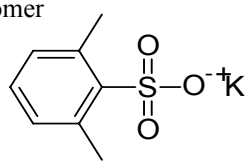
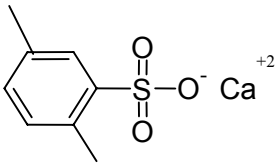
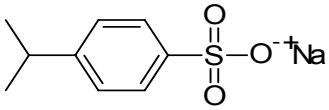
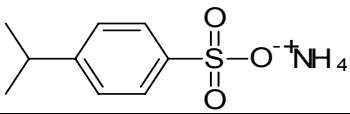
Category Justification for Hydrotropes:

The six sponsored hydrotropes have High Production Volume (HPV) chemical status in one or more OECD regions. However, the Hydrotropes Consortium has identified a total of four

additional hydrotrope substances that are analogues to the six sponsored materials and are also supported by the HPV data. In two cases (CAS Nos. 28088-63-3 and 16106-44-8) these substances provide supporting data for the chemical category. Therefore all ten are included in this SIAR for the purpose of defining and evaluating the chemical category.

The chemicals within the category "Hydrotropes" including chemical name, CAS No. and a representative structure of the commercial mixture (isomer identified) are shown in Table 1.

Table 1: Category of Hydrotropes:

Chemical Name	CAS No.	Structure
Toluene sulfonic acid, sodium salt	**12068-03-0**	para isomer 
Toluene sulfonic acid, potassium salt	16106-44-8	para isomer 
Xylene sulfonic acid, sodium salt	**1300-72-7** 827-21-4	ortho,ortho isomer 
Xylene sulfonic acid, ammonium salt	**26447-10-9**	ortho,ortho isomer 
Xylene sulfonic acid, potassium salt	30346-73-7	ortho,ortho isomer 
Xylene sulfonic acid, calcium salt	28088-63-3	meta,ortho isomer 
Cumene sulfonic acid, sodium salt	**28348-53-0** **32073-22-6**	para isomer 
Cumene sulfonic acid, ammonium salt	**37475-88-0**	para isomer 

*** Sponsored HPV chemicals are shown in bold**. Other substances are supporting compounds.

The Hydrotropes category may be initially considered as three sub-groups: the methyl, dimethyl and methylethyl benzene sulfonates, (or the toluene, xylene and cumene sulfonates). Although the counter ion will also determine the physical and chemical behavior of the compounds, the chemical reactivity and classification for this purpose is not expected to be affected by the difference in counter ion (i.e., Na^+, NH_4^+, Ca^{++}, or K^+). Note that two of the compounds (xylene and cumene sulfonic acid, sodium salts) have more than one CAS number. This is a result of differences in industry nomenclature practice and/or use patterns across geographical regions at the time of notification. This practice has lead to differences in how some substances are identified on national and regional chemical inventories. The structures as well as the physical/chemical and toxicologic properties of these chemical entities are essentially the same although the CAS numbers are different.

In general, the presence of one or two methyl groups or a methylethyl group on the benzene ring is not expected to have a significant influence on chemical reactivity. Alkyl substituents are known to be weak ortho- and para-directing activators, and the difference between methyl and methylethyl will be negligible. On going from methylbenzene (toluene) to dimethylbenzene (xylene) and to methylethylbenzene (cumene), the number of carbon atoms – and thus the organic character - increases. This will improve solubility in apolar solvents and reduce solubility in polar solvents like water. Hence, reactivity in watery solutions may differ somewhat for the hydrotropes. However, the decisive factor in determining water solubility of these compounds will be ionic character, not the number and identity of the alkyl substituents on the benzene ring.

It was therefore concluded that the three sub-groups are expected to be generally comparable and predictable in their chemical behaviour (as such or in solution) and that members from one sub-group may be useful for read across to other sub-groups and to the Hydrotropes category as a whole.

Some of these molecules also exist under the acid form and are commercial products. These products are not ICCA Initiative HPVC, but their chemical structures are close enough that extrapolating some of the test results may be appropriate from the neutralized forms. This is particularly true for tests done under high dilution in water with a pH control (for example, most of the ecotoxicology tests).

1.2 Purity/Impurities/Additives

The hydrotropes are ‘pure’ substances but are produced and transported in either aqueous solutions, typically at a 30-60% level of activity, or in granular solids typically at 90-95% level of activity. The other components of granular solids include sodium sulphate and water.

1.3 Physico-Chemical properties

Table 2 provides the available measured physico-chemical properties of the Hydrotropes category as well as modelled values using the EPIWIN model available at http://www.epa.gov/opptintr/exposure/docs/episuite.htm for those properties lacking measured values. Measured values are typically preferred over modelled values, however, modeled values can provide reasonably accurate directions/trends (e.g., relatively high or low) for these properties. Applicability of these models is addressed on U.S.EPA’s website (shown above) under Exposure Assessment Tools and Models: **“***These tools were designed for exposure screening activities and therefore err on the side of safety (i.e., they estimate high or perhaps higher than actual values of exposure)*”.

Measurements show hydrotropes to be relatively highly soluble in water. There are no reported measurements for vapour pressure; however, a 2000 IUCLID data sheet indicates "non-volatile". This is consistent with the modelled estimates of vapour pressure values ranging from 1.2 x 10^{-11} to 3.47 x 10^{-9} Pa. The single measured low octanol:water partition coefficient (log Kow) is consistent with the modeled estimates.

Table 2: Measured and Modeled Physico-Chemical Properties of Hydrotropes Category

Property	Compound	CAS No.	Modeled Value	Measured Value	Reference	Reliability Rating
Physical state	Pure	All	-	Solid at room temperature	1, 42, 43, 44, 45	n/a
Melting point	Xylene sulfonate, Na	1300-72-7	233° C	>300° C	EPI, 42	4, 4
	Xylene sulfonate, Ca	28088-63-3		>375 ° C	29	1
	Cumene sulfonate, Na	28348-53-0	236° C	182° C and >300° C	EPI, 1, 44	4, 4, 4
	Toluene sulfonate, Na	12068-03-0	228 ° C	-	EPI	4
Boiling point	Xylene sulfonate, Na	1300-72-7	545° C	100° C	3	4
	Xylene sulfonate, NH_4	26447-10-9	468° C	101° C	EPI, 43	4, 4
	Toluene sulfonate, Na	12068-03-0	533° C	-	EPI	4
Relative density	Xylene sulfonate, Na	1300-72-7		1.02-1.08	3	4
	Xylene sulfonate, Ca	28088-63-3		1.3	28	1
Vapour pressure	Xylene sulfonate, Na	1300-72-7	1.52 x10^{-9} Pa	Non-volatile	3	4
	Xylene sulfonate, Ca	28088-63-3	1.2 x10^{-11} Pa	-	EPI	4
	Toluene sulfonate, Na	12068-03-0	3.47 x10^{-9} Pa	-	EPI	4
	Cumene sulfonate, Na	28348-53-0	1.09 x10^{-9} Pa	-	EPI	4
Water solubility	Toluene sulfonate, Na	12068-03-0	1000 g/L	Soluble	EPI, 45	4, 4
	Xylene sulfonate, Na	1300-72-7	1000 g/L	400 g/L	EPI, 3	4, 4
	Xylene sulfonate, Na	1300-72-7		Soluble	42	4
	Xylene sulfonate, NH_4	26447-10-9	54 g/L	Soluble	EPI, 43	4, 4
	Xylene sulfonate, Ca	28088-63-3		553 g/L	31	1
	Cumene sulfonate, Na	28348-53-0	635 g/L	330 g/L , 400 g/L Soluble	EPI, 1, 10, 44	4, 4, 4, 4
Partition coefficient n-octanol /water	Xylene sulfonate, Na	1300-72-7	log Kow = -1.86	-	EPI	4
	Xylene sulfonate, Ca	28088-63-3		log Kow = -2.7	30	1
	Toluene sulfonate, Na	12068-03-0	log Kow = -2.4	-	EPI	4
	Cumene sulfonate, Na	28348-53-0	log Kow = -1.5	-	EPI	4

Note: The Klimisch reliability rating for references #1 and #42-#45 which are Material Safety Data Sheets is 4; the modelled values (reference identified as "EPI") are based on EPIWIN and all model outputs are assigned a reliability rating of 4. "Pa" is Pascal.

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Approximately 29,000 metric tonnes of hydrotropes are produced annually in the U.S. Annual production in Australia and Europe is approximately 1100 (40% concentration) and 19,000 tonnes, respectively. Hydrotropes are used at active concentrations between 0.1 and 15% in consumer cleaning and personal care products. They function as coupling agents in liquid and powder laundry detergents, hand dishwashing liquid detergents, machine dishwashing rinse aids, hard surface cleaners, body washes, shampoos, hair conditioners, liquid face and hand soaps, toilet treatments, solvent hand cleaners, carpet cleaners and optical brightener products. In Australia, a

relatively small volume (about 55 tonnes per year) is used in liquid sulphur textile dyes present at 7.5 – 50%, acidic recirculation cleaning products present at 10-25%, wetting agent for tanning industry present at 10%, enzymatic recirculation cleaner for dairy and food processing applications at 4%, coolant system conditioner at 6.9%, car wash detergents at 1.3–6.3%, cleaners and degreasers at 0.1–6.3%, vinyl, plastic rubber restorer at 0.2% and floor stripper at 2.7–9 %. There are no industrial process intermediate uses of the hydrotropes.

2.2 Environmental Exposure and Fate

Based on its use pattern, the predominant disposal route following use of the products that contain hydrotropes is via wastewater. Hydrotropes are water soluble (>1000 mg/L) and have low volatility (vp~1 x10^{-9} Pa). Hydrotropes are rapidly and completely biodegraded and are effectively removed during biological wastewater treatment (~94%). It has low potential for bioaccumulation (estimated Bioconcentration Factor [BCF] <1 L/kg). These characteristics help to minimize the potential for environmental exposure, and for indirect human exposure via drinking water and/or fish consumption.

2.2.1 Sources of Environmental Exposure

Environmental

Releases to the Environment from Manufacturing and Formulation Processes:

Manufacturing and formulation processes have been designed to maximize production yield and minimize potential environmental releases. A limited amount of hydrotropes may be released as a dilute aqueous solution from washing and rinsing operations in the manufacturing and formulation processes. Atmospheric emissions are considered to be very low. Any minimal release from manufacturing that produce or formulate hydrotropes is discharged to wastewater treatment. Modelling of manufacturing facility effluent discharges using the U.S.EPA Exposure & Fate Assessment Screening Tool (E-FAST) for high end to bounding conditions (see Annex 2) resulted in estimated mean flow and 7Q10 low flow (i.e., the lowest 7-day average flow in a year that occurs during 7 consecutive days on average once every 10 years) stream concentrations of 16.5 µg/L for a large production facility on a mid-size stream and 286.9 µg/L for a large production facility on a small stream, respectively for the high end scenario in the U.S.

Releases to the Environment Following Consumer Use:

Hydrotropes are used primarily in personal care and household/professional cleaning products. Environmental releases from down-the-drain discharges following product use could lead to potential ecological exposure in surface water. However, these hydrotropes are readily soluble (>1000 mg/L) and unlikely to be volatile. Products containing hydrotropes disposed of down-the-drain are transported to wastewater treatment plants where significant removal (~94%) is expected. Residual hydrotropes entering the environment will be completely biodegraded (>80% in ≤ 28 days in standard tests). They have a low potential for bioaccumulation (BCF <1 L/kg) based on modelled results. These characteristics help to minimize the potential for long-term environmental exposure.

For the U.S. modelling (using U.S.EPA E-FAST) of wastewater treatment plant discharges following down the drain disposal of consumer products for high end to bounding conditions (see Annex 2) resulted in estimated mean and low flow (7Q10) stream concentrations of 0.048 µg/L for

a mid-size stream and 0.63 µg/L for a small stream for the U.S. These estimates are based on the annual down-the-drain discharge of approximately 29,000 metric tonnes, which is the entire production plus importation volume estimate for the U.S. There are no monitoring data available to compare to these estimations.

For Australia, total manufacture and importation of hydrotropes amounts to around 1100 tonnes per annum, all of which will be assumed to be disposed of down the drain following consumer use as a worst case scenario. Predicted removal from the sewage treatment plant (STP) using the SIMPLETREAT model (input parameters as follows: LogH<<-4 Pa m^3/mol; Log Kow range of -2.7 to -1.5; readily biodegradable) is 87% by degradation with 13% remaining in the water discharge. Measured data (modified Semi-Continuous Activated Sludge [SCAS] test) indicates removal in the vicinity of 94%. For modelling purposes, a removal rate of 90% will be assumed. Australian modelling considers release to rivers or ocean. Dilution in the event of release to rivers is not assumed as often in Australia. Effluent will constitute the majority, in not all, of river flow in drier months. In the immediate area of ocean release, a dilution of 10:1 is assumed. Assuming wide dispersive release over 365 days of the year, the estimated concentration in surface waters is 8.3µg/L in ocean water and 83µg/L in rivers. There are no monitoring data available to compare to these estimations. Negligible partitioning to sewage sludge, and hence negligible exposure to agricultural soil, is expected.

2.2.2 Photodegradation

No experimental data are available for photodegradation of hydrotropes. Photodegradation rates were estimated for the toluene, xylene and cumene sulfonates using AOPWIN (in EPIWIN 3.11). The predicted atmospheric oxidation half lives were of the order of 40 to 105 hours, indicating a significant atmospheric degradation potential (15). Note that hydrotropes are not volatile, which reduces the importance of atmospheric photodegradation as an environmental fate mechanism, therefore no further consideration is given to this compartment in the assessment.

2.2.3 Stability in Water

No measured data are available for hydrolysis of the Hydrotropes category; however, since commercial products are available in aqueous solutions and these products are stable, the lack of hydrolysis data is not considered a significant deficiency. The salts are expected to dissociate completely in water and hydrotropes are known to be readily biodegradable.

2.2.4 Transport between Environmental Compartments

Fugacity modelling has been conducted to determine the theoretical distribution of hydrotropes in various environmental compartments. Based on EQC Level III modelling, the key compartment for fate of hydrotropes will be surface waters, with a predicted partitioning of 99.9% (15). The EQC Model is a widely used and accepted screening methodology; descriptions, applications and the model itself are available from the Canadian Environmental Modeling Centre (Trent University) at http://www.trentu.ca/cemc/welcome.html and from the U.S.EPA at http://www.epa.gov/opptintr/exposure/docs/hpvscn.htm.

Table 3 presents the output summary for two hydrotropes. First is calcium xylene sulfonate, which is based upon measured physico-chemical property data for all the input parameters except for vapour pressure. Second is sodium cumene sulfonate, which has the lowest estimated water solubility reported among the Hydrotropes category and therefore would be expected to represent a

hydrotrope with the lowest partitioning to water. The modelled physico-chemical input parameters for sodium cumene sulfonate are derived using EPIWIN. Modelled partitioning is nearly identical for both chemicals. Similar partitioning behavior would be expected across the range of Hydrotropes category independent of the benzene substitution (i.e., toluene, xylene or cumene) and counter ion (i.e., Na, K, NH_4, Ca). Hydrotropes are predicted to reside 99+% in the water fraction.

Table 3: EQC Level I output

Calcium Xylene Sulfonate (top row) and Sodium Cumene Sulfonate (bottom row)

MW	Water Solubility (mg/L)	Octanol-Water Partition Coefficient (Log Kow)	Melting Point (°C)	Vapour Pressure (Pa)	Fraction in Soil (%)	Fraction in Air (%)	Fraction in Water (%)	Fraction in Sediment (%)
226	**553 000**	**-2.7**	**375**	**1.2×10^{-11}**	**Negligible**	**Negligible**	**99.9**	**0.1**
222	**330 000**	**-1.5**	**300**	**1.09×10^{-9}**	**Negligible**	**Negligible**	**99.9**	**0.1**

Total mass used as release volume = 1.48×10^{5} kg

2.2.5 Biodegradation

Hydrotropes are fully biodegradable under aerobic conditions. Studies with toluene, xylene and cumene sulfonates are available and are summarized in Table 4. As a group, the Hydrotropes category is considered as readily biodegradable according to OECD criteria. No data are available on anaerobic degradation.

Table 4: Ready Aerobic OECD Biodegradation Screening Tests on Hydrotropes Category

Compound	CAS No.	Ready aerobic biodegradation or Wastewater removability	Method	Ref.	Reliability Rating
Toluene sulfonate	12068-03-0	100% after 3 days	Sewage inoculum	6	2
Xylene sulfonate, Na	1300-72-7	69% degraded in 5 days, 100% in 8 days	Sewage inoculum	6	4
Xylene sulfonate, Na	1300-72-7	74% degraded in 15 days, 88% in 28 days	Modified Sturm; OECD301B	46	2
Xylene sulfonate, Na	1300-72-7	74% degraded in 15 days, 84% in 28 days	Modified Sturm, OECD301B	33	1
Xylene sulfonate, Ca	28088-63-3	>50% degraded in 15days, >80% in 29days	Modified Sturm, OECD301B	27	1
Xylene sulfonate, NH_4	26447-10-9	71% degraded in 26 days	Ultimate biodegradation	17, 50	4,4
Cumene sulfonate, Na	28348-53-0	>60% degraded in 6 days, 100% in 15 day	Modified Sturm, OECD301B	26	1
Cumene sulfonate, Na	28348-53-0	82.5-91.5% degraded	Coupled Unit, OECD301E	7	4
Cumene sulfonate, Na	28348-53-0	100% degraded	Zahn Wellens, OECD301E	43	4
Cumene sulfonate, Na	28348-53-0	73% degraded	Not specified	46	4

2.2.6 Bioaccumulation

No test data are available for bioaccumulation. BCFWIN predictions (15) using the estimated log Kow value of –1.5 L/kg as input parameter (derived for sodium cumene sulfonate), calculated a bioconcentration factor of less than one (<1 L/kg). Thus the potential for bioaccumulation of hydrotropes in aquatic organisms is predicted to be very low.

2.2.7 Other Information on Environmental Fate

Removal of hydrotropes from secondary activated sludge sewage treatment processes is greater than 94%, as observed in a modified SCAS study with calcium xylene sulfonate (34). The protocol followed OECD Guideline 302A. The microbial inoculum was activated sludge mixed liquors from an operating municipal wastewater treatment plant. The concentration of hydrotrope tested was 20 mg carbon/L. The experimental design included duplicate test units, and 7 days each for sludge acclimation, for test substance acclimation, and for test substance removal measurements. The reliability rating for the study was 1. Monitoring data are not available for Hydrotropes category.

2.3 Human Exposure

2.3.1 Occupational Exposure

There is potential for workers to be exposed during manufacturing, formulation and industrial end use of products. Exposure could occur as a result of inhalation and/or dermal contact with aqueous and particulate material. The potential for human exposure to hydrotropes by inhalation is minimized by its low volatility and because most of the production, formulation and industrial end use of products are in aqueous solutions. Inhalation exposure to the solid form is likely to be minimal as dust generation is low. Dermal exposure is possible. Engineering controls (e.g., closed system operations, exhaust ventilation, dust collection) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities further mitigate worker exposure. No special engineering controls or additional personal protective equipment are uniquely specified for Hydrotropes category.

No workplace air monitoring data are available.

2.3.2 Consumer Exposure

Hydrotropes are used in consumer/professional cleaning and personal care products, which may be used “as is”, or diluted prior to or during use. Dermal contact will occur with these products. There is some potential for incidental or accidental ingestion of, inhalation of, and/or eye contact with products during handling and use. Exposure to hydrotropes in formulated consumer products is mitigated by following use and precaution instructions on product labels. Human exposure will be mitigated by the fact that residues from many of these products are washed or rinsed off. Dermal exposure modelling for use of products containing hydrotropes estimates exposure ranging from 1.7 x 10^{-1} to 1 x 10^{-2} mg/kg/day at the high end (see details in the Annex 2). All modelled exposures include a conservative (protective) default assumption of 100% absorption. Environmental releases from production facilities and from down-the-drain discharges following product use may lead to potential environmental exposures in surface waters and indirect human exposures via drinking water and/or fish consumption. Modelled indirect human exposure combining both drinking water and fish consumption following both production facility and down-the-drain discharges is estimated at 1.57 x10^{-3} mg/kg/day (combining modelled estimates from Format C#1 and C#2 in the Annex 2).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

Data on all of the SIDS endpoints are available taking into account all the chemicals included in the Hydrotropes Category. Annex 1 Table B identifies the various endpoints and the data available for them.

3.1.1 Toxicokinetics, Metabolism and Distribution

No ADME (adsorption, distribution, metabolism and elimination) studies for the hydrotropes category were identified during this assessment. However, using the physico-chemical properties of the hydrotropes and available toxicological information a general qualitative comment can be made on absorption. The key physico-chemical properties available for undertaking such an evaluation are the molecular weight, water solubility and octanol/water partition coefficient (Log P) value. The molecular weight of these hydrotropes is 194-226 and a water solubility and Log P value of 553 g/L and –2.7 respectively are available (both from studies with xylene sulfonate calcium and with reliability ratings of 1).

Molecular weights below 500 are favourable for absorption from the gastrointestinal tract. Additionally, absorption of very hydrophilic substances, such as the hydrotropes, can occur by passive diffusions and if the molecular weight is low (less than 200) the substance may pass through aqueous pores. The observation of clinical signs of toxicity, such as decreased activity, weakness and prostration in the acute oral study supports the conclusion that, qualitatively, significant absorption occurs following oral administration of high doses.

In contrast to oral absorption, a molecular weight less than 100 favours dermal uptake. Additionally, if water solubility is above 10 g/L and the log P <0, as is the case for the hydrotropes, the substance is likely to be too hydrophilic to cross the lipid rich environment of the stratum corneum and dermal uptake of these substances will be low. The absence of clinical signs of toxicity in the acute and repeat dermal toxicity studies support the conclusion that, qualitatively, limited absorption occurs following dermal administration.

Therefore, overall, the available data suggests that absorption will be significantly greater following oral exposure compared to topical.

3.1.2 Acute Toxicity

Studies in Animals

Table 5 provides the available acute toxicity results for toluene, xylene and cumene sulfonates and their various salts. Clinical signs observed in some of the acute oral toxicity studies included decreased activity, weakness, prostration, increased salivation and anogenital staining. No clinical effects were reported following inhalation and dermal exposures. A number of the results are reported with limited study detail as part of summary reports. One-half of the oral studies and one dermal study are reported in considerable detail with regard to methods and results. Oral, dermal and inhalation acute toxicity endpoints are addressed. [Note that because purity information was not always available these acute toxicity data are not reported as “a.i.” based on % active ingredient]

Table 5: Acute Mammalian Toxicity of Hydrotropes Category

Compound	CAS No.	Acute Toxicity Endpoints	Method	Reference	Reliability Rating
Toluene sulfonate, Na	12068-03-0	Oral rat LD_{50} 6500 mg/kg	Not specified	50	4
Toluene sulfonate, K	16106-44-8	Oral rat LD_{50} 4400 mg/kg	Not specified	50	4
Toluene sulfonate, Na	12068-03-0	Inhalation rat LC_{50} >557 mg/L	US CPSC CFR1500.40	50, 53	4,4
Xylene sulfonate, Na	1300-72-7	Oral rat LD50 >5000 mg/kg	Not specified	53	4
Xylene sulfonate, Na	1300-72-7	Oral rat LD_{50} 7200 mg/kg	Not Specified	3, 16	2,2
Xylene sulfonate, Na	1300-72-7	Oral rat LD_{50} 16,200 mg/kg	Not Specified	4	2
Xylene sulfonate, Na	1300-72-7	Oral rat LD_{50} >5000-16,200 mg/kg	Not Specified	50	4
Xylene sulfonate, NH_4	26447-10-9	Oral rat LD_{50} >2100 mg/kg	Not Specified	52	4
Xylene sulfonate, Ca	28088-63-3	Oral rat LD_{50} 3346 mg/kg	USEPA 798.1175	24	1
Xylene sulfonate, Ca	28088-63-3	Dermal rabbit 24-hr LD_{50} >2000 mg/kg	USEPA 798.1100	22	1
Xylene sulfonate, NH_4	26447-10-9	Inhalation rabbit 4-hr LC_{50} >6.41 mg/L	Not Specified	52	4
Cumene sulfonate, Na	28348-53-0	Oral rat LD_{50} >7000 mg/kg	OECD 401	7, 10, 11	4,4,2
Cumene sulfonate, Na	28348-53-0	Dermal rabbit $L_{50}D$ >2000 mg/kg	Not Specified	50	4
Cumene sulfonate, Na	28348-53-0	Inhalation rat LC_{50} >770 mg/L	US CPSC CFR1500.40	50, 53	4,4

USCPSC = U.S. Consumer Product Safety Commission CFR = Code of Federal Register (U.S.)

Conclusion

Across the Hydrotropes category, the acute oral LD_{50} in rats ranges from 3346 mg/kg (1044 mg/kg a.i.) to 16,200 mg/kg and the dermal LD_{50} in rabbits is >2000 mg/kg (624 mg/kg a.i. 24-hour exposure period). However the hydrotropes tested were of varying concentrations. Hydrotropes demonstrate a low order of acute oral and dermal toxicity. The results are consistent across the toluene, xylene and cumene sulfonates and their various salts. An acute inhalation study is available in the rabbit that suggests low acute toxicity for ammonium xylene sulfonate (LC50 > 6.41 mg/L/4-hr). However only minimal data was available for this study and the reliability rating of this study is 4.

3.1.3 Irritation

Tables 6 and 7 provide the available skin and eye irritation results for toluene, xylene and cumene sulfonates and their various salts. A number of the results are reported with limited study detail as part of summary reports; however, several studies include considerable detail with regard to methods and results.

Table 6: Skin Irritation Studies of Hydrotropes Category

Compound	CAS No.	Irritation Endpoints	Exposure Duration/Dose	Method	Reference	Reliability Rating
Toluene + xylene sulfonates, Na [50:50]	12068-03-0 + 1300-72-7	Mild to moderate irritation to rabbit skin with 40% soln	Not specified	Not specified	50	4
Xylene sulfonate, Na	1300-72-7	Slight irritation to rabbit skin with 40% soln	24hrs / 0.5ml	Not specified	5	2

Compound	CAS No.	Irritation Endpoints	Exposure Duration/Dose	Method	Reference	Reliability Rating
Xylene sulfonate, Na	1300-72-7	Slight irritation to rabbit skin with 40% soln	Not specified	Not specified	50, 52	4
Xylene sulfonate, NH_4	26447-10-9	Slight irritation to rabbit skin	Not specified	Not specified	52	4
Xylene sulfonate, Ca	28088-63-3	Not irritating to rabbit skin. Purity of the test material-31.2%	4hrs / 0.5ml	US EPA 81-5 & US EPA TSCA 798	36	1
Cumene sulfonate, Na	28348-53-0	Not irritating to rabbit skin with 60% soln	4hrs / 0.5g	OECD 404	14	2
Cumene sulfonate, Na	28348-53-0	Mild to moderate irritation to rabbit skin. Test material- 1% active, undiluted.	Not specified	Not specified	50	4
Cumene sulfonate, Na	28348-53-0	Not irritating to rabbit skin (conc. not indicated)	Not specified	OECD 404	10	4
Cumene sulfonate, Na	28348-53-0	Not irritating to skin (conc. not indicated)	Not specified	Not specified	7	4

TSCA = Toxic Substances Control Act (U.S.)

Table 7: Eye Irritation Studies of Hydrotropes Category

Compound	CAS No.	Irritation Endpoints	Exposure Duration /Dose	Methods	Reference	Reliability Rating
Toluene sulfonate, Na	12068-03-0	Moderate irritation to rabbit eye with 20% soln	Not specified	Not specified	50	4
Toluene sulfonate, K	16106-44-8	Slight irritation to rinsed and non rinsed rabbit eye with 20% soln. Irritation with rinsed 50% solution	Not specified	Not specified	50	4
Xylene sulfonate, Na	1300-72-7	Slight irritation to rabbit eye with 40% soln	Not specified	Not specified	50, 52, 53	4
Xylene sulfonate, NH_4	26447-10-9	Slight irritation to rabbit eye	Not specified	Not specified	52	4
Xylene sulfonate, Ca	28088-63-3	Mild irritation to rabbit eye. Purity of test material-31.2%	0.1ml	US EPA TSCA 798.4500	37	1
Cumene sulfonate, Na	28348-53-0	Irritating to rabbit eye depending on diluted or not, and rinsed or not at 10% soln	Not specified	Not specified	50	4
Cumene sulfonate, Na	28348-53-0	Not irritating to rabbit eye	Not specified	Not specified	7	4
Cumene sulfonate, Na	28348-53-0	Not irritating to rabbit eye	Not specified	OECD 405	10	4
Cumene sulfonate, Na	28348-53-0	Mild irritation to rabbit eye with 60% soln, 96% purity of test substance	50mg	OECD405	13	2

Conclusion

Varying results were observed in the skin and eye irritation studies. Either slight or no skin irritation has been observed with 31-60% solutions, and mild eye irritation with a 60% solution. Consequently, the Hydrotropes category is considered to possess a low skin and eye irritation potential

3.1.4 Sensitization

Studies in Humans

Skin

In the only available study, no evidence of skin sensitization was reported in a human repeat insult patch test of 0.5% aqueous sodium cumene sulfonate in a 0.1 % aqueous solution of granular laundry detergent product (50). However, the available information does not allow the reliability of the study to be determined (reliability rating of 4).

Studies in Animals

No animal studies investigating the skin sensitization potential of hydrotropes were identified.

Conclusion

No animal data or reliable human data is available to determine the skin sensitization potential of the hydrotropes category.

3.1.5 Repeated Dose Toxicity

Oral and dermal subchronic repeat dose toxicity studies conducted in rats and mice are available for the Hydrotropes category. The results are summarized in Table 8.

Studies in Animals

Dermal

Two subchronic dermal toxicity studies in both rats and mice were conducted using technical grade sodium xylenesulfonate in water (in 17-day) and ethanol (in 90-day) vehicles (51). All four studies are detailed in a 1998 U.S. National Institutes of Health report and have been assigned a reliability rating of 2. Five doses and a vehicle only were applied 5 days per week to clipped skin. In the 17-day study, doses ranged from 10-800 mg active ingredient (a.i.)/kg body weight (bw) for male rats, 13-1030 for female rats, 20-1600 for male mice and 26-2000 for female mice. In the 90-day study, doses ranged from 6-500 mg a.i./kg bw for male rats, 10-800 for female rats, 17-1300 for male mice, and 20-1620 for female mice. The 17-day study exposed 5 animals per sex per dose and the 90-day study exposed 10 animals per sex per dose. Rats were 5-6 weeks old and mice were 6-7 weeks old at study initiation. Endpoints in the 17-day study were mortality, body and organ weight, clinical signs and histopathology of skin from site of application, skin from an untreated site, and gross lesions. Endpoints in the 90-day study were the same as 17-days but also included hematology, clinical biochemistry and complete histopathology at necropsy on control mice and rats as well as on rats and mice in the top dose group (1620 mg a.i/kg bw/day in females and 1300 mg a.i./kg bw/day in males). No treatment-related deaths occurred in either study.

No treatment related effects were observed in the 17-day study for either species. The highest doses were 2000 mg a.i./kg bw for mice and 1030 mg a.i./kg bw for rats. The relative liver weights of male and female rats at the two highest doses were significantly greater than those of the control groups but the absolute weights were similar. The biological significance of the differences in relative liver weights was unclear. Similar observations, and conclusions, were reported in the mouse study at all the doses for males at and at the highest dose for females. No treatment related effects were observed in the 90-day study for rats. The highest dose was 800 mg a.i./kg bw in females and 500 mg a.i./kg bw in males. The absolute and relative liver weights of males at the mid (60 and 170 mg a.i./kg bw) and upper (500 mg a.i./kg bw) doses were significantly less than those of the controls. There were no treatment-related histopathologic alterations in the livers, thus the biological significance of the decreased liver weights was unclear.

No treatment related effects were observed in the 90-day study for female mice at the highest dose which was 1620 mg a.i./kg bw. There was, however, a gain in mean body weight and kidney weight in male mice at the highest dose of 1300 mg a.i./kg bw. The gain in body weight though statistically significant was <10%of the controls and is not considered to be toxicologically significant. There were no clinical findings related to sodium xylenesulfonate administration. There was some epidermal hyperplasia (reported as "typically minimal in severity" multifocal increase in the thickness of the epidermis) observed in male and female mice at the highest doses. However, the results of the 2-year study (51) conducted by the same investigators (reported below) showed no evidence that these lesions progressed to skin neoplasms. The No Observed Adverse Effect Level (NOAEL) for local effects, based on epidermal hyperplasia at the site of application, was 440 mg a.i./kg bw for male mice and 540 mg a.i./kg bw for female mice.

Oral

Three subchronic 90-day feeding studies in rats were conducted; two with sodium xylene sulfonate (2 and 54) and the other with sodium cumene sulfonate (18). One of the studies also included mice (54).

In the first study (2), 15 Wistar rats per sex per dose level were exposed to purified sodium xylene sulfonate at 0, 0.2, 1.0 and 5.0% in the diet. Mean administered doses were 0, 140, 710 and 3800 mg/kg bw for males and 0, 160, 820 and 4400 mg/kg bw for females. The purity of the test substance was at least 93% (3). Therefore, the doses based on active ingredient (a.i.) are 130, 660 and 3534 mg a.i./kg bw for males and 149, 763 and 4092 mg a.i./kg bw for females. Endpoints were those specified in OECD 408 with the exception of clinical signs, functional observations, ophthalmoscopy, cholesterol, sodium and potassium as part of clinical chemistry and platelets and blood clotting potential as part of hematology. No treatment related effects other than some sporadic clinical chemistry and haematology changes were observed in males at up to the highest dose (3534 mg a.i./kg bw). A loss of relative spleen weight in females, along with some clinical chemistry and haematology changes, was observed at the highest dose (4092 mg a.i./kg bw). The NOAEL from this study is 1% in the diet or 763 mg a.i./kg bw in females and 5 % in the diet or 3534 a.i. mg/kg bw in males.

In the second study (54), ten male and ten female Fischer rats and B6C3F1 hybrid mice were exposed per dose level to sodium xylene sulfonate at 0, 0.125%, 0.25%, 0.5%, 1% and 2% in the diet over a 91-day period. A nuclear magnetic resonance spectrum was run on the test material to determine purity. The conclusion of this analysis was that the major component of the test material was xylene sulfonate although an exact percent purity was not stated in the report. These dietary levels equate to 0, 152, 305, 610, 1220 and 2439 mg/kg bw daily doses for male mice, 0, 154, 308, 617, 1234 and 2467 mg/kg bw for female mice, 0, 89, 179, 357, 715 and 1429 mg/kg bw for male

rats, and 0, 98, 195, 390, 781 and 1561 for female rats. Body weights and food consumption were recorded. Animals were observed for clinical signs and mortality. No haematology or clinical chemistry tests were undertaken. Gross pathology was recorded when observed and histopathology was performed on all controls and high dose animals. There were no significant dose-related treatment effects on food consumption, or body weight in any group for either species. There were also no treatment-related gross or microscopic lesions noted at necropsy in either rats or mice. The NOAELs are, therefore, 2439 and 2467 mg/kg bw/day for male and female mice respectively and 1429 and 1561 mg/kg bw/day for male and female rats respectively.

In the third study (18), 20 CD rats per sex per dose level were exposed to sodium cumene sulfonate at 0, 0.005, 0.05 and 0.5% in the diet. Mean administered doses were 0, 2.6, 26 and 270 mg/kg bw for males and 0, 3.6, 36 and 375 mg/kg bw for females. Taking into account the content of active ingredient, 42.3%, these doses equate to 1.1, 11 and 114 mg a.i./kg bw and 1.5, 15 and 159 mg a.i./kg bw, respectively. The intervals between dose levels are large (factor of 10), while OECD TG 408 prefers 2 – 4 fold intervals and an additional group if factors are > 6 – 10. Endpoints were mortality, body and organ weight, food consumption, haematology, and histopathology. The methodology of this study was not available for assessment and was deduced from the results provided, No treatment related effects were observed in males at up to the highest dose (114 mg a.i./kg bw). A reduction in body weight gain was reported females (4%, 5% 12% as compared to controls at 1.5, 15 and 159 mg a.i./kg bw, respectively). The study report stated that this decrease in body weight gain was within the established ranges for animals of this species and age and was therefore not considered an adverse effect by the authors. The feed efficiency of the high dose females was statistically higher than the controls. The decrease in body weight gain of the high dose females was not associated with histopathological changes or any other effects. The NOAEL for sodium cumene sulfonate is therefore 114 mg a.i./kg bw for males and 159 mg a.i./kg bw in females.

Two 14 day studies in rats (55, 56) and one (55) in mice are available for sodium xylene sulfonate. One of the studies was a two-week range-finding study in both mice and rats (55) and preceded a 90-day study (54) described above. The dose concentrations in this study were 0, 0.25, 0.5, 1, 2% and 4%. Body weight and food consumption were recorded and the animals were observed for clinical signs and mortality. There were no clinical signs of toxicity or mortality at any of the doses in mice. Body weight gain was higher than the controls at the 0.25 and 0.5% levels in both sexes of mice. A reduction in body weight gain was observed at 1, 2 and 4% levels (2, 2 and 6% respectively). Reduced weight gain at the higher dose levels may be related to feed consumption which was slightly decreased in the first week with an increase in feed consumption in the second week. This could be the result of a palatability issue with acceptability of the feed in the second week in mice. Animals were observed scratching the food out of their dishes beginning about day 5.

In rats, deaths occurred at 2% (2) and 4% (4) in males and in females one each at the 0.5, 1, 2 and 4% doses. The deaths in males occurred on days 7, 8 and 12. Body weight gains were reduced at the 1 and 2% levels in males and at the 1, 2 and 4% levels in females. Food consumption was generally higher in the second week. Palatability was reported to be a problem as many animals were scratching the feed out of the dish, developed rough coats, loss of weight followed by death of some of the animals.

Subsequent to the 90-day study (54), a second two-week study (56) was conducted because of the lack of toxicity noted in the subchronic study (54) and in light of the mortalities reported in the first two-week range-finding study (55). This study was to determine if the mortalities observed in the first 14 day study were reproducible and due to the toxicity of sodium xylene sulfonate. The dose concentrations in this study were 0, 1, 2, and 4%. No mortality was observed at any dose levels.

Reduced body weight gains were reported at 1, 2 and 4% in both sexes (6, 5 and 17% in males and 3, 2 and 5% in females respectively) however there was no dose-response relationship between test material concentration and body weight gain. Palatability appeared to be an issue in the 4% group as animals were observed scratching their feed from the feeders during the last eight days of the study at this level. An accurate measurement of food consumption was not possible because of the food spillage issues.

Overall Conclusion:

The Hydrotropes category has been assessed in repeated dose oral and dermal studies in rats and mice. Test durations ranged from 17 days up to 2 years and exposure doses ranged from 6 to 2000 mg/kg bw by the dermal route and from 1.1 up to 4092 mg a.i./kg bw/day by the oral route. LOAELs ranged from 1300 mg a.i./kg bw/day in dermal studies to 4092 mg a.i./kg bw/day in oral studies. The corresponding NOAELs were 440 mg a.i./kg bw/day in dermal studies and 763 mg a.i./kg bw/day in oral studies. Local effects in the dermal study (mouse) were epidermal hyperplasia at the site of application. The only systemic effect observed was a body weight gain in males, but this change was not considered to be biologically significant.

One oral study reported a LOAEL of 4092 mg a.i./kg bw and a NOAEL of 763 mg a.i./kg bw. Effects observed were a decrease in spleen weight in females. No adverse effects were reported for males. A reduction in body weight gain was reported in an oral study with sodium cumene sulfonate. Given that two other well reported 90 day studies did not report a reduction in body weight gain at much higher doses, the effect in the sodium cumene sulfonate study is considered not to be reliable and its finding should be set aside in favor of the more robust studies. The most appropriate NOAEL for systemic toxicity from mammalian toxicity studies was therefore determined to be 763 mg a.i./kg bw/day based on a reduction in spleen weight in female rats.

Table 8: Summary of Repeat Dose Toxicity Tests of the Hydrotropes Category

Compound	CAS No.	Species	Route of Exposure	Study Duration	NOAEL mg/kg bw	LOAEL mg/kg bw	Doses mg/kg bw	Ref ŦŦ	Reliability Rating
Xylene sulfonate, Na	1300-72-7	Rat	Dermal	17-day	No effects at high dose (1030)	N/A	♂ 10, 30, 90, 260, 800 a.i. ♀ 13, 40, 120, 330, 1030 a.i.	51	2
Xylene sulfonate, Na	1300-72-7	Mouse	Dermal	17-day	No effects at high dose (2000)	N/A	♂ 20, 60, 190, 540, 1600 a.i. ♀ 26, 80, 220, 680, 2000 a.i.	51	2
Xylene sulfonate, Na	1300-72-7	Rat	Dermal	90-day	No effects at high dose (800)	N/A	♂ 6, 20, 60, 170, 500 a.i. ♀ 10, 30, 90, 260, 800 a.i.	51	2
Xylene sulfonate, Na	1300-72-7	Mouse	Dermal	90-day	540 for ♀ 440 for ♂	1620 for ♀ 1300 for ♂ epidermal hyperplasia	♂ 17, 50, 140, 440, 1300 a.i. ♀ 20, 60, 170, 540, 1620 a.i.	51	2

Compound	CAS No.	Species	Route of Exposure	Study Duration	NOAEL mg/kg bw	LOAEL mg/kg bw	Doses mg/kg bw	Ref ŦŦ	Reliability Rating
Xylene sulfonate, Na	1300-72-7	Mouse	Dermal	2-years	No systemic effects at high dose (727)	N/A	182, 364, 727 a.i.	51	1
Xylene sulfonate, Na	1300-72-7	Rat	Dermal	2-years	No systemic effects at high dose (240)	N/A	60, 150, 240 a.i.	51	1
Xylene sulfonate sodium	1300-72-7	Rat	Oral feed	14 days	Mortalities at 2, 4% levels. Palatability problem		0, 0.25, 0.5, 1, 2, 4% of diet	55	2
Xylene sulfonate sodium	1300-72-7	Rat	Oral feed	14 days	No effects 4 %		0, 1, 2 and 4% of diet	56	2
Xylene sulfonate sodium	1300-72-7	Mouse	Oral feed	14 days	No effects 4%		0, 0.25, 0.5, 1, 2, 4% of diet	55	2
Xylene sulfonate, Na	1300-72-7	Rat	Oral feed	28-day	No effects 3% of diet	N/A	1% and 3% of diet	3	4
Xylene sulfonate, Na	1300-72-7	Rat	Oral feed	90-day	763 for ♀ No effects at high dose (3534) for ♂	4092 for ♀ relative spleen wt loss	♂ 130, 660, 3534 a.i. ♀ 149, 763, 4092 a.i.	2	2
Xylene sulfonate, Na	1300-72-7	Rat	Oral feed	90-day	No effects at high dose (1429 for ♂ 1561 for ♀)	N/A	♂ 89, 179, 357, 715, 1429 a.i. ♀ 98, 195, 390, 781, 1561 a.i.	54	2
Xylene sulfonate, Na	1300-72-7	Mouse	Oral feed	90-day	No effects at high dose (2439 for ♂ 2467 for ♀	N/A	♂ 152, 305, 610, 1220, 2439 a.i. ♀ 154, 308, 617, 1234, 2467 a.i.	54	2
Cumene sulfonate, Na	28348-53-0	Rat	Oral feed	91-day	No systemic effects at high dose (159)	N/A	♂ 1.1, 11, 114 a.i. ♀ 1.5, 15, 159 a.i.	18	2

ŦŦ Reference numbers refer to the OECD HPV Dossier references

3.1.6 Mutagenicity

The Hydrotropes category has been assessed for mutagenic potential in a variety of *in vivo* and *in vitro* assays. Specifically mouse micronucleus assays with calcium xylene sulfonate and sodium cumene sulfonate, an Ames assay, mouse lymphoma, sister chromatid exchange, and chromosome aberration assay with sodium xylene sulfonate, an Ames assay with calcium xylene sulfonate and an Ames assay with sodium cumene sulfonate. All studies have a reliability rating of 1.

In vitro Studies

Ames Assays: The mutagenic potential of sodium xylene sulfonate (51), calcium xylene sulfonate (21) and sodium cumene sulfonate (8), were tested up to 10,000, 5,000 and 2000 µg a.i./plate, respectively, in the bacterial reverse mutation (Ames) assay using S*almonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 in the presence and absence of metabolic activation. There was no evidence of mutagenicity observed for any of the three compounds with and without metabolic activation. Positive controls for sodium xylene sulfonate and calcium xylene sulfonate were reported to give results that confirmed the validity of the test. The negative result for sodium xylene sulfonate is corroborated by an Albright & Wilson study (1987) reported in the IUCLID (3)

Mouse Lymphoma Test: Technical grade (65% a.i.) sodium xylene sulfonate was tested for mutagenicity potential in L5178Y mouse lymphoma cells up to 5000 µg/mL with metabolic activation and without metabolic activation using supplemented Fischer's medium and 2500 µg/mL without metabolic activation using DMSO (51). Test concentrations were reported to be selected based on cytotoxicity. There were two independent tests with duplicate cultures per treatment per test concentration. The exposure period was 4 hours with and without metabolic activation and the incubation period was 48 hours. There was no mutagenic activity without metabolic activation and an equivocal result was reported with activation. The result was considered equivocal because the significant increase in mutant colonies noted in the first trial with S9 was not repeated in the second trial. Positive results were seen at the highest doses where cytotoxicity was also reported.

Sister Chromatid Exchange (SCE) Test: Technical grade (65% a.i.) sodium xylene sulfonate was tested at 500 – 5000 µg/mL (should convert to active ingredient) in Chinese hamster ovary cells with and without metabolic activation (51). There were two independent tests with an exposure period of 2 hours with metabolic activation (plus 25.5 hours incubation time) and initially up to 25.5 hours without metabolic activation. However, cytotoxicity (cell cycle delay) was reported at 2513 – 5000 µg/mL without metabolic activity that was addressed by lengthening the exposure time to 32.5 hours to ensure a sufficient number of scorable (second-division metaphase) cells. No clastogenic activity was recorded with metabolic activation. A significant increase in SCEs was observed without metabolic activity but only at dose levels that were reported to produce cell cycle delay. Positive controls produced clear increases in SCEs.

Chromosome Aberration Test: Technical grade (65% a.i.) sodium xylene sulfonate was tested in Chinese hamster ovary cells with and without metabolic activation (51). Test concentrations were 2513, 3750 and 5000 µg/mL. Exposure with metabolic activation was 2 hours and 18 hours without metabolic activation. Cells were harvested at 12 and 18 hours with and without metabolic activation, respectively. There was no clastogenic activity with and without metabolic activation. Positive controls gave results that confirmed the validity of the test.

In vivo Studies

Three mouse micronucleus cytogenetic assays were reported. One study with calcium xylene sulfonate (35) used a single intra-peritoneal (i.p.) injection of 0, 145, 290 or 580 mg a.i./kg bw (5 per sex per dose). Doses were selected from a preliminary dose ranging study. Two oral (gavage) studies are available with sodium cumene sulfonate. One study (12) used a single administration of 0 or 4467 mg a.i./kg bw (5 per sex per dose) with the dose selected from a preliminary dose ranging study, and the other (9) total doses of 400, 2000 and 4000 mg a.i./kg bw delivered in two equal applications 24 hours apart (7 per sex per dose). One male and 1 female died at the top dose in this repeated dose study. Negative results were obtained in all three studies. In all 3 assays the positive controls gave results that confirmed the validity of the test.

Conclusion

No positive results were seen *in vitro* or *in vivo*. Thus the available data indicates that the Hydrotropes category is not genotoxic.

3.1.7 Carcinogenicity

Chronic toxicity/carcinogenicity data exist for the Hydrotropes category for both rats and mice dermally exposed for 2 years (51). Both studies have reliability ratings of 1.

Dermal

F344/N rats (50 per sex per dose) and B6C3F1 mice (50 per sex per dose) received dermal application to clipped skin 5 days per week) of technical grade sodium xylene sulfonate (65% a.i.) in 50 % ethanol in a 2-year carcinogenicity study. Doses in the rat study were 0, 60, 120 and 240 mg a.i./kg bw/day and 0, 182, 364 and 727 mg a.i./kg bw/day in the mouse study. Observations were as per OECD 453 Guideline with the exception of clinical signs recorded monthly, and no observations of food consumption (feeding was *ad libitum*), blood parameters, urinalysis and organ weights were undertaken. Stability of the test compound in ethanol was confirmed. Body weight gain was not affected by the exposures in either species. No treatment related effects were observed with the exception of epidermal hyperplasia at the application site in female rats only at 120 and 240 mg a.i./kg bw/day and in female mice at 0, 364 and 727 mg a.i./kg bw/day and in male mice at 364 and 727 mg a.i./kg bw/day. There was no evidence of carcinogenic activity.

Conclusion

The Hydrotropes category demonstrated no evidence of a carcinogenic potential in dermal chronic toxicity/carcinogenicity rodent studies.

3.1.8 Toxicity for Reproduction

Developmental toxicity in rats including fertility was evaluated for calcium xylene sulfonate (32). No fertility studies are reported for the Hydrotropes category. However, the 91-day oral rat feeding study with sodium cumene sulfonate (18), the 90-day feeding study with sodium xylene sulfonate (2) and the 90-day and 2-year dermal studies with sodium xylene sulfonate (51) included examination of sex organs. No treatment related effects on reproductive organs were reported.

Developmental Toxicity

Calcium xylene sulfonate (31% a.i.) was administered via gavage to female rats (30 per dose) at 0, 150, 1500 or 3000 mg/kg bw in water on days 6 to 15 of gestation (32). EPA TSCA Guideline 1985 was followed, and the reliability rating of this study is 2. Clinical symptoms were noted daily from day 6 to 20. Body weight gain and food consumption were recorded on day 0, 6, 9, 12, 16 and 20. All females were macroscopically examined on day 20 (or on day of death). The uteri were removed, weighed and examined for number of *corpora lutea*, number of implantation sites and number and location of fetuses and resorptions. Fetuses were inspected on total number, sex, weight and external, visceral (one-half) and skeletal (one-half) defects.

Only one animal died during the study (mid-dose). No treatment related effects were observed. An increase in food intake observed at the highest dose was considered to be within ranges of biological variation for this species. The NOAEL for maternal and fetal toxicity was the highest dose tested; 3000 mg/kg bw/day that corresponds to 936 mg a.i./kg bw/day.

Conclusion

The Hydrotropes category has been evaluated for the potential to cause developmental toxicity in rats. Hydrotropes were not developmental toxicants. While a reproductive study is not available for the Hydrotropes category, reproductive organs were examined in 90-day oral and 90-day and 2-year dermal repeated dose studies. There is no evidence from these repeat dose studies to suggest that these chemicals would have an adverse effect on fertility.

3.2 Initial Assessment for Human Health

Toxicological studies have been conducted with numerous members of the Hydrotropes category. Data on all SIDS-endpoints are available. These data demonstrate consistent results and a relatively low toxicity for these compounds. The quality of data is variable and while some of these studies were conducted prior to the effective date for Good Laboratory Practices (GLPs) or were non-guideline, some studies are generally of good scientific quality, show consistent results and are acceptable to support the overall profile of the category.

The available acute toxicity data indicate that the Hydrotropes category has a low hazard potential. These tests were conducted with varying concentrations of hydrotropes. Acute oral LD_{50} values for rats range from 3346 – 16,200 mg test material/kg bw. Acute dermal LD_{50} value was >2000 mg/kg bw (624 mg a.i./kg bw following 24 hr exposure). No acute inhalation studies with reliability ratings of 1 or 2 are available; 3 studies with reliability ratings of 4 (insufficient detail) are reported.

In a series of studies in rabbits varying results were observed in the skin and eye irritation studies. Either slight or no skin irritation was observed with 31-60% solutions, and mild eye irritation with a 60% solution. The Hydrotropes category is therefore considered to have a low skin and eye irritation potential. No animal studies, or reliable human data, investigating skin sensitization potential are available.

In repeated dose exposure to hydrotropes via oral and dermal routes, no significant toxicity was observed in 9 of 14 studies. The NOAELs in the 9 studies ranged from 159 - 2467 mg a.i./kg bw. One dermal study (mouse) reported a LOAEL of 1300 mg a.i./kg bw and a NOAEL of 440 mg a.i./kg bw in males for local effects. Effects observed were epidermal hyperplasia at the site of application. The only systemic effect observed was a body weight gain in males, but this change was not considered to be biologically significant. One oral study reported a LOAEL of 4092 mg a.i./kg bw and a NOAEL of 763 mg a.i./kg bw. Effects observed were a decrease in spleen weight

in females. No adverse effects were reported for males. A reduction in body weight gain was reported in an oral study with sodium cumene sulfonate. Given that two other well reported 90 day studies did not report a reduction in body weight gain at much higher doses, the effect in the sodium cumene sulfonate study is considered not to be reliable and its finding should be set aside in favor of the more robust studies. The most appropriate NOAEL for systemic toxicity from mammalian toxicity studies was therefore determined to be 763 mg a.i./kg bw/day based on a reduction in spleen weight in female rats. The most appropriate NOAEL for local effects was determined to be 440 mg a.i./kg/bw based on epidermal hyperplasia at the site of application (dermal exposure) in male mice. The results of a 2-year dermal study conducted by the same investigators showed no evidence that these lesions progressed to skin neoplasms.

No evidence of genotoxicity was seen in *in vitro* and *in vivo* assays. No evidence of carcinogenicity was seen in 2-year dermal studies in rats and mice.

No developmental effects or maternal toxicity were observed in a developmental toxicity study where female rats were gavaged with up to 936 mg a.i./kg bw/day of calcium xylene sulfonate.

The results are consistent across the toluene, xylene and cumene sulfonates and their various salts where comparative data are available (i.e., acute oral and dermal eye and skin irritation, repeated dose and genotoxicity).

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Reliable data are available on all SIDS-endpoints for selected members of the category and analogues. Annex 1 Table A identifies the various endpoints and the data available for them. The data cover fish, invertebrates and algae for xylene sulfonate (sodium, ammonium and calcium salts) and cumene sulfonate (sodium salt). Chronic toxicity to *Daphnia magna* and bacterial toxicity was reported for sodium cumene sulfonate. While the toluene benzene derivative is not represented in the available data set, the xylene and cumene benzene representatives are represented. Results are consistent for the chemicals tested, providing confidence in the ability to read-across for other category members.

Acute Toxicity Test Results

Based on hazard data, acute toxicity is considered to be uniformly low across the category (Table 9). Green algae are considered the most sensitive species with EC_{50} values of 230-236 mg/L a.i. and No Observed Effect Concentrations (NOECs) of 31-75 mg a.i./L. when tested with the sodium and calcium salts of xylene sulfonic acid, respectively. Fish and invertebrates did not demonstrate acute sensitivity at concentrations tested (>318 mg a.i./L) of xylene and cumene sulfonates (ammonium, calcium and sodium salts). However some sublethal effects were noted in two of the studies at the higher concentrations and included surfacing, loss of equilibrium, swimming on the bottom of the tank, dark discoloration, labored respiration and quiescence in some fish.

Table 9: Acute Aquatic Toxicity of the Hydrotropes Category

Compound	CAS No.	Acute Toxicity Endpoint Species and Duration EC50 / LC50 (mg/L)[1]	Method	Ref.	Reliability Rating
		Fish			
Xylene sulfonate, Na	1300-72-7	Rainbow trout 96-hr LC50 >408 a.i.	EPA 797.1400	48	2
Xylene sulfonate, Na	1300-72-2	Fathead minnow 96-hr LC50 >400 a.i.	EPA 797.1400	20	2
Xylene sulfonate, NH_4	26447-10-9	Bluegill 96-hr LC50 = 1060	Not specified	17	4
Xylene sulfonate, Ca	28088-63-3	Rainbow trout 96-hr LC50 >490 a.i.	EPA 797.1400 (flow through)	40	1
		Invertebrate			
Xylene sulfonate, Na	1300-72-7	*Daphnia magna* 48-hr EC50 >408 a.i.	EPA 797-1300	49	2
Xylene sulfonate, Na	1300-72-7	*Daphnia magna* 48-hr EC50 >400 a.i.	EPA 797-1300	39	2
Xylene sulfonate, Na	1300-72-7	*Artemia sp.* 48-hr EC50 >400	Not specified	3	4
Xylene sulfonate, Ca	28088-63-3	*Daphnia magna* 48-hr EC50 >318 a.i.	EPA 797-1300 (flow through)	23	1
		Algae			
Xylene sulfonate, Na	1300-72-7	*Selenastrum* 96-hr EC50 = 230 NOEC = 31	EPA 797.1050	47	2
Xylene sulfonate, Ca	28088-63-3	*Selenastrum* 96-hr EC50 = 236 a.i. NOEC = 75 a.i.	EPA 797.1050	25	1
		Fish			
Cumene sulfonate, Na	28348-53-0	Fathead minnow 96-hr LC50 >450 a.i.	EPA 797.1400	41	2
Cumene sulfonate, Na	28348-53-0	*Leuciscus idus* 48-hr LC50 >1000	DIN 38412, T15	7, 10	4,4
		Invertebrate			
Cumene sulfonate, Na	28348-53-0	*Daphnia magna* 48-hr EC50 >450 a.i.	EPA 797-1300	19	2
Cumene sulfonate, Na	28348-53-0	*Daphnia magna* 24-hr EC50 >1000	DIN 38412, T11	10	4
		Algae			
Cumene sulfonate, Na	28348-53-0	*Scenedesmus* 72-hr EC50 >1000	Algenwachstums-hemmtest - UBA	10	4
		Bacteria			
Cumene sulfonate, Na	28348-53-0	*Pseudomonas putida* 48-hr EC50 >16,000	Bringmann-Kuehn	10	4

[1] "a.i." indicates active ingredient for those studies where test substance purity was reported.

EC50 = Effect concentration for 50 percent of organisms tested

LC50 = Lethal concentration for 50 percent of organisms tested.

Conclusion

The Hydrotropes category demonstrates a low level of acute aquatic toxicity to fish, invertebrates, algae and bacteria.

Chronic Toxicity Test Results

A single chronic study is reported for *Daphnia magna*. [Note: the 96-hour algal toxicity tests reported in Table 9 may also be considered chronic results.] There are limited details of presumably the same study in both a journal article citation (7) and an IUCLID (sodium cumene sulfonate, CAS No. 28348-53-0, 18 Feb 2000)(10). Both references have reliability ratings of 4. The description is a 21-day exposure with reproduction endpoint following method "Verlaengerter Toxizitaetstest bei *Daphnia magna* nach UBA (1984 standard)" with no analytical monitoring. The 21-day EC50 is reported as 154 mg/L and the NOEC is reported as >30 mg/L in Greim et al. (7) and <30 mg/L in the IUCLID (10). The study sponsor does not have a full laboratory report but did indicate that "Testing was done in 1987 without formal GLP but that GLP certification of the

laboratory was received in 1989/1990. Test substance concentrations were 30, 100 and 300 mg/L as active ingredient (with no analysis performed)." The sponsor also provided tables summarizing the number of parent animals and offspring during the course of the study. These tables are appended to reference 10 for the purpose of this SIAR. The tables show no significant test substance related mortality of parent animals over the 21-day exposure period. The average number of offspring produced per day was 43 in the controls, 38 at 30 mg/L, 29 at 100 mg/L and 13 at 300 mg/L. These equate to 88% of control, 67% of control and 30% of control at 30, 100 and 300 mg/L, respectively. There are insufficient data to establish a statistically derived NOEC. It is uncertain whether the 88% of control response is a significant reduction in the number of young produced, but the data in the table do indicate that the "NOEC >30 mg/L" as reported in Greim et al. (7) appears to be in error. The NOEC could be = 30 mg/L or < 30 mg/L. A chronic NOEC of approximately 30 mg/L would be consistent with the lowest algal chronic NOEC value of 31 mg/L and would also be in the range of a predicted NOEC based on the *Daphnia magna* acute LC50 value of >450 mg/L divided by 10 (i.e., >45 mg/L).

4.2 Terrestrial Effects

No terrestrial toxicity data are available for members of the Hydrotropes category. Given the low potential for hydrotropes reaching the terrestrial compartment (EQC modelling results), the lack of persistence (ready biodegradability under aerobic conditions) or bioaccumulation (BCFWIN modelling results), and the low likelihood of these chemicals partitioning to soil (EQC modelling results), generation of data in this area is not considered necessary.

4.3 Other Environmental Effects

Results of a microbial toxicity test are reported for sodium cumene sulfonate. The 48-hr EC10 for the bacteria *Pseudomonas putida* exposed in a Bringmann-Kuehn-Test is reported as >16,000 mg/L (10).

4.4 Initial Assessment for the Environment

Effects assessment: Relatively low level toxicity, ready biodegradation and low potential for bioaccumulation indicate that the Hydrotropes category does not pose a significant environmental hazard. The suggested aquatic Predicted No Effect Concentration (PNEC) is 2.3 mg/L (2,300 µg/L) calculated as the lowest EC50 for three species (algae, fish, daphnid) divided by the recommended assessment factor of 100. The lowest EC50 is 230 mg/L (algal toxicity; sodium xylene sulfonate) divided by 100 equals 2.3 mg/L. This PNEC is consistent with what would be predicted using the chronic *Daphnia magna* NOEC divided by 10, or using the 96-hour algal NOEC as a chronic endpoint divided by 10.

5 RECOMMENDATIONS

The chemicals in the Hydrotropes category are currently of low priority for further work.

Human Health: The chemicals are currently of low priority for further work because of their low hazard potential.

Environmental: The chemicals are currently of low priority for further work because they do not pose a significant environmental hazard.

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ANNEX 1. MATRIX OF THE MEASURED DATA OF ACCEPTABLE QUALITY* FOR SIDS ENDPOINTS:

These tables provide a matrix of the measured physico-chemical and ecotoxicity data (A), and mammalian toxicity data (B) of acceptable quality available for the Hydrotropes category.

Table A. Measured data of acceptable quality for selected SIDS endpoints[@]:

Chemical Name	**CAS No.**		**Physico-Chem.**			**Environmental Fate**				**Ecotoxicity**		
		M.W.	Sol.	LogKow	V.P.	Photo	St. wat.[*]	Transp.[#]	Biodeg	Fish	Daph.	Algae
Toluene sulfonic acid, sodium salt	12068-03-0	194.18	-	-	-	-	-	-	Maybe	-		
Toluene sulfonic acid, potassium salt	16106-44-8	210.29	-	-	-	-	-	-	-	-		
Xylene sulfonic acid, sodium salt	1300-72-7 827-21-4	208.21	-	-	-	-	-	-	Yes	Yes	Yes	Yes
Xylene sulfonic acid, ammonium salt	26447-10-9	203.24	-	-	-	-	-	-				
Xylene sulfonic acid, potassium salt	30346-73-7	224.32	-	-	-	-	-	-	-	-		
Xylene sulfonic acid, calcium salt	28088-63-3	226.31	Yes	Yes	-	-	-		Yes	Yes	Yes	Yes
Cumene sulfonic acid, sodium salt	28348-53-0 32073-22-6	222.24	-	-	-	-	-		Yes	Yes	Yes	
Cumene sulfonic acid, ammonium salt	37475-88-0	217.27	-	-	-	-	-	-	-	Yes		

For data to be considered acceptable quality, it must be rated 1 or 2 on the Klimisch scale and is expressed as "Yes".

Sol, water solubility; LogKow, octanol:water partition; V.P., vapour pressure; Photo, photodegradation; Transp, transport between environmental compartments; St.wat., stability in water; Transp., transport between environmental compartments; Biodeg, biodegradation; Daph., *Daphnia magna* .

*Stability in water is not considered a relevant endpoint as commercial hydrotrope products are used in aqueous solutions to help solubilize otherwise water insoluble ingredients.

#Transport between environmental compartments are modelled for use in the SIAR. Modelling puts >99% of hydrotropes in the water compartment.

- No data available

@Additional testing for all of the above endpoints is not considered necessary given the known high degree of water solubility, low volatility and ready biodegradability of hydrotropes.

The purpose of this table is to show the number of studies of reliability rating 1 or 2 that is available for this category and that the data set is complete for the SIDS endpoints. Supporting data, including studies with a reliability rating 4, are not included here.

Table B. Measured data of acceptable quality for selected SIDS endpoints:

Chemical Name	CAS No.	Toxicity Data										
		AO	**AD**	**AI**	**SI**	**EI**	**SE**	**Rep.**	**Geno**	**Repro**	**Dev**	**Car**
Toluene sulfonic acid, sodium salt	12068-03-0		-		-		-	-	-	-	-	-
Toluene sulfonic acid, potassium salt	16106-44-8		-	-	-		-	-	-	-	-	-
Xylene sulfonic acid, sodium salt	1300-72-7 827-21-4	**Yes (2)**	-	-	**Yes**		-	**Yes (4)**	**Yes (3)**	-	-	**Yes (2)**
Xylene sulfonic acid, ammonium salt	26447-10-9		-				-	-	-	-	-	-
Xylene sulfonic acid, potassium salt	30346-73-7	-	-	-	-	-	-	-	-	-	-	-
Xylene sulfonic acid, calcium salt	28088-63-3	**Yes**	**Yes**	-	**Yes**	**Yes**	-	-	**Yes (2) #**	-	**Yes**	**Yes**
Cumene sulfonic acid, sodium salt	28348-53-0 32073-22-6	**Yes**			**Yes**	**Yes**		**Yes**	**Yes**	-	-	-
Cumene sulfonic acid, ammonium salt	37475-88-0	-	-	-	-	-	-	-	-	-	-	-

*For data to be considered acceptable quality, it must be rated 1 or 2 on the Klimisch scale and expressed as 'Yes" with number of studies in bracket.

AO, acute oral; AD, acute dermal; AI, acute inhalation; SI, skin irritation; EI, eye irritation; SE, sensitisation; Rep, repeated dose toxicity; Geno, genotoxicity; Repro, reproductive toxicity; Dev, developmental toxicity; Car, carcinogenicity.

Substance identity not available from reports

- No data available

The purpose of this table is to show the number of studies of reliability rating 1 or 2 that is available for this category and that the data set is complete for the SIDS endpoints. Supporting data, including studies with a reliability rating of 4, are not included here.

ANNEX 2: HYDROTROPES USE AND EXPOSURE INFORMATION

Purpose:

To provide high end to bounding estimates of the potential environmental and human exposure to hydrotropes from its manufacture and its use in consumer products in the United States (U.S.) to complement an OECD SIDS Programme review of this category.

Coverage:

The report covers manufacturing and professional and consumer use for hydrotropes in the United States (U.S.) and in Australia.

Synthesis of Key Assessment Results:

Hydrotropes are used as coupling agents to solubilize water insoluble and otherwise. incompatible functional ingredients in personal care and household/professional cleaning products. Hydrotropes are produced by sulfonation of aromatic hydrocarbon solvents (i.e., cumene, toluene, and xylene). The resulting aromatic sulfonic acid is neutralized utilizing the appropriate base (e.g., sodium hydroxide) to produce the sulfonate or hydrotrope. The category includes ammonium, calcium, potassium and sodium salts that are described by 10 CAS numbers (6 are ICCA-sponsored and have HPV status in one or more OECD regions; 4 are non-HPV status and are included as supporting chemicals in the category).

Approximately 29,000 metric tonnes of hydrotropes are produced annually in the U.S. Annual production in Australia and Europe is approximately 1,100 and 19,000 tonnes, respectively. Hydrotropes are used at active concentrations between 0.1 and 15% in consumer cleaning and personal care products. They function as coupling agents in liquid and powder laundry detergents, hand dishwashing liquid detergents, machine dishwashing rinse aids, hard surface cleaners, body washes, shampoos, hair conditioners, liquid face and hand soaps, toilet treatments, solvent hand cleaners, carpet cleaners and optical brightener products.

In Australia, a relatively small volume (about 55 tonnes per year) is used in liquid sulphur textile dyes present at 7.5 – 50%, acidic recirculation cleaning present at 10-25%, wetting agent for tanning industry present at 10%, enzymatic recirculation cleaner for dairy and food processing applications at 4%, coolant system conditioner at 6.9%, car wash detergents at 1.3–6.3%, cleaners and degreasers at 0.1–6.3%, vinyl, plastic rubber restorer at 0.2% and floor stripper at 2.7–9 %. There are no industrial process intermediate uses of the hydrotropes. The predominant disposal route following use of the products that contain hydrotropes is via wastewater.

Hydrotropes are water soluble (>1000 mg/L) and have low volatility (vp~1 $x10^{-9}$ Pa). Hydrotropes are rapidly and completely biodegraded and are effectively removed during biological wastewater treatment (~94%). It has low potential for bioaccumulation (estimated BCF <1 L/kg). These characteristics help to minimize the potential for human and environmental exposure. Engineering controls (e.g., closed system operation, exhaust ventilation, dust collection) and personal protective equipment (e.g., protective clothing, eyewear, and gloves) at manufacturing and formulation facilities and industrial end uses such as textile dye mitigate worker exposures and no special engineering controls or additional personal protective equipment are uniquely specified for hydrotropes.

The aquatic PNEC of hydrotropes is 2,300 µg/L. Aquatic life exposure occurs as a result of process loss discharge at production facilities (Format C #1) and/or from down-the-drain discharge following private (consumer) use of laundry/cleaning and personal care products (Format C #2). The down-the-drain scenario represents the major disposal route to the environment. E-FAST exposure modelling predicts upper-bound, in-stream concentrations of 286.9 µg/L for a hypothetical large production facility in the U.S. on a small stream under low flow (7Q10) conditions, 16.5 µg/L for a large production facility on a mid-size stream under low flow (7Q10) conditions, 0.63 µg/L for

a wastewater treatment facility following down-the-drain consumer disposal into a small stream under low flow (7Q10) conditions, and 0.048 µg/L for a wastewater treatment facility following down-the-drain consumer disposal into a mid-size stream under average flow conditions. The U.S. conditions were specifically modelled due to the significant production and consumption in this geography. For Australia, the estimated concentration in surface waters is 8.3 µg/L in marine, and 83 µg/L in river surface water, assuming wide dispersive release over 365 days of the year.

The most appropriate NOAEL for systemic toxicity (oral exposure) from mammalian toxicity studies was therefore determined to be 763 mg a.i./kg bw/day based on a reduction in spleen weight in female rats. The most appropriate NOAEL for local effects was determined to be 440 mg a.i./kg/bw based on epidermal hyperplasia at the site of application (dermal exposure) in male mice. Modeled estimates of environmental concentrations leading to indirect human exposure from drinking water and fish consumption (Formats C#1 and C#2) range from 1.23 $x10^{-5}$ to 2.63 x 10^{-8} mg/kg/day. The highest estimated human exposures (Format C#3) are from residuals following personal care product use. They range from 0.02-0.14 mg/kg/day for shampoos and hair conditioners to 0.11- 0.17 mg/kg-day for liquid face and hand soaps. Exposure estimates for cleaning product use and residuals on clothing range from 0.01- 0.08 mg/kg-day. All exposure evaluations include conservative (protective) input assumptions (e.g. all modeled human exposures are conservative due to use of a default assumption of 100% absorption). However, the physico-chemical data and available toxicological data suggest that dermal absorption is likely to be minimal. Consequently, the contribution to total body burden arising from dermal exposure to personal care products will be significantly less than the reported exposure values.

In the particular case of hydrotropes, use of all the noted product categories by a single consumer is plausible. A conservative estimate of aggregate daily exposure could be achieved by a simple addition of the daily exposure estimates for each of the product categories plus exposure estimates for drinking water and fish consumption. However, as stated, the body burden from dermal exposure will be significantly over-estimated and hence the margin of exposure between the calculated body burden and NOAEL would be considerably greater.

Identity of Organization

Hydrotropes Consortium
The Soap and Detergent Association, c/o Kathleen Stanton (kstanton@sdahq.org)
1500 K St. NW, Suite 300, Washington, DC 20005. USA.

Table of Contents **Page No.**

Format A: General Information

I. Substance Information

(1) Category Name:
Hydrotropes Category

(2) Substance Name(s) and CAS Numbers:
Hydrotropes are classified into one category and include the following ICCA-sponsored HPV CAS numbers and corresponding chemical names:

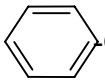
1300-72-7	xylenesulfonic acid, sodium salt
26447-10-9	xylenesulfonic acid, ammonium salt
12068-03-0	toluenesulfonic acid, sodium salt
28348-53-0	cumenesulfonic acid, sodium salt
32073-22-6	cumenesulfonic acid, sodium salt
37475-88-0	cumenesulfonic acid, ammonium salt

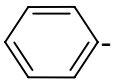
In addition, four CAS numbers that are not HPV hydrotropes and are not ICCA sponsored but are among the hydrotropes reported by the Hydrotrope Consortium member companies are:

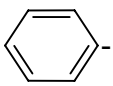
827-21-4	xylene sulfonic acid, sodium salt
28088-63-3	xylenesulfonic acid, calcium salt
30346-73-7	xylenesulfonic acid, potassium salt
16106-44-8	toluenesulfonic acid, potassium salt

Synonyms are listed in Section 1.1 of the SIAR

(3) Substance Formula and Structure:
Diagrams of sodium salts for each of the three hydrotropes (without isomer orientation) are depicted below. Commercial toluene and cumene sulfonates consist of mixtures of 3 isomers (ortho-, meta- and para-). Commercial xylene sulfonic acid consists of mixtures of 6 isomers. An ortho-isomer would have adjacent attachment points to the benzene ring; a para-isomer would have attachments at opposite ends of the benzene ring; and a meta-isomer would have one open carbon between attachments on the benzene ring.


$-CH_3$ $-SO_3Na$ toluenesulfonic acid, sodium salt


$-(CH_3)_2$ $-SO_3Na$ xylenesulfonic acid, sodium salt


$-CH.(CH_3)_2$ $-SO_3Na$ cumenesulfonic acid, sodium salt

(4) Physical Form: Solid at room temperature; melting point >100°C. Supplied to formulators as aqueous solutions (30-60% active substance) or solids containing >88 to 100% active substance.
(5) Other Constituents (If Applicable): Not applicable

II. Summary

(1) Data Collection Efforts:

Information in this assessment was assembled from a number of sources:

1) Member company surveys of the Hydrotropes Consortium (including producers and formulators representing the majority of hydrotrope production in the U.S. and Europe), The Soap and Detergent Association (SDA) (U.S.), and the Cosmetics, Toiletries and Fragrances Association (CTFA)(U.S.) were used to collect data on hydrotrope production volumes, uses, releases, and potential exposures. To protect proprietary information, an independent third party compiled the survey data. The compiled results were confirmed by comparison with a 2002 economic review in the Chemical Economics Handbook by SRI international, and US EPA's summary of 2002 Inventory Update Rule (IUR) information. (Format A).

2) The Australian Government agency the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) conducted a survey on hydrotrope production volumes, product formulations and uses, releases, and potential exposures for Australia. (Format A).

3) Potential hydrotrope exposures are estimated via conservative modelling and summarized in Format C attachments. Potential aquatic exposures resulting from hypothetical U.S. manufacturing facility upper-bound discharges to wastewater are modelled using the E-FAST model from USEPA. The modelled scenario is a general manufacturing release assessment with very high-end release assumptions, not a site specific assessment with actual release data. The model also permits estimation of indirect human exposure from drinking water and consumption of fish downstream of effluent discharges. Similarly, E-FAST is also used to estimate potential upper-bound aquatic exposures and indirect human exposures resulting from consumer use of hydrotrope-containing products (i.e., down-the-drain releases). Finally, direct, upper-bound exposures from consumer uses of products containing hydrotropes are examined using general exposure models for four exposure scenarios: 1) use of diluted liquid detergents (hand-wash of dishes, hand washing of laundry, laundry pre-treatment); 2) use of undiluted hard surface cleaning products; 3) exposure to laundry product residue on clothing (liquid and powder laundry detergents); and 4) exposure to personal care products during and after use (shampoo, hair conditioner, body wash, liquid hand & face soap).

(2) Discussions of Key Uncertainties, Limitations, Data Gaps:

Exposure estimates for aquatic life are based on releases of 100% of total production/importation volume in a geographic region. While there is some uncertainty in the precision of these estimates, the tonnages represent the data from the major manufacturers and are the volumes reported, as required, to regulatory authorities. The models used to predict receiving water concentrations are based upon conservative models that are generally accepted by authorities for screening-level evaluations. The human exposure assessment also uses a conservative (protective) approach to modelling, selecting inputs based on conservative values for each parameter. For example, all

modelled exposures include a default assumption of 100% dermal absorption of hydrotropes. This leads to an overestimate of exposure. A few of the consumer use scenarios are not modelled (e.g., toilet treatments, carpet cleaners), however, formulation information presented for all products and general knowledge of use patterns/frequency establish these scenarios as being adequately represented by the product use scenarios that are modelled in detail.

(3) Exposure Results:
The following tables show the estimated exposure for the scenarios assessed, and the PNEC or NOAEL hazard values.

Environmental Exposure Scenarios

Exposure Scenario	Concentration (µg/L)	PNEC (µg/L)
Modeled Surface Water Concentrations for Hypothetical U.S. Manufacturing Facility		
Aquatic Exposure – 0.1 tonnes/day		
Mid-size stream with average flow	16.5	
Small stream with low (7Q10) flow	286.9	2,300
Modeled Surface Water Concentrations for Consumer down-the-drain Release		
Aquatic Exposure – 28,684 tonnes/yr (~79 tonnes/day)		
Mid-size stream with average flow	0.048	
Small stream with low (7Q10) flow	0.63	2,300

Consumer Exposure Scenarios

Exposure Scenario	Estimated Exposure (mg/kg/day)	NOAEL (mg/kg/day)
Indirect Exposure – Manufacturing Effluent Modelling		
Drinking Water Consumption -		
Mid-size stream with average flow	1.1×10^{-4}	763
Small stream with low (7Q10) flow	1.56×10^{-3}	
Fish Consumption -		
Mid-size stream with average flow	4.72×10^{-8}	
Small stream with low (7Q10) flow	6.69×10^{-7}	
Indirect Exposure – Consumer down-the-drain Modelling		
Drinking Water Consumption -		
Small stream with low (7Q10) flow	1.23×10^{-5}	763
Fish Consumption -		
Small stream with low (7Q10) flow	2.63×10^{-8}	
Dermal Modelling		
Face and hand soaps (liquid)	0.11 – 0.17	
Shampoos	0.03 – 0.14	440
Hair conditioners	0.02 – 0.11	
Others – including laundry detergents, hand dishwashing liquid detergent, machine dishwashing rinse aid, hard surface cleaners and body washes	0.01 – 0.08	

Note : range of estimated exposures for dermal modelling represent the range of hydrotrope concentration in product formulations

III. Production, Import and Use

(1) Estimated Volumes (tonnes/yr):

U.S. - 28,684 (2001 data; consistent with USEPA 2002 IUR)

Europe - 19,348 (2001 data)

Australia - 1,100 (2003 data)

(2) Function/Product Use Categories:

Hydrotropes are used as coupling agents to solubilize water insoluble and otherwise incompatible functional ingredients. Major uses are in personal care and household/professional cleaning products including liquid and powder laundry detergents, hand dishwashing liquid detergents, machine dishwashing rinse aids, hard surface cleaners, body washes, shampoos, hair conditioners, liquid face and hand soaps, toilet treatments, solvent hand cleaners, carpet cleaners and optical brightener products. It is estimated that 60-70% of the total tonnage is used in dishwashing liquids. There are also some relatively small volume, commercial/professional uses in liquid sulphur textile dyes, acidic recirculation cleaners, wetting agent for tanning, enzymatic recirculation cleaner for dairy and food processing, coolant system conditioner, car wash detergents, cleaners and degreasers, vinyl plastic rubber restorer, and floor strippers.

IV. Activities, Releases and Exposures – Factors that Mitigate or Exacerbate Exposures

Manufacture

(1) Process Description:

Hydrotropes are produced by sulfonation of aromatic hydrocarbon solvents (i.e., cumene, toluene, xylene). The resulting aromatic sulfonic acid is neutralized utilizing the appropriate base (e.g., sodium hydroxide) to produce the sulfonate or hydrotrope. Liquid product is produced in a closed system. Granular product is produced by spray drying that includes source control and dust collection. Hydrotropes are manufactured for industrial/professional and consumer use and are not used as intermediates/derivatives for further chemical manufacturing processes or uses. In Australia, the process is partially closed at one site and complete closed at a second site.

(2) General Description of Potential Releases and Exposures:

Hydrotropes are water soluble (>1000 mg/L) and have very low volatility (vp ~1 $x10^{-9}$ Pa). They are effectively removed in biological wastewater treatment (~94%) and are rapidly and completely biodegraded (>60% in ≤28 days). These characteristics reduce environmental exposure. Based on EQC Level I modelling (i.e., environmental partitioning estimation as detailed in Mackay et al., 1996 and included in Format C), hydrotropes do not partition to any significant degree into soil, sediment, air or biota. The water compartment is the focus for environmental exposure.

For Australia:

Exposures: For facility with partially closed process, unheated, pumped solution is manually packaged into drums. Takes approximately 30 hours and is done 6 times per year.

For U.S.:

Releases: Potential releases to the environment include some stack emission, discharge to wastewater treatment systems and to landfills. Daily release to wastewater treatment is estimated at 0.15% (USEPA default process loss) of annual volume of chemical produced at typical U.S. facility.

Exposures: Estimated receiving water exposures are provided in Format C. Workplace occupational exposures are possible as a result of dermal contact and/or inhalation and ingestion of dust, but are not further quantified.

(3) Discussion of Factors that Decrease or Increase Releases and Exposures:

For Australia:

For facility with partially closed process, there is general and point source ventilation, workers wear goggles, protective clothing, and gloves (acid resistant). For facility with closed process, there is exhaust ventilation; workers wear overalls, eye protection, protective footwear and rubber gloves.

For U.S.:

Environmental releases are regulated as part of overall facility emissions. Mitigation includes using good manufacturing practices, best available technology and engineering controls. As a result of engineering controls (e.g., exhaust ventilation systems and dust collection) and personal protective equipment (e.g., protective clothing, eyewear and gloves) that would normally be in place at facilities that manufacture liquid and granular materials and/or that formulate products with hydrotropes, the exposure incidental to hydrotropes is decreased. No special engineering controls or additional personal protective equipment are specified for hydrotropes. MSDS information and product labels for the hydrotropes themselves instruct persons to avoid contact with skin and eyes and to wear eye protection and gloves when handling.

(4) Remarks:

Formulation
(1) Volumes: Essentially all the production volume of hydrotropes is going into product formulation.
(2) Process Description: Depending upon the amount of formulated product and level of hydrotrope, hydrotropes can be received in a variety of ways, from totes to truck trailers to rail cars. In Australia, liquid products are formulated by decanting pump or direct manual addition. For example, hand pumping from 200 L drums into 25 liter pails which are then sealed until required for formulation. Packing processes include: gravity filling by weight into packs ranging from 10-1000 liters; hydraulic filling of small packs by volume; semi-manual decanting through a hose with tap and dip-leg; semi-automated dosing; and pump through filling lines to bulk storage tanks. No heating was involved at any stage. For granular product, there is a partially closed process where bags containing the pellet form are cut open and added to a tank via a manhole. Addition time is 10 minutes, total mix time is 8 hours, approximately 5 batches per year. This is a heated process (60-65 °C). Samples are collected with a scoop and there are both automated and manual packing processes. In the U.S., for liquid dish or laundry cleaning products, hydrotropes are received in trailers, rail cars or tankers and pumped into heated storage tanks (32-50°C) to prevent salt precipitation. Dish or laundry products can be produced in continuous liquids process (CLP) or batch processes that consist of pipes, mixing tanks, mixers, pumps, heat exchangers, fillers and packaging equipment. The hydrotropes are added to the formulation by controlled flow in-line injection or pumping (batch). The CLP is a completely closed system. The batch system is partially closed.
(3) General Description of Potential Releases and Exposures: Product formulation, the blending of hydrotropes with other ingredients, is not expected to result in releases or workplace or environmental exposures that exceed those for hydrotrope production facilities. For Australia: Formulation processes ranged from open to partially-closed to fully enclosed. The chemical was added to tanks via decanting, pump, or direct manual addition. Batches on average took 2-4 hours, although some were longer (e.g., one full day), and were done daily, to several times a week, to once or twice a year. No atmospheric monitoring is undertaken during this process.
(4) Discussion of Factors that Decrease or Increase Releases and Exposures: For Australia: No heating of the product was involved at any of the sites. PPE was worn at all sites. For U.S.: Environmental releases are regulated as part of overall facility emissions. Mitigation includes using good manufacturing practices, best available technology and engineering controls. As a result of engineering controls (e.g., exhaust ventilation systems and dust collection) and personal protective equipment (e.g., protective clothing, eyewear and gloves) that would normally be in place at facilities that manufacture liquid and granular materials and/or that formulate products with hydrotropes, the incidental exposure to hydrotropes is decreased. No special engineering controls or additional personal protective equipment are specified for hydrotropes. MSDS information and

product labels for the hydrotropes themselves instruct persons to avoid contact with skin and eyes and to wear eye protection and gloves when handling.
(5) Remarks:

Commercial/Occupational (or Industrial) Use
(1) Volumes: In Australia, approximately 55 tonnes per year is used as an ingredient in liquid sulphur textile dyes present at 7.5 – 50%, acidic recirculation cleaning present at 10-25%, wetting agent for tanning industry present at 10%, enzymatic recirculation cleaner for dairy and food processing applications at 4%, coolant system conditioner at 6.9%, car wash detergents at 1.3–6.3%, cleaners and degreasers at 0.1–6.3%, vinyl, plastic rubber restorer at 0.2% and floor stripper at 2.7–9 %. In U.S., the fraction of the total 28,684 tonnes per year is not quantified, however, commercial/professional products include hard surface cleaner products where hydrotropes are present at 0.1 to 5.0%.
(2) Process Description: In Australia, information was available on the use textile dyes containing hydrotropes to dye cotton and viscose fibers. Dyes are transferred from 1000 L transport tanks to storage tanks in a closed process. The tanks in which dying takes place are also enclosed. After passing through a dye bath the fabric is subjected to a steam process for the dye to react with the fabric fibers. The fabric then passes through water baths with oxidizing agent to fix the dye to the fabric. Steaming and washing operations and subsequent fabric drying all take place within enclosed systems with exhaust ventilation.
(3) General Description of Potential Releases and Exposures: (a) Releases: Environmental release from down-the-drain discharges following product use. (b) Exposures: Receiving waters may be exposed to hydrotropes following wastewater treatment. Dermal exposure may occur with commercial/professional product use. Exposure from incidental / accidental ingestion, inhalation, and/or eye contact is expected to be less than for dermal contact. In Australia, any waste liquor from the dyeing operation will be highly diluted as a result of large volumes of water which is used for washing off the oxidized dyestuff. No skin contact by workers is expected due to the enclosed or semi-enclosed tank systems in use and precautionary PPE.
(4) Discussion of Factors that Decrease or Increase Releases and Exposures: Hydrotropes are highly water soluble (>1000 mg/L) and have very low volatility (vp ~1 x10^{-9} Pa). They are effectively removed in biological wastewater treatment (~94%) and are rapidly and completely biodegraded (>60% in ≤28 days). These characteristics reduce environmental exposure. Human exposure via inhalation is likely minimal due to low volatility of hydrotropes. Dermal exposure is minimised by use of personal protective equipment. In the Australian dyeing operation, waste liquids are processed via a settling pond and on-site water treatment plant. Operators are equipped with protective gloves, glasses and protective clothing.
(5) Remarks: Human exposures are not modelled separately for commercial/occupational (industrial) uses in this evaluation since the consumer use scenario would represent a more highly exposed individual as a result of frequency of use and the direct application to skin of products containing hydrotropes.

Consumer Use

(1) Function/ Product Use Description:
Hydrotropes are expected to have wide spread and dispersive uses in the following consumer products:

Product Type	Concentration in Products in U.S. (range)	Concentration in Products in Australia (range)
laundry detergents		0.9 - 1.375%
- powders	0.1 – 0.5 %	
- liquids	1 – 10 %	
hard surface cleaners, including dilutable forms	0.1 – 5.0 %	0.1 - 0.9%
machine dishwashing rinse aid	1 – 5%	4.1 - 5.5%
hand dishwashing liquid detergents	1 – 5 %	1.2 - 5.5%
body washes	0.1 – 0.5 %	-
shampoo	1 – 5 %	0.4 - 0.8%
hair conditioner	1 – 5 %	-
face and hand soap (liquid)	10 – 15 %	-
toilet treatments	-	0.2%
solvent hand cleaner	-	0.8%
carpet cleaners	-	1%
optical brightener product	-	3%

Except where noted, the concentration (%) in products shown above is in the formulated product and does not take into account any dilution prior to or during use.

(2) General Description of Direct Exposures to Private (Consumer) Products and of Potential Releases to the Environment Leading to Ecological Exposures and Indirect Human Exposures:
(a) Releases: Environmental release from down-the-drain discharges following product use.
(b) Exposures: Receiving waters may be exposed to hydrotropes following wastewater treatment. Exposure estimates are presented in Format C.
The personal care products are applied as is, typically diluted during use and then rinsed off. Dermal contact does occur with personal care products and may occur with laundry and/or cleaning products. There is some potential for incidental / accidental ingestion of, inhalation of, and/or eye contact with product during handling and use. Personal care products are likely to be used daily. Laundry and cleaning products may be used as is, or diluted prior to or during use. Exposure estimates are presented in Format C.

(3) Discussion of Factors that Decrease or Increase Releases and Exposures:
Hydrotropes are highly water soluble (>1000 mg/L) and have very low volatility (vp ~1 x10^{-9} Pa). They are effectively removed in biological wastewater treatment (~94%) and are rapidly and completely biodegraded (>60% in ≤28 days). Based on physico-chemical properties, the potential for bioaccumulation in aquatic organisms is low. These characteristics reduce environmental exposure. Human exposure as a result of using laundry/cleaning products is decreased by following use/precaution instructions on product labels. Product labels are written to reflect the entire range of chemical components in any given product. Laundry and cleaning products might include eye and skin irritancy cautionary and first aid information (e.g., to rinse thoroughly if exposed). Low volatility minimizes the potential for inhalation. Human exposure as a result of using personal care products will be reduced for those that are washed/rinsed off. Exposures may increase by frequent and concurrent use of one or more consumer products.

(4) Remarks :
Direct oral exposures are not modelled in this evaluation since these would only occur via accidental ingestion. None of the uses of hydrotropes are in products intended for human consumption. Potential oral indirect exposure via drinking water and fish ingestion are included in Format C #1 and #2. Also not modeled is indirect oral exposure from deposition on dishes washed with products containing hydrotropes. Due to the use of dilute solutions of dishwashing products and the rinsing/draining of dishes following the wash, exposure from this source is considered to be insignificant compared to the direct, dermal exposures that are modelled. A few products with very low hydrotrope concentrations and/or products that are infrequently used are not modelled (e.g., toilet treatment, carpet cleaners). Potential exposures from these products are considered negligible compared to the products that are modeled.

Format B: Monitoring Evaluations

I. Identification Information

(1) Study Title: None available
(2) Activity Associated with Monitoring Information: Monitoring not considered necessary for exposure assessment of the hydrotropes category. Conservative modelling exposure estimates (see format C) indicate low concern associated with human and environmental exposures. In addition, these chemicals are well removed in wastewater treatment, are rapidly and completely biodegraded, and have low potential for bioaccumulation following environmental release.

II. Monitoring Study Design

(1) Monitoring Study Objective and Scenario Description:

III. Sampling and Analytical Methods

(1) Media Sampled:
(2) Sampling:
(3) Method/ Procedure:

IV. Results and Reliability Description

(1) Results:
(2) Reliability Rating:
(3) Remarks:

FORMAT C: MODELING EVALUATION #1
Release and Exposure from US Production Facility

I. Identification Information

(1) Activity Associated with Modeling Information: U.S. manufacturing/production facility effluent discharge – Environmental exposure including both aquatic life and indirect human exposure

II. Modelling Objective

(1) Modeling Study Objective: Screening level estimate (high-end to bounding) of surface water concentration as well as aquatic life, drinking water and fish consumption exposures as a result of manufacturing/production facility effluent discharge.
(2) Description of Modeled Scenario: Accounts for wastewater treatment, in-stream dilution and bioaccumulation potential. Daily process loss/release is estimated at 0.15% (USEPA default process loss) of annual volume of chemical produced. Daily release estimated for a hypothetical "largest" U.S. manufacturing facility and assumes 350 days of operation per year (15 days for annual maintenance). The modelled scenario is a general manufacturing release assessment with very high-end release assumptions (e.g., half the total U.S. production is from this single, hypothetical facility), not a site specific assessment with actual release data. Release from formulation process is not expected to exceed those for production facility.

III. Description of Model and Model Validation/ Peer Review

(1) Tool or Model: E-FAST (Exposure & Fate Assessment Screening Tool); Provides screening level estimates of the concentrations of chemicals released to the environment from industrial discharge. Designed to provide high-end to bounding estimates of exposure. Chemical-specific and facility-specific data or defaults can be used. Modeling conducted 2003.
(2) Validation/ Peer Review: Standard model (USEPA 2002) used by USEPA Office of Pollution Prevention and Toxics in screening level assessments
(3) Availability and Documentation: www.epa.gov/oppt/exposure/docs/efast.htm

IV. Inputs, Outputs, and Quality Description

(1) Media Modeled: Surface water, drinking water and edible fish tissue
(2) Inputs: Pre-treatment release (process losses) per facility = 0.1 tonnes (or 100 kg)/day; estimated as follows: - 28,684 tonnes/yr = annual production - 82 tonnes/day = daily production assuming 350 days/year

- 0.123 tonnes/day = daily process loss assuming 0.15% loss
- based on survey conducted by SDA, no single facility produces more than half the total annual production, therefore a conservative assumption is that the maximum daily process loss for a single facility is 0.123 tonnes (or 123 kg)/day or one-half the total daily process loss for the total USA production.

SIC Code is Soaps, Detergents, etc. Manufacture (2841-2844)
Release days = 350
Wastewater treatment removal = 94%
BCF estimate <1 based on log Kow <1.0 (based on BCFWIN model; USEPA 2003)
PNEC = 2.3 mg/L (lowest EC_{50} for 3 species [fish, daphnid and algae] = 230 mg/L ÷ 100 = 2.3 mg/L) = 2,300 µg/L; where 100 is the recommended assessment factor (Cowan et.al., 1995; OECD 2003; EU 2003).

(3) Model Outputs :
Results following wastewater treatment; where 50% ile represents a large facility on a mid-size stream and 10% ile represents a large facility on a small stream. Two stream flow scenarios (7Q10 = low flow ; mean flow) are modelled.

Aquatic life exposure -
50% ile facility -
Mean stream concentration = 5.9 µg/L
7Q10 stream concentration = 16.5 µg/L
[7Q10 is the lowest 7-day average flow in a year that occurs during 7 consecutive days on average once every 10 years]
10% ile facility -
Mean stream concentration = 83.4 µg/L
7Q10 stream concentration = 286.9 µg/L

Drinking water exposure -
50% ile facility -
Average Daily Dose (ADD) =
1.1×10^{-4} mg/kg/day (chronic non-cancer)
10% ile facility -
Average Daily Dose (ADD) =
1.56×10^{-3} mg/kg/day (chronic non-cancer)

Fish consumption exposure –
50% ile facility -
Average Daily Dose (ADD) =
4.72×10^{-8} mg/kg/day (chronic non-cancer)
10% ile facility -
Average Daily Dose (ADD) =
6.69×10^{-7} mg/kg/day (chronic non-cancer)

(4) Reliability Rating:
The reliability rating is 2 (reliable with restrictions). The model has not been validated but is sufficiently conservative and accepted by authorities. The modelling for hydrotropes falls into the applicability domain of the model and appropriate (conservative) inputs were used. Modelling can be useful in first tier approach for exposure assessment. Model outputs reflect E-FAST model assumptions that are designed to provide high-end to bounding estimates of exposure.

(5) Remarks:
The aquatic PNEC = 2300 ug/L (as described in "(2) Inputs"). The high-end to bounding PEC estimates range from 3.9 to 286.9 µg/L and include medium size stream with average flow to small stream with low (7Q10) flow. The most appropriate NOAEL for an oral exposure scenario is 763 mg a.i./kg bw/day based on a reduction in spleen weight in female rats. The highest estimated average daily doses (ADDs) are 1.56 $x10^{-3}$ mg/kg/day (drinking water) and 6.69 $x10^{-7}$ mg/kg/day (fish consumption) for the small stream and low (7Q10) flow scenario.

Format C: Modelling Evaluation #2
Release and Exposure from Consumer Use

I. Identification Information

(1) Activity Associated with Modelling Information: U.S. wastewater treatment facility effluent discharge following consumer use and down-the-drain disposal; environmental exposure including both aquatic life and indirect human exposure.

II. Modelling Objective

(1) Modelling Study Objective and Scenario Description: Screening level estimate (high-end to bounding) of surface water concentration (including drinking water and fish consumption exposures) as a result of daily consumer usage of personal care and cleaning products.
(2) Description of Modelled Scenario: Down-the-drain release of total U.S. annual production volume into total volume of U.S. municipal wastewater system. Accounts for wastewater treatment and in-stream dilution. Accounts for bioaccumulation potential.

III. Description of Model and Model Validation

(1) Tool or Model: E-FAST (Exposure & Fate Assessment Screening Tool): Provides screening level estimates of the concentrations of chemicals released to the environment from consumer products. Designed to provide high-end to bounding estimates of exposure. Chemical specific data or defaults can be used. Modelling conducted 2003.
(2) Validation/ Peer Review: Standard model (USEPA 2002) used by USEPA Office of Pollution Prevention and Toxics in screening level assessments.
(3) Availability and Documentation: www.epa.gov/oppt/exposure/docs/efast.htm

IV. Inputs, Outputs, and Quality Description

(1) Media Modelled: Surface water, drinking water and edible fish tissue.
(2) Inputs: Release = 28,684 tonnes/yr = annual USA production Wastewater treatment removal = 94% BCF estimate <1 (based on log Kow <1) (based on BCFWIN model; USEPA 2003) PNEC = 2.3 mg/L (lowest EC_{50} for 3 species [fish, daphnid and algae] is 230 mg/L ÷ 100 = 2.3 mg/L) = 2,300 µg/L; where 100 is the recommended assessment factor (Cowan et.al., 1995; OECD 2003; EU 2003).

(3) Model Outputs:

Aquatic life exposure -

The surface water concentration estimate under median stream flow conditions = 0.048 µg/L. The surface water concentration estimate under low stream flow (7Q10) conditions = 0.63 µg/L. Indirect human exposure estimates under low stream flow (7Q10) conditions are:

Drinking water exposure :

Average Daily Dose (ADD) =
1.23×10^{-5} mg/kg/day (chronic non-cancer)

Fish consumption exposure :

Average Daily Dose (ADD) =
2.63×10^{-8} mg/kg/day (chronic non-cancer)

(4) Reliability Rating:

The reliability rating is 2 (reliable with restrictions). The model has not been validated but is sufficiently conservative and accepted by authorities. The modelling for hydrotropes falls into the applicability domain of the model and appropriate (conservative) inputs were used. Modelling can be useful in first tier approach for exposure assessment. Model outputs reflect E-FAST model assumptions that are designed to provide high-end to bounding estimates of exposure.

(5) Remarks:

The aquatic PNEC = 2300 µg/L (as described in "(2) Inputs"). The high-end to bounding PEC estimates range from 0.048 to 0.63 µg/L and include medium size stream with average flow to small stream with low (7Q10) flow. The most appropriate NOAEL for an oral exposure scenario is 763 mg a.i./kg bw/day based on a reduction in spleen weight in female rats. The highest estimated average daily doses (ADDs) are 1.23×10^{-5} mg/kg/day (drinking water) and 2.63×10^{-8} mg/kg/day (fish consumption) for the small stream and low (7Q10) flow scenario.

Format C: Modelling Evaluation #3
Dermal Exposures from Consumer Uses of Products

I. Identification Information

(1) Activity Associated with Modelling Information:
Human dermal exposures from use of laundry/cleaning and personal care products.

II. Modelling Objective

(1) Modelling Study Objective:
The objective of the dermal exposure model for consumer product uses is to estimate "screening" levels of human exposure (in daily dose, i.e. mg/kg/day) and compare to the most sensitive toxic endpoint (e.g. lowest NOEL/NOAEL) in order to assess exposure and risk potential. Exposure and risk estimations could then be subjected to further refinement as needed. Because of the conservative nature of the screening level assessment, when product uses are determined to be of low concern, no further evaluation would be conducted.

(2) Description of Modelled Scenarios:
Dermal exposures to hydrotropes that are modelled include:

Exposure during the activity/use of products[1]
Laundry detergent: hand washing clothes
Laundry detergent: pre-treatment
Dishwashing liquid detergents: hand washing dishes
Hard surface cleaners (diluted and undiluted)

[1)] Exposure during the activity/use of personal care products are not modelled because these exposures (lasting just minutes) are very small in comparison to exposure to residuals that last until the next use (e.g., for a day).

Exposure from residuals on clothing
Laundry detergents on clothing following washing

Exposure from residuals after using products

Shampoos	Face and hand soap (liquid)
Hair conditioners	Body washes

The exposure scenarios encompass conservative, screening-level assumptions including: the high-end frequency of product use, the high-end amount of product per use, the high-end percent of product retained on skin or clothes following use, and 100% dermal absorption. SDA member companies provided formulation information and the entire range of hydrotropes in specified product types are used in this assessment. Direct oral exposures are not modelled in this evaluation since these would only occur via accidental ingestion. None of the uses of hydrotropes are in products intended for human consumption. Incidental oral exposure via drinking water and fish ingestion are included in Format C#1 and C#2. Inhalation exposures are not modelled for hydrotropes. Trigger-spray hard surface cleaners have the potential to aerosolize product, however, the low volatility of hydrotropes and the relatively infrequent use of these products (in comparison to products involving dermal contact) was the basis for not including an inhalation modelling scenario.

III. Description of Model and Model Validation

(1) Tool or Model:

The modelling presented here uses simple, first principle equations, which, when combined with conservative (protective) input values err on the side of being protective.

General Exposure Model

Potential Chemical Exposure (PE) =
Exposure to Product (EXP) x Chemical Concentration in Product Formulation (PF)

Dermal Exposure

1. **Exposure during the activity/use of diluted and undiluted laundry and dishwashing products, and diluted and undiluted hard surface cleaning products:**

$$\frac{[FQ \times CA \times PC \times FT \times CF \times TF \times DA]}{BW} \times PF$$

2. **Exposure to laundry product residual on clothing:**

$$\frac{[A \times PR \times PT \times DA \times CF]}{BW} \times PF$$

["FQ" (frequency of use) is 1 wash load/day for clothing]

3. **Exposure to residual after using personal care products:**

$$\frac{[FQ \times A \times PR \times DA \times CF]}{BW} \times PF$$

Where:

FQ: frequency of use (use/day)
CA: body surface contact area (cm^2)
PC: product concentration (g/cm^3)
FT: film thickness on skin (cm)
CF: conversion factor (1000 mg/g)
TF: time scaling factor (unit less)
DA: dermal absorption (%)
BW: female body weight (kg)
A: amount per use (g/day or g/wash)
PF: Hydrotrope concentration in product formulation (%)
PR: percent retained on clothing or on skin (%)
PT: percent transferred from clothing to skin (%)

(2) Validation/ Peer Review:

These exposure calculations use first principle equations and are mathematically consistent with EPA Exposure Guidelines (1992) with regard to modelling dermal doses.

(3) Availability and Documentation:

USEPA 1992. Guidelines for Exposure Assessment. Washington, DC. Office of Research and Development, Office of Health and Environmental Assessment. EPA/600/Z-92-001.

IV. Inputs, Outputs, and Quality Description

(1) Media Modeled:

The exposure media are the hydrotrope-containing products used by consumers. The Hydrotrope Consortium fielded a survey among producers and formulators to provide the range of hydrotrope contained in each of the product forms. For each product category containing hydrotropes, the minimum and maximum of the range was utilized as inputs for the dermal exposure models. The product formulations reported by Australia (also shown in Format A) are generally comparable; therefore, the human exposure estimates can be considered representative of uses in both countries.

(2) Inputs:

1. Exposure during the activity/use of diluted and undiluted laundry and dishwashing products, and diluted and undiluted hard surface cleaning products:

$$\frac{[FQ \times CA \times PC \times FT \times CF \times TF \times DA]}{BW} \times PF$$

	Laundry Pre-treatment	Laundry Hand-wash	Hand Wash Dishes	Hard Surface Cleaners
FQ (use/day)	1 [a]	1 (liq.and powd.) [a]	3 [a]	1 [d]
CA (cm^2)	360 [b]	1680 [f]	1680 [f]	360 [b]
PC (g/cm^3)	0.6 [a]	0.01 [a]	0.0015 [a]	0.2 [a]
FT (cm)	0.0024 [c]	0.0024 [c]	0.0024 [c]	0.0024 [c]
CF (1000mg/g)	1000	1000	1000	1000
TF (unitless)	0.007 [d]	0.007 [d]	0.03 [d]	0.014 [a]
DA (%) [h]	100%	100%	100%	100%
Female BW (kg)	60 [e]	60 [e]	60 [e]	60 [e]
PF (%)[g]	1-10% (liquid) 0.1-0.5% (powder)	1-10% (liquid) 0.1-0.5% (powder)	1-5%	0.1-5%

References:
a: SDA Habit and Practice Survey
b: Palms surface area (USEPA Exposure Factors Handbook)
c: USEPA 1985 (Methods of assessing exposure to chemical substances)
d: HERA project 2002
e: female body weight (USEPA Exposure Factors Handbook)
f: hands and forearms (USEPA Exposure Factors Handbook)
g: Hydrotrope Survey, Min-Max values (see table in section IV. Consumer Use (1))
h: default assumption

2. Exposure to laundry product residual on clothing:

$$\frac{[A \times PR \times PT \times DA \times CF]}{BW} \times PF$$

	Liquid Laundry detergent	Powder Laundry detergent
A (g/wash)	121[a]	121[a]
PR (%)	1%[a]	1%[a]
PT (%)	1%[a]	1%[a]
DA(%)	100%[b]	100%[b]
CF (mg/g)	1000	1000
BW (kg)	60 [c]	60 [c]
PF (%)	1-10%[d]	0.1-0.5%[d]

References:
a: SDA Habit and Practice Survey
b: Default assumption
c: female body weight (USEPA Exposure Factors Handbook)
d: Hydrotrope Survey, Min-Max values (see table in section IV. Consumer Use (1))

3. Exposure to residual after using personal care products:

$$\frac{[FQ \times A \times PR \times CF \times DA]}{BW} \times PF$$

	Shampoo	Hair Conditioner	Body Wash	Hand & Face Soap (liquid)
FQ	1[a]	1 [a]	1[a]	8[a]
A	16.4[a]	12.7[a]	12 [a]	1.7[a]
PR	1% [b]	1% [b]	0.5% [a]	0.5% [a]
CF	1000	1000	1000	1000
DA[e]	100%	100%	100%	100%
BW	60 [c]	60 [c]	60 [c]	60 [c]
PF[d]	1-5%	1-5%	0.1-0.5%	10-15%

References:
a: SDA Habit and Practice Survey
b: CTFA 2003 data; Min-Max values
c: female body weight (EPA Exposure Factors Handbook)
d: Hydrotropes Survey, Min-Max values (see table in section IV. Consumer Use (1))
e: Default assumption

(3) Model Outputs:

Product Category	Dermal – potential exposure (mg/kg/day) [a]
Face and hand soaps (liquid)	0.11 – 0.17
Shampoos	0.03 – 0.14
Hair conditioners	0.02 – 0.11
Others [b]	0.01– 0.08

Footnotes:
a: range based on Min. and Max. "PF" values (i.e., hydrotrope concentration in product formulation)
b: includes laundry detergent (powders and liquids), machine dishwashing rinse aid, hand dishwashing liquid detergent, hard surface cleaners and liquid body washes

(4) Reliability Rating:

The reliability rating is 1 (reliable without restrictions). The model used first principal equations, which are sufficiently conservative, have undergone peer review and are generally accepted by authorities. The modelling for hydrotropes in consumer products falls into the applicability domain of the model and appropriate (conservative) inputs were used. The model used is applicable for screening-level assessment. The selected model inputs reflect best available information and conservative estimates where applicable (i.e., high-end frequency of product use, high-end amount of product per use, high-end percent of product retained, and 100% dermal absorption).

(5) Remarks:
Indirect oral exposure from deposition on dishes was not modelled. Due to the use of dilute solutions of dishwashing products and the rinsing/draining of dishes following the wash, exposure from this source is insignificant compared to the direct, dermal exposures that are modelled. A few products with very low hydrotrope concentrations and/or products that are infrequently used are not modelled (e.g., toilet treatments, carpet cleaners). Potential exposures from these products are considered negligible compared to the products that are modeled. In the particular case of hydrotropes, use of all the noted product categories by a single consumer is plausible. That is, an individual could be using laundry cleaning products, machine and/or hand dishwashing detergents, hard surface cleaners, liquid body wash, face and hand soap, shampoos and hair conditioners. A conservative estimate of aggregate daily exposure could therefore be achieved by a simple addition of the daily exposure estimates for each of the product categories. Exposure estimates for drinking water and fish consumption (Format C, Model Evaluation #1 (production facility) and #2 (consumer use); section IV (3) in each) could be added to the total as well.

Appendix 1: References

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European Union (EU) 2003. Technical Guidance Document on Risk Assessment in Support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances. 337 pp.

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Hydrotropes Survey. 2002. Survey of production, use and exposure information provided by the member companies of the Hydrotropes Consortium and the SDA HPV Task Force.

Mackay, D, A DiGuardo, S Peterson and C Cowan. 1996. Evaluating the Environmental Fate of a Variety of Types of Chemicals Using the EQC Model. *Environ. Toxicol.Chem*. **15(9)**: 1627-1637.

OECD. 2003. Manual for Investigation of HPV Chemicals. http://www.oecd.org/document/7/0,2340,en_2649_34379_1947463_1_1_1_1,00.html

SDA Habit and Practice Survey. 2002. Survey conducted by the Soap and Detergent Association and its member companies.

USEPA. 1985. Methods of assessing exposure to chemical substances. Vol. 7, Versar. EPA 560/5-85-007.

USEPA. 1987. Exposure Factors Handbook. August 1987.

USEPA. 1992. Guidelines for Exposure Assessment. Washington, DC. Office of Research and Development, Office of Health and Environmental Assessment. EPA/600/Z-92-001.

USEPA. 2002. E-FAST model. Office of Pollution Prevention and Toxics. Washington, DC. http://www.epa.gov/oppt/exposure/docs/efast.htm

USEPA 2003. BCFWIN model in EPI Suite. http://www.epa.gov/oppt/exposure/docs/episuitedl.htm

Appendix 2: Data Search Strategy

Consortium member companies contributed in-house studies of physical-chemical properties, environmental fate and transport, ecotoxicity, and mammalian toxicity for the chemicals in the category. To supplement the industry data, literature searches were conducted employing a strategy utilizing databases available from the U.S. Chemical Information Systems and the European International Uniform Chemical Information Database (IUCLID) and Institute for Systems, Informatics and Safety (ISIS) Environmental Chemicals Data Information Network (ECDIN) databases. These databases include:

- Registry of Toxic Effects of Chemical Substances (RTECS)
- Hazardous Substances Database (HSDB)
- Aquatic Toxicity Information Retrieval (AQUIRE)
- Toxic Substances Control Act Test Submissions (TSCATS)
- Integrated Risk Information System (IRIS)
- The Environmental Teratology Information Center (ETIC)
- The Developmental and Reproductive Toxicology Database (DART)
- The Catalog of Teratogenic Agents (CTA)
- ENVIROFATE, DATALOG, AQUIRE, PHYOTOX and TERRATOX
- Chemical Carcinogenesis Research Information (CCRIS)
- The Environmental Mutagen Information Center (EMIC)
- GENETOX
- Sax's Dangerous Properties of Industrial Materials
- Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles
- International Uniform Chemical Information Database (IUCLID)
- Environmental Chemical Data Information Network (ECDIN)
- TOXLINE
- www.chemfinder.com
- Standard scientific data compendia such as Verschueren (1996), CRC Handbook of Chemistry and Physics and The Merck Index.

CAS Registry Numbers were used to match records available in each database. All reports identified were subject to a reliability check for determining adequacy in developing the Robust Summaries.

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

CASE STUDY: TRICLOCARBAN (TCC)

Data Availability and Screening Level Assessment

Triclocarban
CAS #: 101-20-2

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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

CASE STUDY: TRICLOCARBAN (TCC)

[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

($C_{13}H_9Cl_3N_2O$):

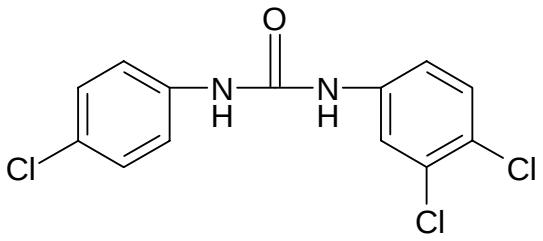

Figure 1. Structure of Triclocarban

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 (µg/L)	PNEC (µg/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

	RESULT	Unit	REFERENCE
Molecular Weight	315.6	g/mol	Hawley's Chemical Dictionary, 11th ed.
Melting Point	250	^oC	Hawley's Chemical Dictionary, 11th ed.
Boiling Point	>300	^oC	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^oC	Bayer AG data; MPBWIN ver1.65, EPIWIN Estimation Program; Modified Grain Method
Partition Coefficient	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 μg/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 μg/L	OECD Guideline 202
Chronic toxicity to fish	***Pimephales promelas***	NOEC (35 day) = 5 μg/L	Critical 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.

	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:

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 µg/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 µg/L, and the high-end concentration was 0.017 µg/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 μg/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.

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

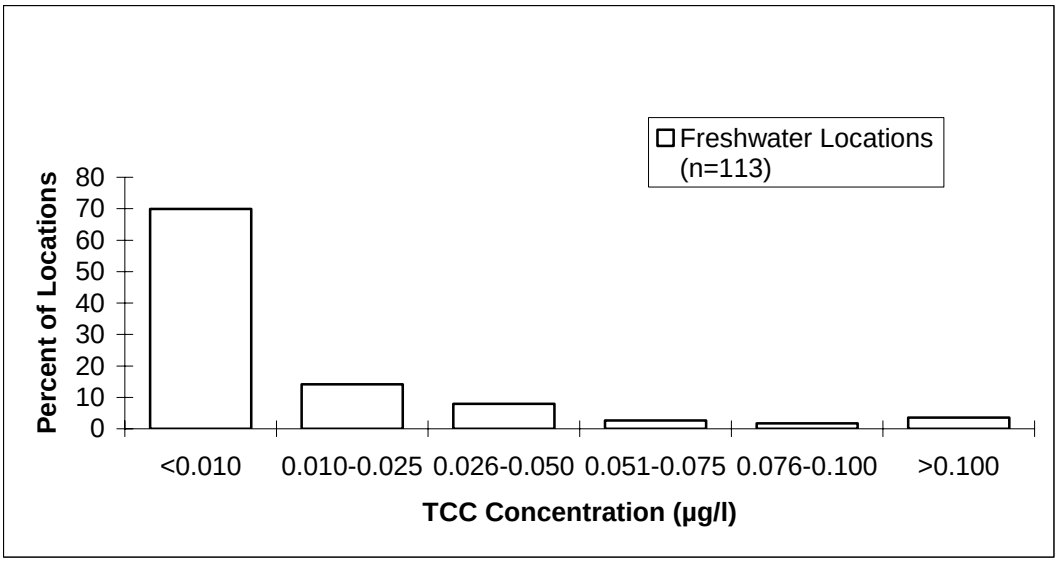

Table 2.5. Measured Concentrations of TCC in U.S. Surface Waters in 1985 and 1987.

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 µg/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 (μg/L)	PNEC (μg/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

[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 μg/plate in the preliminary toxicity dose range-finding studies and 125-4000μg/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 μg/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 not a primary irritant, a fatiguing agent, or 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)

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):

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

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

Assumptions:

1. Product is used an average of 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):

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

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

Assumptions:

1. Product is used an average of 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 1.36×10^{-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 1.38×10^{-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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