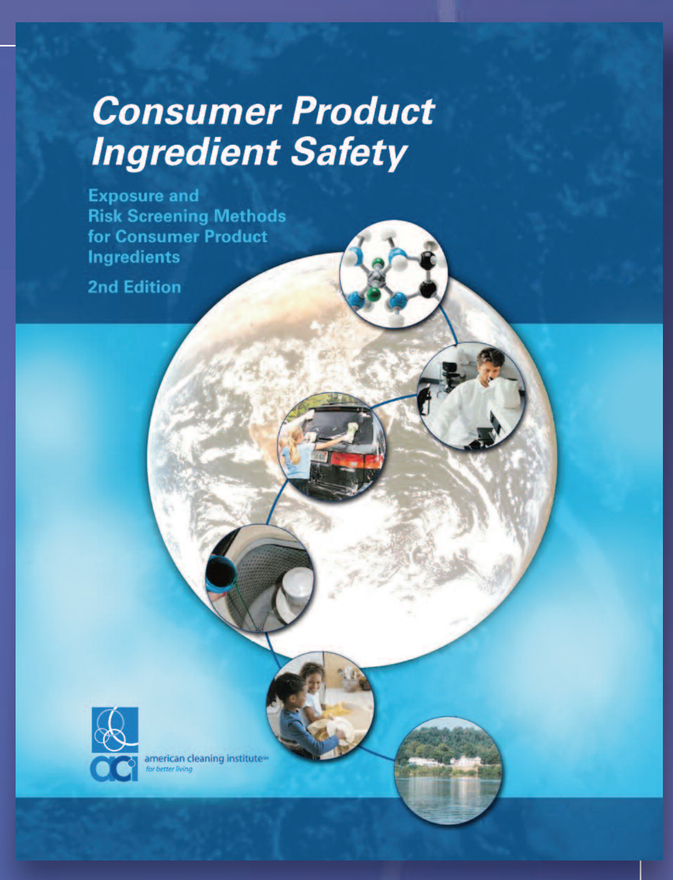
Consumer Product Ingredient Safety:

Exposure and Risk Screening Methods for Consumer Product Ingredients – Human Safety.

C.E. Cowan-Ellsberry[1], R.I. Sedlak[2], P.C. DeLeo[2], H. Sanderson[3]

1. CE[2] Consulting, LLC, Cincinnati, OH USA
2. American Cleaning Institute (formerly The Soap and Detergent Association), Washington, DC, USA
3. Aarhus University, National Environmental Research Institute, Roskilde, Denmark



Introduction/Abstract

In support of ongoing chemical management programs around the world that are focused on both legacy and high production volume (HPV) chemicals, the American Cleaning Institute (formerly The Soap and Detergent Association) compiled a book that presents methodologies and specific consumer exposure information that can be used for screening-level risk assessments of environmental and human exposures to chemicals through the manufacturing and use of consumer products, mainly laundry, cleaning, and personal care products. The screening-level risk assessment approach can be applied to other consumer products when manufacturing and consumer use information is available. These screening-level risk assessment methods use 1) available exposure information, 2) simple models that are widely accepted by the scientific and regulatory communities and 3) deliberately conservative default assumptions to compensate for gaps in the data and uncertainties, and to avoid risk decisions based on "false negatives." These methodologies allow hazard information to be put into context by using exposure information to characterize risk. Screening-level risk assessments are efficiently used to prioritize chemicals for future work. More refined assessments, which are designed to closely simulate a particular exposure scenario, can be conducted based on the results of the screening-level risk assessment, if warranted.

Framework for Human Health Screening-Level Risk Assessment

$$\text{Margin of Exposure (MOE)} = \frac{\text{Dose — Response Threshold}}{\text{Product Exposure (PE) X Ingredient Concentration (IC)}}$$

1) Selection of Dose-Response Threshold for screening-level risk characterization is based on No Observed Adverse Effect Level (NOAEL) by considering:

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

2) Product Exposure (PE) is based on:

- Screening exposure equations and input parameters derived from government and non-government sources including government agency documents, consumer product manufacturers' surveys regarding product use, habits-and-practices data, and the published literature.
- A Product Exposure (PE) data matrix provides 1) exposure factors (e.g., frequency of use, duration of use, amount of use per occasion), and 2) equations used to estimate dermal, oral, and inhalation exposure. Conservative exposure factors (e.g., high-end frequency of product use, longer duration of product contact, largest amount of product use per occasion) are used.
- These exposure factors result in a PE value for that route of exposure and type of exposure scenario.

3) Ingredient concentration (IC) ranges:

- For conducting a screening-level assessment, minimum and maximum Ingredient Concentrations (IC) for an entire category of chemicals were generated for each product use category based on a survey of companies using the ingredient in their products.

4) Screening-Level Exposure Estimates (PE x IC):

Screening-level exposure estimates for the various Product Exposure scenarios may be **aggregated**:

- **Within each product category** by adding the scenario exposures within a product category.
- **Across product categories** by adding the exposures from all the individual products. If there were duplicate types of product (e.g., both liquid and granule laundry detergents), the product resulting in the higher exposure would be used. Differences in product use patterns between males and females, ages, and ethnicity were considered to determine relevant product combinations when adding the exposures.

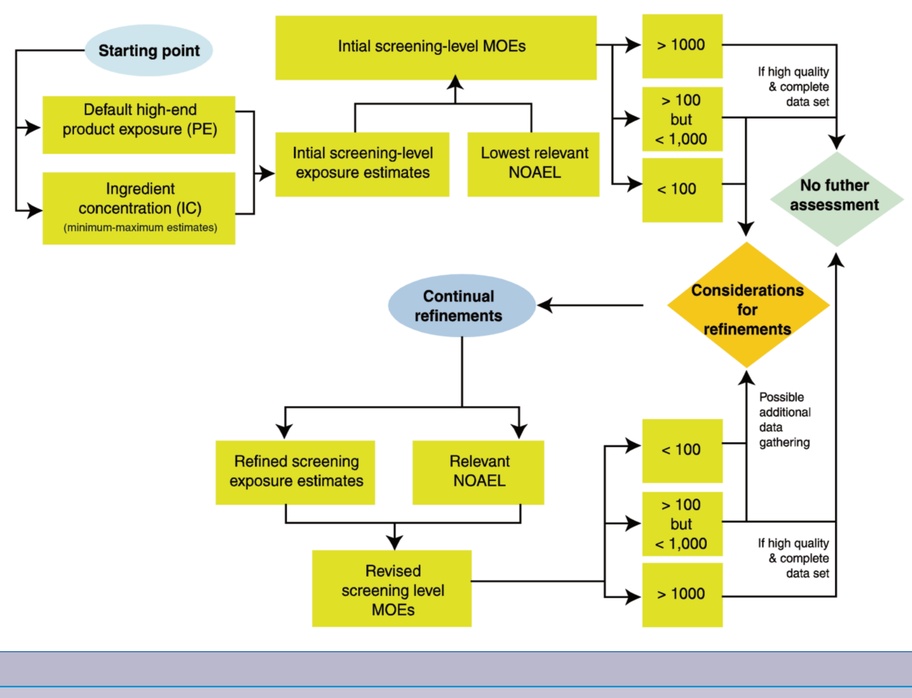
5) Interpretation of MOEs and appropriate responses

If the margins of exposure (MOEs) are not adequate, then product categories with the lowest MOEs can proceed to a more refined assessment. The more refined assessment would focus on identifying both the most appropriate NOAEL for the chemical based on the product and its exposure scenarios and more realistic exposure information as illustrated below.

Various factors to consider when determining if a MOE of less than 1,000 but greater than 100 is adequate or refinement is needed include:

- the quality and comprehensiveness of the toxicity database,
- the quality and duration (e.g., 28 days vs. 90 days vs. 6 months or greater) of the study upon which the NOAEL is based,
- the seriousness of the effect observed,
- the steepness of the dose-response curve, and
- what is known about the toxicokinetics and toxicodynamics in animals vs. humans.

Figure 1. Screening-Level Risk Assessment – Continual Refinement Process



Case Study: Amine Oxide HPV Chemical Category

Amine oxides are amphoteric surfactants that are used in consumer cleaning and personal care products where they function as foam stabilizers, thickeners and emollients, emulsifying and conditioning agents. Amine Oxide is an HPV chemical category because approximately 26,000 metric tonnes are produced annually in the U.S. and 16,000 and 6,800 tonnes, respectively in Europe and Japan.

1) Selection of Dose-Response Threshold

A NOAEL for the repeat-dose study of 80 mg amine oxide/kg-BW/day is the most relevant because of the high quality of the study from which it is derived and its consistency with the NOAELs from the other toxicity endpoints.

2) Product Exposure Equations and Input Parameters for Direct Dermal Exposure to Amine Oxide Containing Products

Relevant PE Scenario	PE Model	Parameters
Exposure during activity/use of: Laundry detergent: hand-washing clothes Laundry detergent: laundry pretreatment Dish detergent: hand-washing dishes Nondilutable hard surface cleaners	NA and EU approach: $\frac{FQ \times CA \times PC \times FT \times CF \times TF \times DA}{BW}$	FQ: frequency of use (use/day) CA: body surface contact area (cm2) PC: product concentration (g/cm3) FT: film thickness on skin (cm) CF: conversion factor (1,000 mg/g) TF: time scaling factor (unitless) DA: dermal absorption (100%) BW: female body weight (60 kg)
Exposure after activity/use (residual): Adult rinse-off products: Hair conditioners Hand/body/face soaps Shampoos Adult leave-on products: Aftershave Hand/body moisturizer Styling/tonic gel	NA and EU approach: $\frac{FQ \times A \times PR \times CF \times DA}{BW}$	FQ: frequency of use (use/day) A: amount used (g/use) PR: percent retained (%) CF: conversion factor (1,000 mg/g) DA: dermal absorption (100%) BW: female body weight (60 kg); male body weight (70 kg) (shaving products); child body weight (15 kg) (baby care products)

3) Ingredient Concentrations for Amine Oxide in Products

Product Type	Range of Concentration in Products (%)
Body Moisturizer	0.2 – 0.6
Hair Care	0.1 – 5
Aftershave	0.5 – 1
Laundry Detergent – liquid	1 – 5
Bar Soap	0.1 – 5
Cleansing Products	0.04 – 9
Dish Detergent – liquid	0.1 – 10
Hard Surface Cleaner – liquid	0.05 – 5

4) Dermal Exposure to Amine Oxide by Product Category

	Screening-Level Product Dermal Exposure Estimates* (mg AO/kg-BW/day)
Product Category	**Minimum to Maximum**
Body Moisturizer	1.1 to 3.2
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
Hard Surface Cleaner – liquid	1.1E-4 to 5.5E-3

*Inhalation does not contribute significantly to the overall exposure because the vapor pressure of AO is very low (i.e., 2.6 x 10-7 to 4.6 x 10-5 Pa). Oral exposure is not considered because AO is not used in products that are intended to be ingested.

5) Screening-Level MOEs from Amine Oxide Exposures by Product

Product Type	Range of Margins of Exposure (MOEs)	
Body Moisturizer	72.7	25
Hair Care	7,270	333
Aftershave	1,143	571
Laundry Detergent – liquid	26,667	5,333
Bar Soap	195,122	4,000
Cleansing Products	347,826	1,569
Dish Detergent – liquid	6,666,667	66,667
Hard Surface Cleaner – liquid	727,273	14,545

Interpretation of MOEs and appropriate responses

In the case of AO, with the exception of the body moisturizers, hair care, and aftershave products, all products have MOEs greater than 1,000 and thus further assessment is not necessary. Although the MOEs for body moisturizers, hair care, and aftershave use are below 1,000, refinements are not necessary because:

- the MOE was based on a high-quality, repeat-dose toxicity study;
- chemical category AO has a comprehensive toxicity data set that includes chronic toxicity data (i.e., developmental , reproductive, as well as carcinogenicity); and
- the MOE is greater than 100, except for body moisturizer, and thus is sufficient to account for the 10-fold uncertainty factor for interspecies variability and the 10-fold uncertainty factor for intraspecies variability (Health Canada, 1994; Kodell and Gaylor, 1999).
- the MOEs for body moisturizer were extremely conservative including assumptions of 100% retained on skin (PR) and 100% dermal adsorption (DA).

For More Information:

SDA (The Soap and Detergent Association). 2010. *Consumer Product Ingredient Safety: Exposure and Risk Screening Methods for Consumer Product Ingredients*. Washington, D.C., pp. 208. Available at http://www.aciscience.org.

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Kodell R, Gaylor D. 1999. Combining uncertainty factors in deriving human exposure levels of noncarcinogenic toxicants. Ann NY Acad Sci. 895:188–195.

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1331 L Street, NW Suite 650
Washington, DC 20005
www.cleaninginstitute.org