# American Cleaning Institute
# Cleaning Product Ingredient Safety Initiative
# Methodology

The American Cleaning Institute (ACI) has developed the Cleaning Product Ingredient Safety Initiative (CPISI) as one of its many efforts to promote the responsible management of cleaning products and their ingredients. The Initiative focuses on laundry care, dish care, and hard surface cleaning products.

This document describes the methods associated with each major step of the CPISI.

## Ingredient Inventory Compilation

Member company lists were used as the starting point for preparing the Ingredient Inventory. Each manufacturer's web site was surveyed to identify laundry care, dish care, and hard surface cleaning products intended for home use in the United States. Industrial cleaning products, specialty cleaning products (e.g. oven cleaners), and disinfectants/sanitizers were not included in the inventory. Disinfectants or sanitizers have been evaluated under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA).

Once the relevant products for each manufacturer were identified, the name for each ingredient in each product was entered into a database exactly as listed by the manufacturer. The use of the product (i.e. dish detergent, fabric softener, etc.) and its form (i.e. liquid, powder, spray, etc.) were recorded. Other information such as CAS registry numbers were recorded as they were available. Because assessing risks from ingredients requires the use of exposure models and the model used will vary based on the intended use of the product, the product use category associated with specific products and ingredients was also collected for the inventory. Information regarding the concentration of each ingredient associated with different product uses was also compiled as part of the Ingredient Inventory. Ingredient function information was also gathered from company websites where available.

Ingredients were entered for over 900 products made by 13 manufacturers distributed over 30 product use and form categories. The initial list of ingredients totaled over 13,000 entries with over 1000 unique listed ingredient names. Many ingredients are used in more than one product, so many of the 13,000 entries that formed the initial list were repeats of the same ingredient name. Therefore, the list of ingredients was consolidated and differences in naming resolved. Each listed ingredient was reviewed and one or more common names were assigned using naming conventions from trade literature and chemical nomenclature. Ingredients that are in fact durable articles such as wool, polyester or fabric were removed from the database.

Where ingredients were identified by generic names or by chemical category names, they were replaced by more specific ingredient names. To be as inclusive as possible, it was assumed that any of the chemicals represented by a generic name or included in a chemical category could be used in those products. Past studies, other inventories, and trade literature, provided sources of more specific ingredient names that could be used for generic names and chemical categories.

Replacing generic names and chemical category descriptors with specific chemical names resulted in a final list of 588 unique name-CAS combinations.

Some of the ingredients included in the Ingredient Inventory were not listed directly on consumer cleaning products; however, due to their similarity to ingredients listed in products, they were added to the Inventory in order to support the listed ingredients by providing useful hazard data during the hazard data collection process. Once these supporting compounds were compiled, they were separated from the actual Ingredient Inventory, resulting in approximately 588 unique ingredients and 236 supporting compounds.

A chemical grouping/category was assigned to each ingredient to aid in satisfying several data quality objectives. Assignment of chemical groupings provided a means of selecting any additional ingredients for inclusion in the Inventory, improved use of read-across in searching and applying chemical hazard data to each ingredient, and, in some cases, aided in assigning chemical function where data gaps existed. Functional classes were identified for each of 588 unique ingredients. The first step in this process was completed during initial collection of ingredient listings; function was collected where provided by ACI member companies. Reliable databases were used to fill gaps in function information. An initial functional class was assigned per ingredient based on review of the occurrence of the ingredient in the products evaluated and the function information provided across the sources used. Where data gaps still existed, a read-across approach was used to assign a functional class to ingredients with a similar composition or chemical structure. The last step was the harmonization of the initial functional class assignments to match the recently published OECD list of functional classes.

## Hazard Data Collection

The primary goal of hazard data collection was to identify publicly available human safety data that describes potential adverse effects associated with ingredients found in home use cleaning products for the purpose of conducting a screening level risk assessment (SLRA). In addition, environmental hazard data, which describes potential adverse effects on critical ecosystem components, and physical and chemical properties of the ingredients were identified.

The collection of the publicly available human health hazard data was conducted in several steps. During the first step, databases were searched for hazard data for each unique ingredient. First tier sources included:

- Past ACI risk assessments (i.e. Sanderson et al. 2006);
- High Production Volume Information System (HPVIS) (USEPA 2015a);
- Organization for Economic Cooperation and Development High Production Volume (OECD HPV) database (OECD 2015); and
- European Chemicals Agency (ECHA CHEM) (ECHA 2016).

Additional sources included:

- Aggregated Computational Toxicology Resource (ACToR) (USEPA 2015b);
- Studies cited in Cosmetic Ingredient Review (CIR) reports (CIR 2015);

- Food and Drug Administration (FDA) Allowable Daily Intake (FDA 2015);
- Human and Environmental Risk Assessment (HERA) project (HERA 2015);
- FDA, FD&C, listings of ingredients as governed by specific regulations; and
- Other publicly available industry and agency study citations.

Hazard data to support human health risk assessment were collected as part of this multi-tiered process. Data were entered into a standard format capturing test type, organism, endpoint, effects, exposure route, dose descriptor, duration, citation, and other parameters. Webpages were archived and web links entered. In some cases, quantitative hazard data for an ingredient were unavailable, but the FDA had performed evaluation of this ingredient and/or synonymous or similar ingredients as part of previous studies. Where these evaluations found the ingredient either to be generally regarded as safe for consumer use, or to be approved for uses with exposures greater than those expected for cleaning products, such findings were entered into the hazard database with references to the applicable regulation.

At the conclusion of hazard data collection, 409 ingredients were determined to have publicly available hazard data sufficient for use in SLRA or a relevant and defensible risk assessment finding from past studies. A total of 46 ingredients were not able to be studied because they are proprietary; safety information is maintained by their manufacturer. Another 48 ingredients are the subject of further review; data are available for many of these, but were not usable for the SLRA. Research into these ingredients is ongoing.

**Development of Exposure Assessments**

ACI developed the exposure estimates associated with the use(s) of each of ingredient listed in the Ingredient Inventory as part of a consolidated Development of Exposure Assessments Inventory. The goal was to characterize the exposure for each ingredient, in the framework of the product types and their typical applications. The planned approach was an extension of that undertaken by ACI (as the then Soap and Detergent Association), and published in the peer-reviewed literature in 2006 (Sanderson et al., 2006). Exposure modeling focused on the products examined during compilation of the Ingredient Inventory, their chemical composition, their intended uses, and data from surveys of habits and practices for the use of these products.

The information collected included, but was not limited to:

- Product types in which each ingredient is used (e.g., all-purpose cleaner-liquid, laundry detergent-powder);
- Function of each ingredient (e.g., solvent, humectant, surfactant, chelating agent); and
- Habits and practices for typical and intended use of each cleaning product containing the ingredients evaluated in the CPISI.

Ingredient and product information collected during compilation of the Ingredient Inventory was revisited to gather the connections between ingredients and product types and to pull any information collected on concentration ranges for each ingredient. Ingredients with no primary concentration data were then compared to established lists of functional classes from reliable

sources to identify concentration ranges. Examples of these classes include chelating agents, surfactants, and solvents. If gaps existed after searching available sources, functions assigned to other ingredients within a group were reviewed and a determination made as to whether it applies to the ingredient in the same grouping. After functional classes were compiled, the list was standardized to the Organisation for Economic Co-operation and Development (OECD) nomenclature for ingredient functions.

The data described above was used to determine the ways in which a user could potentially be exposed to a particular ingredient as a result of intended use of the product. Each product type under the scope of the CPISI has a specific application which is expected to cause exposure through one or more of the traditional routes (inhalation, ingestion, dermal). Previous work was used to connect each ingredient to its relevant routes and models of exposure. These exposure equations, generated under regulatory and risk assessment paradigms in the US, were gathered and published by ACI (Sanderson et al., 2006). Based on the typical use patterns for the products that fall under the scope of this project, 16 possible exposure models were applied.

The successful gathering and curation of the exposure model data allowed for calculation of estimated exposure for each ingredient for each route using the equations from Sanderson et al., 2006. The completion of these exposure models generated estimates of exposure for individual routes of exposure under normal and intended use of the cleaning products under the scope of the CPISI. These exposure estimates were calculated as mg/kg/day. When individual ingredients were used in more than one product type, aggregate exposure estimates to each ingredient were generated by summing the single-route values. In some cases, product uses were identified as overlapping for daily use; in such cases, the product use and form with the higher exposure estimate were included in the sum. The end result was the summation of exposures to produce a daily exposure estimate arising from multiple product exposures. The minimum and maximum of the ranges of concentrations expected in each product type was used to develop minimum and maximum estimated exposures for use in SLRA.

## Development of Screening-Level Risk Assessments

The tiered approach to hazard data collection resulted in over 7,830 records of data. To use these data to derive NOAELs for use in risk assessment, an approach was developed that included data selection criteria, data source prioritization, and methods to address uncertainty. Criteria were established to ensure the quality and relevance of data. Data were limited to:

- Test type: In vivo whole organism testing for named species.
- Endpoint/Effect: Stated reproduction, developmental, carcinogenic, growth, and survival endpoints.
- Exposure pathway: Inhalation, dermal, or oral pathways.
- Duration: Documented duration as acute, subchronic, or chronic.
- Dose descriptor: NOAEL, LOAEL, ED and LD doses expressed in terms of body weight per day; for inhalation only, concentration data where respiration rate could be determined allometrically to convert to dose.
- Data quality: Studies with a reported Klimisch reliability rating (KRR) of 2 or lower or where reporting sources only considered low KRR data.

Based on these and other quality-based criteria, 4,056 records were identified as potentially useful for NOAEL derivation. Data sources were identified as authoritative and prioritized if they were publicly available; defensible in terms of quality; transparent in methodology; and drew from many studies. Priority was given to quantitative data in the following general order:

- Past ACI risk assessments
- FDA Allowable Daily Intakes (ADIs)
- OECD Derived No Effects Levels reported in ECHA CHEM
- HERA Project derived NOAELs
- Hazard data compiled under CPISI from individual studies
- GRAS or safe-for-use listings from FDA and FD&C
- Read across was used to fill data gaps, with the following order of priority:
- Direct name-CAS matches
- Name only or synonym matches
- Read across used or referenced by authoritative sources
- Read across based on one of 56 groupings derived from chemical structure considering OECD guidance (OECD 2014)

NOAEL and LOAEL data were prioritized over LD50 data. Extrapolation across exposure pathways was used selectively, with preference given to data specific to the target pathway. In some cases, oral NOAELs were used to fill data gaps for inhalation or dermal exposures.

To address uncertainties in the NOAEL derivation process, assessment factors (AFs) consistent with those used under REACH were applied to increase the conservativeness of hazard data where study duration was less than chronic; effect severity was greater than no effect; and species other than humans were used. Additionally, when multiple studies provided a NOAEL for a single ingredient exposure, the lowest available calculated NOAEL was selected as a conservative measure.

Two approaches were used for SLRA. The first was to rely on risk assessments already conducted using defensible and comparable methodologies. The second was to perform quantitative modeling of exposure and risk. A SLRA presents a general indication of the potential for risk (or lack of risk) from a particular substance. The SLRAs performed for the CPISI ingredients can provide an estimate of the chance that an ingredient in a cleaning product may pose a risk during use. A total of 85 ingredients were identified as unlikely to produce risks based on the findings of past risk assessments and studies. Another 409 ingredients were assessed via a quantitative SLRA in which exposure estimates and hazard data were combined to calculate a risk characterization ratio (RCR). AN RCR below 1 indicates minimal potential for risk while an RCR above 1 indicates a possible risk. A total of 390 ingredients demonstrated were found unlikely to pose risks because their RCR values were below 1 even under conservative maximum case exposure scenarios. A small number of ingredients (19) had RCR above 1 under maximum case scenarios; these were found to warrant additional study via refining risk assessment methods. The models used to develop the RCR were examined for any areas of potential uncertainties associated with the collected hazard or exposure data. These data may have included ingredient concentration ranges, application of uncertainty factors, or the ingredient-product exposure combinations that were evaluated. Additionally, more input was solicited as needed from ACI members regarding specific ingredients in specific products to secure more updated hazard or exposure data. For most

of these 19 ingredients with an RCR greater than 1, risks were associated with conservative ingredient concentrations or conservative assessment factors that warrant additional research and review.

In summary, the CPISI project produced SLRA results in the form of risk models or review of past findings for over 80% of the 588 ingredients studied, and found that 95% of those ingredients were unlikely to produce risks even when highly conservative exposure models and hazard values were used. There are 46 ingredients which were not able to be studied because they are proprietary; safety information is maintained by their manufacturer. Another 48 ingredients are the subject of further review; data are available for many of these, but were not usable for the screening level risk assessment.

## References


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