

ULE P 113



Procedure

Preparation of a Toxicological Assessment

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Procedure for the Preparation of a Toxicological Assessment, ULE P 113

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October 25, 2010

1

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CONTENTS

GLOSSARY	3
1.0 INTRODUCTION	4
2.0 THE PREPARATION AND REVIEW OF THE TOXICOLOGICAL ASSESSMENT	5
2.1 Preparation	5
2.2 Review	5
2.3 Self-Certification to UL Environment Standards	6
3.0 RESOURCES	6
3.1 General Databases	6
3.2 Specialized Databases	7
3.3 Other Sources of Information	7
4.0 CATEGORIES AND PARAMETERS	7
4.1 Regulatory Status	8
4.2 Exposure Pathways	8
4.3 Environmental Fate (Persistence and Bioaccumulation)	9
4.4 Toxicity to Wildlife	10
4.5 Toxicity to Humans	11
5.0 ADDRESSING DATA GAPS	14
5.1 Search the scientific literature for additional information	14
5.2 Consider performing a structure-similarity search	15
6.0 ACCEPTABLE HAZARD PROFILE	15
6.1 Definition	15
6.2 Decision Flow for Determining Hazard Profile Status	15
7.0 COMPILING THE TOXICOLOGICAL ASSESSMENT	18
Step 1: Input the product formula	18
Method A: Homogenous Materials	18
Method B: Products Comprised of Component Ingredients	18
Step 2: Review each ingredient	19
Step 3: Summarize each ingredient	19
Step 4: Review the formulation	19
Step 5: State whether the product has an acceptable hazard profile	19
Step 6: Prepare an abstract	19
Step 7: Approve the Assessment	20
Step 8: Compile the final document	21
8.0 UPDATES TO THIS PROCEDURE	21
9.0 REFERENCES	21
APPENDIX A: TEMPLATE FOR INGREDIENT REVIEW	23
APPENDIX B: TEMPLATE FOR TOXICOLOGICAL ASSESSMENT	26

GLOSSARY

For the purpose of this procedure, the following definitions apply.

ACUTE LETHALITY – The ability of a substance to cause death after a short-term or single exposure.

ACUTE TOXICITY – The toxicity of a substance after a single dose or multiple doses administered over a period of time less than one week.

BIOACCUMULATION – The accumulation of a substance, such as a toxic chemical, in various tissues of a living organism.

CARCINOGENICITY – The degree to which something causes cancer.

CHRONIC TOXICITY – The toxicity of a substance after multiple doses administered over a period of time.

DEVELOPMENTAL TOXICITY – Any adverse effect on the normal development of the offspring.

ENDOCRINE EFFECTS – The mimicking of an endogenous hormone by a chemical, such as an environmental estrogen. Chemicals with endocrine effects are commonly referred to as endocrine disruptors.

ENVIRONMENTAL FATE – The processes by which a chemical moves through and is transformed by the environment. (Reprinted from EPA <http://www.epa.gov/dfe/pubs/tools/ctsa/>)

ENVIRONMENTAL PERSISTENCE – The potential length of time that a compound may remain into and environment into which it has been introduced.

EXPOSURE PATHWAYS – The ways in which an organism comes in contact with a chemical.

FORESEEABLE MISUSE – Application of the product for a purpose other than its primary purpose or directed use, whether intentional or accidental, provided that the misuse is reasonably foreseeable.

GENOTOXICITY – The degree to which something causes damage to or mutation of DNA.

LOG K_{OW} – The log of the octanol-water partition coefficient (K_{OW}). The octanol-water partition coefficient is the ratio of the concentration of a chemical in octanol and water at equilibrium and at a specified temperature. This parameter is a surrogate that can indicate the fate of chemicals in the environment.

REGULATORY STATUS – The restrictions and prohibitions on the use of a chemical or class of chemicals as defined by regulatory authorities on a state, national or international level.

REPRODUCTIVE TOXICITY – Any adverse effect on the sexual function and fertility of adult males and females.

TOXICOLOGICAL ASSESSMENT – A review of the physical, chemical and toxicological properties of each ingredient followed by an overall summary of the potential hazards of a product.

1.0 INTRODUCTION

A heightened awareness arose in the latter half of the twentieth century of the impact of chemicals on the environment and human health. In addition to multiple well-publicized chemical releases that were environmental disasters with significant impacts on human health, there was also a much more subtle disaster occurring silently in the office buildings of the world. The 1980s saw the development of well insulated, energy efficient buildings that ushered in the era of “sick building syndrome”. As a result, consumers, workers, and employers became much more aware that not all disasters involve a chemical release of significant proportion. Rather, it was the continuous onslaught of emissions from the materials around them that was associated with the symptoms of sick building syndrome.

As products are redesigned to optimize resource utilization, it is essential that safety not be compromised. In general terms, a material that may provide superior energy efficiency, for example, may pose a greater risk of harm to workers and building occupants.

To fully appreciate the sustainability of a product, one shall consider the potential environmental and human health impacts. To that end, UL Environment Standards and Interim Sustainability Requirements incorporate, as appropriate, a Toxicological Assessment (“assessment”) criterion. The assessment identifies ingredients in a product and characterizes the hazards associated with exposure to the ingredients.

The purpose of this document is to provide a procedure for preparing a toxicological assessment in compliance with a UL Environment Standard or Interim Sustainability Requirement (ISR). Use of this Procedure does not constitute a representation, warranty or guarantee by UL Environment that any toxicological assessment will be recognized or accepted.

In many instances, the information needed to compile the assessment is readily available and has likely been collected for other purposes, including creation of a Material Safety Data Sheet (MSDS) for the finished product. This guidance describes the most commonly used and helpful sources for locating environmental and human health effects information about the ingredients in the product being evaluated.

A toxicological assessment prepared to comply with a UL Environment Standard or ISR will typically include the available information within each of the following five categories:

- a) Regulatory Status - US and internationally, including pending action
- b) Exposure Pathways - inhalation, oral and dermal
- c) Environmental Fate - environmental persistence and bioaccumulation
- d) Toxicity to Wildlife - including endocrine effects
- e) Toxicity to Humans - occupational and end use

As described above, this information is gathered and summarized for each ingredient present at a concentration $\geq 0.1\%$ in the final product or as otherwise specified in the specific Standard or ISR to which a product is being evaluated. This Procedure does not address intermediates or process chemicals that may have occupational consequences but are not present in the finished product. This Procedure provides a detailed definition for each of the above categories along with instructions for identifying sources of information. This Procedure identifies each endpoint that shall be included in the toxicological assessment and provides guidance on which value to include if multiple values are reported for an endpoint.

The manufacturer may prepare the entire assessment or just part of the assessment. However, a qualified toxicologist shall review and approve all parts of the assessment prepared by the manufacturer. Alternately, the manufacturer may elect to have a qualified toxicologist prepare the assessment. In any event, to certify to a UL Environment Standard or ISR containing the Toxicological Assessment criteria, the manufacturer shall produce an assessment that has been reviewed and approved by a qualified toxicology professional. This Procedure defines the characteristics of a “qualified” toxicologist.

The assessment will contain proprietary information including but not limited to detailed formulation information. As such, at no time is the content of the assessment intended for public dissemination. The conclusions of the assessment may be made publicly available depending upon the policies or practices of the organization certifying the product to the UL Environment Standard or ISR and/or any applicable laws or regulations.

This Procedure includes templates to assist manufacturers with preparing the ingredient reviews and the final toxicological assessment. These templates are provided as examples; an individual preparing an assessment may use whatever format they consider most appropriate provided that the finished assessment addresses all requirements identified in this document.

The completed assessment shall be signed by the preparer and reviewer (as appropriate) and submitted to satisfy the Toxicological Assessment criteria. Additionally, the UL Environment Standard or ISR may contain optional criteria that award points for products determined to have acceptable hazard profiles. Therefore, the conclusion of the toxicological assessment shall include a statement of whether the product meets the optional criteria for an acceptable hazard profile. The definition of a product with an acceptable hazard profile, in the context of UL Environment Standard or ISR, is defined in this Procedure.

2.0 THE PREPARATION AND REVIEW OF THE TOXICOLOGICAL ASSESSMENT

2.1 Preparation

2.1.1 Who may prepare the assessment?

Anyone with the relevant scientific training and/or experience may prepare the assessment. Qualified individuals may include, but are not necessarily limited to, the following: toxicologists, industrial hygienists, and environmental health and safety professionals.

2.1.2 How long will it take?

Using publicly available databases, a formulation containing 10 ingredients or fewer will require approximately one week of full time effort to complete the assessment.

2.2 Review

2.2.1 What is required for this criterion?

The assessment is considered complete only when reviewed and approved by a toxicologist of appropriate training and experience. The toxicologist may elect to draft the document on behalf of the manufacturer or may serve as a reviewer of an assessment prepared by the manufacturer. In any event, a toxicologist of appropriate training and experience shall approve the assessment prior to submission as partial requirement for certification to a UL Environment Standard or ISR.

2.2.2 What defines a toxicologist of appropriate training and experience?

For the purposes of UL Environment Interim Sustainability Requirements containing the toxicological assessment criteria, an individual is considered qualified to review and approve the assessment provided the following:

A toxicologist of sufficient skill and experience is one whom has achieved certification by a certification body that establishes standards for professional competency in the field of toxicology. As defined here, an acceptable certification body is one that defines eligibility for certification based on training and experience, administers a certification examination, and requires recertification on a defined schedule. The American Board of Toxicology is one such certifying body and a toxicologist with a DABT is considered qualified.

The organization certifying a product to a UL Environment Standard or ISR shall make the final determination and take responsibility for the sufficiency of the qualifications of the toxicology professional.

2.2.3 Why is there a requirement on who can approve the assessment?

The assessment reviews a wide range of information about the potential human health and environmental hazards of the finished product. As there is no single authoritative source for all information (i.e. no

“checklist”) the evaluation is, in part, the professional judgment of the reviewer. Requiring a board certification in toxicology is one way to ensure consistency and minimum qualifications among individuals approving these materials.

2.3 Self-Certification to UL Environment Standards

2.3.1 Does this mean that a manufacturer can't self-certify to a UL Environment Standard or ISR with this prerequisite?

No. A manufacturer may still self-certify and has the discretion to identify the individual to approve the assessment. The manufacturer may have a qualified toxicologist on staff or may elect to retain the services of an individual or firm engaged in toxicology. Where the manufacturer is the certifier, the manufacturer shall make the final determination and take responsibility for the sufficiency of the qualifications of the toxicology professional.

3.0 RESOURCES

There are various commercial databases available specific to toxicological data. Many of these are also employed for Environmental Health and Safety purposes. Any database providing accurate, peer-reviewed information is an appropriate source for the preparation of the dossier. Rather than limit the resources used to prepare an assessment, the following is intended to serve as a source list.

3.1 General Databases

ChemIDPlus is a free database published by the National Library of Medicine. It can be found online at:

<http://chem.sis.nlm.nih.gov/chemidplus/>

While not exhaustive, ChemIDPlus provides basic information for preparation of an assessment. There will be some additional information available only through fee-for-use databases (e.g. RTECS) that the manufacturer may elect to add to the dossier or may be added by the toxicologist during review. By this mention, UL Environment does not seek to endorse a particular database. ChemIDPlus is provided as an example of an appropriate database because it is publicly available for no charge and can be readily accessed by individuals without specialized training.

Other relevant databases or toxicology information source documents include, but are not limited to, the following:

- ATSDR - Agency for Toxic Substances and Disease Registry
- CPDB - Carcinogenic Potency Database
- CCRIS - Chemical Carcinogenesis Research Information System
- DART - Developmental and Reproductive Toxicology Database
- ECOTOX - ECOTOXicology database
- EPA Ambient Water Quality Guidelines
- ECETOC - European Centre for Ecotoxicology and Toxicology of Chemicals
- Environmental Health Criteria (EHC) Monographs
- GENETOX - Genetic Toxicology Data Bank
- HPVIS - High Production Volume Chemical Information System
- HSDB - Hazardous Substances Data Bank
- IARC - International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risks to Humans
- IRIS - Integrated Risk Information System
- ITER - International Toxicity Estimates for Risk
- NTIS - National Technical Information Service, Toxicology Document and Data Depository
- NTP - National Toxicology Program
- Cal/EPA PROP 65
- REPROTOX - Reproductive Effects of Chemical, Physical and Biologic Agents

- RTECS - Registry of the Toxic Effects of Chemical Substances
- TSCATS - Toxic Substance Control Act Test Submission Database

Note that these databases are cross-referenced in ChemIDPlus. As such, a search of ChemIDPlus will provide links to relevant information on the ingredient in other relevant databases. There may be additional sources of information the manufacturer and/or toxicologist may elect to include. This list is only provided as an example and highlights the disperse nature of human health and environmental hazard data available for ingredients and further underscores why any information shall be reviewed by a qualified toxicology professional.

There are several databases that report environmental toxicity information that may be used in addition to those named previously. Those listed below are examples of common databases but other sources of information may be relevant:

- ECOTOX (USEPA)
- Cal/ECOTOX

When no data are available for a chemical, the screening-level tool, Persistent Bioaccumulative Toxic (PBT) Profiler, can provide estimates of the potential of a chemical to persist and to bioaccumulate. PBT Profiler is provided at no charge by the USEPA and is available at:

www.pbtprofiler.net

3.2 Specialized Databases

If an ingredient is a drug or pesticide, it will be registered with the FDA or USEPA, respectively. Whether an ingredient is a drug or pesticide can be determined in one of several ways that include, but are not limited to, the following:

1. The MSDS for the ingredient bears registration information
2. A ChemIDPlus search will reveal links to specific databases related to drugs and pesticides. These include but are not limited to:
 - a. Drug Portal
 - b. FIFR (EPA Pesticide Active Ingredients)
 - c. EPA PPIS (Pesticide Product Information System)

In some instances, an ingredient may be listed as both a pesticide and a drug. One example where this is common is with anti-fungal ingredients. Registered products (drug or pesticides) are required to submit detailed safety information to the registering agency. In those instances, the USA.gov search engine can be a useful tool for locating data.

3.3 Other Sources of Information

Other sources of information (including proprietary data) may be included in the assessment. At no time is the content of the assessment intended for public dissemination. The conclusions of the assessment, specifically with respect to whether the product has an acceptable hazard profile, may be made publicly available depending upon the policies of the organization certifying the product to the UL Environment Standard or ISR.

4.0 CATEGORIES AND PARAMETERS

Each category for the toxicological assessment is explained with respect to purpose and sources of information. Endpoints to consider are identified.

4.1 Regulatory Status

4.1.1 What is it?

As used in the toxicological assessment, *regulatory status* is intended to describe any pending or implemented restrictions or prohibitions on the use of the chemical in the United States or elsewhere.

4.1.2 Why is it relevant?

A pending or implemented restriction or prohibition on a chemical is a strong indication that a chemical specific issue has been identified. This is a good first place to start to appreciate concerns regarding the toxicity of the chemical.

4.1.3 When is this not relevant?

This category should be relevant for all ingredients.

4.1.4 What kind of information should be reported?

At a minimum the following regulatory agencies shall be consulted as to the status of the ingredient:

- DSL - Environment Canada Domestic Substances List
- ECHA - European Chemicals Agency: List of Pre-registered Substances
- EINECS - European Inventory of Existing Commercial Substances
- EPA - United States Environmental Protection Agency
- FDA - United States Food and Drug Administration
- INCI - Cosmetic Ingredients Inventory
- TSCA - EPA Toxic Substances Control Act Inventory

Regulatory status can be determined in any number of ways, including consulting the web pages of various regulatory authorities. While not endorsing any software or database, ExPub from EBSCO is a database that provides reporting of regulatory status. Additionally, a publicly available database such as ChemIDPlus will typically index the regulatory authorities listed above.

It is the responsibility of the individual preparing and approving the assessment to ensure that the list is complete and accurate. State or international requirements, where they are a recapitulation of existing national requirements, need not be reported in the assessment.

4.1.5 Reconciling conflicting information?

Where differences in regulatory status are reported, refer to the relevant body with jurisdiction for the location of the manufacture and sale of the product (e.g. The United States of America). Ensure that regulatory status is confirmed directly from the regulatory body (e.g. their webpage, their memoranda or public announcements on the topic) and not from a secondary source. Where conflicting status reports exist that appear to come from valid sources, report all information in the assessment. The final determination is at the discretion of the reviewing toxicologist.

4.2 Exposure Pathways

4.2.1 What is it?

As used in the toxicological assessment, *exposure pathways* describe the various means by which exposure to a chemical may occur. This includes oral, inhalation and dermal exposure. To estimate whether inhalation exposure is a route of concern, for example, considerations include the vapor pressure of the chemical, or whether handling or use scenarios allow for dusts or aerosols to become airborne. Once the presence of the chemical at the site of contact is confirmed, a second important consideration is the degree to which it is absorbed (except for direct contact effects). Whether the chemical may be readily absorbed through the skin or mucous membranes (such as in the respiratory or gastrointestinal tract) is another critical consideration in identifying the relevance of potential exposure pathways for assessing human health hazard potential.

4.2.2. Why is it relevant?

The route of exposure to a chemical is as important as the toxicity of the chemical. There are often significant differences in the toxicity of a chemical when administered by different routes of exposure.