IAPMO IGC 1123-2022

PUBLIC REVIEW DRAFT

California Proposition 65 Compliance – Products or Materials.

IAPMO Standard

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Preface

This is the first edition of IAPMO IGC 1123, California Proposition 65 Compliance for Products or Materials.

This Standard was developed by the IAPMO Standards Review Committee (SRC) in accordance with the policies and procedures regulating IAPMO industry standards development, Policy S-001, Standards Development Process. This Standard was approved as an IAPMO Industry Standard on Month DD, YYYY.

Notes:

(1) The use of the singular does not exclude the plural (and vice versa) when the sense allows.

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(3) This standard was developed using an open process and in accordance with IAPMO Standards Policy S-001, Standards Development Process*, which is available on the IAPMO Standards website (www.IAPMOstandards.org).*

(4) During its development, this Standard was made available for public review, thus providing an opportunity for additional input from stakeholders from industry, academia, regulatory agencies, and the public at large. Upon closing of public review, all comments received were duly considered and resolved by the IAPMO Standards Review Committee.

(5) This Standard was developed in accordance with the principles of consensus, which is defined as substantial agreement; consensus implies much more than a simple majority, but not necessarily unanimity. It is consistent with this definition that a member of the IAPMO Standards Review Committee might not be in full agreement with all sections of this Standard.

(6) Although the intended primary application of this Standard is stated in its scope, it is important to note that it remains the responsibility of the users of the Standard to judge its suitability for their particular purpose.

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- *(a) standard designation (number);*
- *(b) relevant section, table, or figure number, as applicable;*
- *(c) wording of the proposed change, tracking the changes between the original and the proposed wording; and*
- *(d) rationale for the change.*

(8) Requests for interpretation should be clear and unambiguous. To submit a request for interpretation of this Standard, you may send the following information to the International Association of Plumbing and Mechanical Officials, Attention Standards Department, at standards@IAPMOstandards.org or, alternatively, at 4755 East Philadelphia Street, Ontario, California, 91761, and include "Request for interpretation" in the subject line:

- *(a) the edition of the standard for which the interpretation is being requested;*
- *(b) the definition of the problem, making reference to the specific section and, when appropriate, an illustrative sketch explaining the question;*
- *(c) an explanation of circumstances surrounding the actual field conditions; and*
- *(d) the request for interpretation phrased in such a way that a "yes" or "no" answer will address the issue.*

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Introduction

California Proposition 65, officially known as the Safe Drinking Water and Toxic Enforcement Act of 1986, was enacted as a ballot initiative in November 1986. The proposition protects the state's drinking water sources from being contaminated with chemicals known to cause cancer, birth defects or other reproductive harm, and requires businesses to inform Californians about exposures to such chemicals. Proposition 65 requires the state to maintain and update a list of chemicals known to the state to cause cancer or reproductive toxicity.

These chemicals can be in the products that Californians purchase, in their homes or workplaces, or may be ones that are released into the environment. By requiring that this information be provided, Proposition 65 enables Californians to make more informed decisions about their exposures to these chemicals.

To guide businesses in determining whether a warning is necessary, the Office of Environmental Health Hazard Assessment (OEHHA) has developed safe harbor levels for many Proposition 65 chemicals. A safe harbor level identifies a level of exposure to a listed chemical that does not require a Proposition 65 warning. A business does not need to provide a warning if exposure to a chemical occurs at or below these levels. These safe harbor levels consist of No Significant Risk Levels (NSRLs) for chemicals listed as causing cancer and Maximum Allowable Dose Levels (MADLs) for chemicals listed as causing birth defects or other reproductive harm.

If OEHHA has not established a safe harbor level for a chemical, businesses that expose individuals to that chemical would be required to provide a Proposition 65 warning, unless the business can show that the anticipated exposure level will not pose a significant risk of cancer or reproductive harm[1]. OEHHA has adopted regulations that provide guidance for businesses in calculating their own safe level of exposure in the absence of an OEHHA safe harbor level. Regulations are available at Article 7 and Article 8 of Title 27, California Code of Regulations.

Determining anticipated levels of exposure to listed chemicals can be very complex. Although a business has the burden of determining if a warning is required, a business is discouraged from providing a warning that is not necessary (*i.e.,* over-warning for hazards).

The purpose of this Standard is to determine if a specific product requires labeling in accordance with Proposition 65 regulations. The Standard outlines methods for determining if humans may be exposed to chemicals associated with products/materials and if the levels of exposure are high enough such that Proposition 65 labeling of the product is warranted. If it is determined that a specific product may expose an individual to a chemical(s) on the Proposition 65 list at a harmful level, this Standard provides instructions for labelling the product in accordance with the most up-to-date Proposition 65 guidelines, including what chemical(s) is of concern and what health effect(s) is of concern.

[1] Under Proposition 65, toxicity of chemicals that affect either the ability of a human to reproduce or that causes direct toxicity to a fetus during development (birth defects) are grouped together in labeling, even though reproductive toxicity and developmental toxicity are two very different types of toxic effects, with some chemicals only affecting reproduction and others only linked with toxicity to a developing fetus.

IAPMO IGC 1123-2022
California Proposition 65 Compliance – Products or Materials.

1 General

1.1 Purpose

The purpose of this Standard is to establish methods to address the compliance of consumer products or materials with California Proposition 65 requirements. Product compliance is determined in accordance with this Standard and input from a product manufacturer and supplier.

1.2 Scope

This Standard is intended to cover specific consumer materials or products and may include, but are not limited to:

- Drinking Water Treatment Products
- Plumbing Products
- Pool and Spa Equipment
- Drinking Water Treatment Chemicals

The California Code of Regulations defines “consumer product” in § 25600.1. Definitions. as “any article, or component part thereof, including food, that is produced, distributed, or sold for the personal use, consumption or enjoyment of a consumer.” This Standard does not address any potential exposures which may occur during the initial installation of a consumer product, whether the installation is by a professional or a consumer. This Standard specifies acceptable laboratory testing methods for various products/materials and exposure pathways. In addition, this Standard specifies methods used to derive safe harbor levels, (No Significant Risk Levels (NSRLs) for cancer-causing chemicals and Maximum Allowable Dose Levels (MADLs) for chemicals causing reproductive toxicity), for chemicals specified on the Proposition 65 list for which no safe harbor levels have been derived. The Standard is intended to be used by risk managers.

1.3 Terminology

In this Standard,

(a) "shall" is used to express a requirement, i.e., a provision that the user is obliged to satisfy to comply with the Standard;
(b) "should" is used to express a recommendation, but not a requirement;
(c) "may" is used to express an option or something permissible within the scope of the Standard; and
(d) "can" is used to express a possibility or a capability.

Notes accompanying sections of the Standard do not specify requirements or alternative requirements; their purpose is to separate explanatory or informative material from the text. Notes to tables and figures are considered part of the table or figure and can be written as requirements.

1.4 Units of Measurement

SI units are the primary units of record in global commerce. In this Standard, the inch/pound units are shown in parentheses. The values stated in each measurement system are equivalent in application, but each unit system is to be used independently. All references to gallons are to U.S. gallons.

1.5 Limitations

The methodology outlined in this Standard is only applicable to California Proposition 65 requirements. Ultimately, the manufacturer and/or supplier is responsible for determining if a warning label should be used for a specific product. This Standard also does not include continuous compliance management, sometimes seen in other standards or industry guidance documents. Use of this standard is not a substitute for legal guidance regarding California Proposition 65 warning label requirements.

1.6 Significant Figures and Rounding

To determine conformance with the specifications in this Standard, the Absolute Method in ASTM E29 Standard Practice for Using Significant Digits in Test Data to Determine Conformance with Specifications shall be used. The rounding procedure in Section 6.4 of ASTM E29 shall be used when rounding numbers.

2 Reference Publications

This Standard refers to the following publications and, where such reference is made, it shall be to the current edition of those publications, including all amendments published thereto.

ASTM International

ASTM E29
Standard Practice for Using Significant Digits in Test Data to Determine Conformance with Specifications

ISO
ISO 10993-1
Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process

NSF International
NSF/ANSI/CAN 61
Drinking Water System Components - Health Effects

NSF/ANSI 42
Drinking Water Treatment Units - Aesthetic Effects

NSF/ANSI 44
Residential Cation Exchange Water Softeners

NSF/ANSI 53
Drinking Water Treatment Units - Health Effects

NSF/ANSI 55
Drinking Water Treatment Units - Aesthetic Effects

NSF/ANSI 58
Reverse Osmosis Drinking Water Treatment Systems

NSF/ANSI 62
Drinking Water Distillation Systems

NSF/ANSI 401
Drinking Water Treatment Units - Emerging Compounds / Incidental Contaminants

NSF/ANSI/CAN (NSF) 600
Health Effects Evaluation and Criteria for Chemicals in Drinking Water

U.S. EPA (U.S. Environmental Protection Agency)
U.S. Environmental Protection Agency (U.S. EPA). 1991. Guidelines for Developmental Toxicity Risk Assessment. EPA/600/FR-91/001. United States Environmental Protection Agency, Washington, DC, USA. Available at: https://www.epa.gov/sites/default/files/2014-11/documents/dev_tox.pdf.

U.S. Environmental Protection Agency (U.S. EPA). 1996. Guidelines for Reproductive Toxicity Risk Assessment. EPA/630/R-96/009. United States Environmental Protection Agency, Washington, DC, USA. Available at: https://www.epa.gov/sites/production/files/2014-11/documents/guidelines_repro_toxicity.pdf.

U.S. Environmental Protection Agency (U.S. EPA). 1998 - 2003. Series 870 – Health Effects Test Guidelines. United States Environmental Protection Agency, Washington, DC, USA . Available at: https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-870-health-effects-test-guidelines.

U.S. Environmental Protection Agency (U.S. EPA). 2005. Guidelines for Carcinogen Risk Assessment.
Risk Assessment Forum. EPA/630/P-03/001B. United States Environmental Protection Agency, Washington, DC, USA. Available at: https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment

U.S. Environmental Protection Agency (U.S. EPA). 2019. Guidelines for Human Exposure Assessment. (EPA/100/B-19/001). Washington, D.C.: Risk Assessment Forum, U.S. EPA. Available at: https://www.epa.gov/sites/default/files/2020-01/documents/guidelines_for_human_exposure_assessment_final2019.pdf.

U.S. Environmental Protection Agency (U.S. EPA). 2022. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency, Washington, DC, USA. Available at: https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface.

U.S. Environmental Protection Agency (U.S. EPA). 2022. EPA ExpoBox (A Toolbox for Exposure Assessors). United States Environmental Protection Agency, Washington, DC, USA. Available at: https://www.epa.gov/expobox.

U.S. FDA (U.S. Food and Drug Administration)
U.S. Food and Drug Administration (U.S. FDA). 2020. Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process." United States Food and Drug Administration, Silver Spring, MD, USA. Available at: https://www.fda.gov/media/85865/download.

California Office of Environmental Health Hazard (OEHHA)
California Office of Environmental Health Hazard Assessment (OEHHA). Proposition 65 Website. Available at: https://oehha.ca.gov/proposition-65.

California Office of Environmental Health Hazard Assessment (OEHHA). Initial Statement of Reasons Title 27, California Code of Regulations, Proposed Amendment to Section 25703, Subsection (a)(6) Quantitative Risk Assessment, Safe Drinking Water and Toxic Enforcement Act of 1986 Proposition 65. Available at: https://oehha.ca.gov/media/downloads/crnr/072911isor25703.pdf.

California Office of Environmental Health Hazard Assessment (OEHHA). 2001. Process for Developing Safe Harbor Numbers. Available at: https://oehha.ca.gov/media/downloads/crnr/2001safeharborprocess.pdf.

California Office of Environmental Health Hazard Assessment (OEHHA). California Proposition 65 Glossary. Available at: https://www.p65warnings.ca.gov/glossary.

California Safe Drinking Water and Toxic Enforcement Act of 1986. Available at: https://govt.westlaw.com/calregs/Browse/Home/California/CaliforniaCodeofRegulations?guid=I42D79370D45011DEA95CA4428EC25FA0&originationContext=documenttoc&transitionType=Default&contextData=(sc.Default).

3 Definitions and Abbreviations

3.1 Definitions

The following definitions shall apply in this Standard:

Consumer Information - Warnings, directions for use, ingredient lists, and nutritional information. “Consumer information” as it relates to Proposition 65 does not include the brand name, product name, company name, location of manufacture, or product advertising.

Consumer Product - Any article, or component part thereof, including food, which is produced, distributed, or sold for the personal use, consumption or enjoyment of a consumer.

Consumer Product Exposure - An exposure that results from a person's acquisition, purchase, storage, consumption, or any reasonably foreseeable use of a consumer product, including consumption of a food.

Chronic Exposure - Repeated exposure by the oral, dermal, or inhalation route for more than approximately 10% of the life span in humans (more than approximately 90 days to 2 years in typically used laboratory animal species).

Exposure - Coming into contact with a substance, for example by swallowing, breathing, or touching the skin or eyes.

Exposure Assessment - The process of estimating or measuring the magnitude, frequency and duration of exposure to an agent and the size and characteristics of the population exposed (U.S. EPA 2019).

Exposure Duration - The length of time of contact with an agent (e.g., one year).

Exposure Frequency - The number of exposure events in an exposure duration (e.g., 365 days per year).

Hazard — Is a characteristic of a chemical that defines its potential to cause harm or adverse effects in humans. Hazard is the potential for harm.

Risk — The nature and probability of occurrence of an unwanted adverse effect on human life or health, or on the environment. Thus, risk is the chance that someone may actually be harmed by a hazard.

Genotoxic – A term used when a chemical is able to interact with and damage the genetic material, DNA, of a cell, often causing a mutation. The tests that are used to assess the potential of a chemical to damage DNA are known as “genotoxicity” studies.

Leachate – Any liquid that, in the course of passing through matter, extracts soluble or suspended solids, or any other component of the material through which it has passed.

Mutation – A heritable change in the structure or sequence of the DNA that carries the "blueprint" for the normal function of a cell, and which changes the function or behavior of the cell.

Developmental toxicant – An agent that causes developmental toxicity. A chemical that causes adverse effects on the developing embryo, fetus, or child resulting from exposure during or before pregnancy. Developmental toxicity, therefore, occurs when a chemical causes adverse effects on the developing embryo, fetus, or child resulting from exposure during or before pregnancy.[2]

Label - A display of written, printed or graphic material that is printed on or affixed to a product or its immediate container or wrapper.

Labeling - Any written, printed, graphic, or electronically provided communication that accompanies a product, such as a package insert.

Reproductive toxicant -- An agent that can cause reproductive toxicity. Reproductive toxicity occurs when a chemical interferes with the ability to produce normal, healthy offspring. This includes effects on the female and male reproductive systems, and effects on the developing embryo, fetus, or child, resulting from exposure during pregnancy. Under Proposition 65, "reproductive toxicity" includes "developmental toxicity," "female reproductive toxicity," and "male reproductive toxicity".[3]

Safe Harbor Levels – A level of exposure to a listed chemical that does not require a Proposition 65 warning. A business does not need to provide a warning if exposure to a chemical occurs at or below these levels. These safe harbor levels consist of No Significant Risk Levels (NSRLs) for chemicals listed as causing cancer and Maximum Allowable Dose Levels (MADLs) for chemicals listed as causing birth defects or other reproductive harm.

Note:

(1) Definition Retrieved December 1, 2020, from: https://www.p65warnings.ca.gov/faq/businesses/what-are-safe-harbor-numbers

(2) The Proposition 65 list is updated by OEHAA in an ongoing basis. The reference to the Proposition 65 list in this document refers to the current Proposition 65 list. A copy of the current Proposition 65 list can be found at https://oehha.ca.gov/proposition-65/proposition-65-list/.

Safe Harbor Warning - A clear and reasonable warning that provides a "safe harbor" against enforcement actions for businesses that choose to use them.

Systemic Effects – Health effects that occur in tissues distant from the site of contact between the body and the toxicant.

Toxicity – The characteristic of being toxic or poisonous

[2] https://www.p65warnings.ca.gov/glossary#letter_d

[3] https://www.p65warnings.ca.gov/glossary#letter_r

Drinking Water Treatment Unit Standards — Series of standards used for evaluation of drinking water treatment units which include NSF 42, 44, 53, 55, 58, 60, 61, 62, and 401.

3.2 Abbreviations

The following abbreviations apply in this Standard:

DWTUS — Drinking Water Treatment Unit Standards

BOM — Bill of Materials

CAS — Chemical Abstract Service

PMI — Product Material Information

MADL — Maximum Allowable Dose Levels

NSRL — No Significant Risk Levels

OEHHA — California Office of Environmental Health Hazard Assessment

OECD — Organization for Economic Co-operation and Development

U.S. EPA— United States Environmental Protection Agency

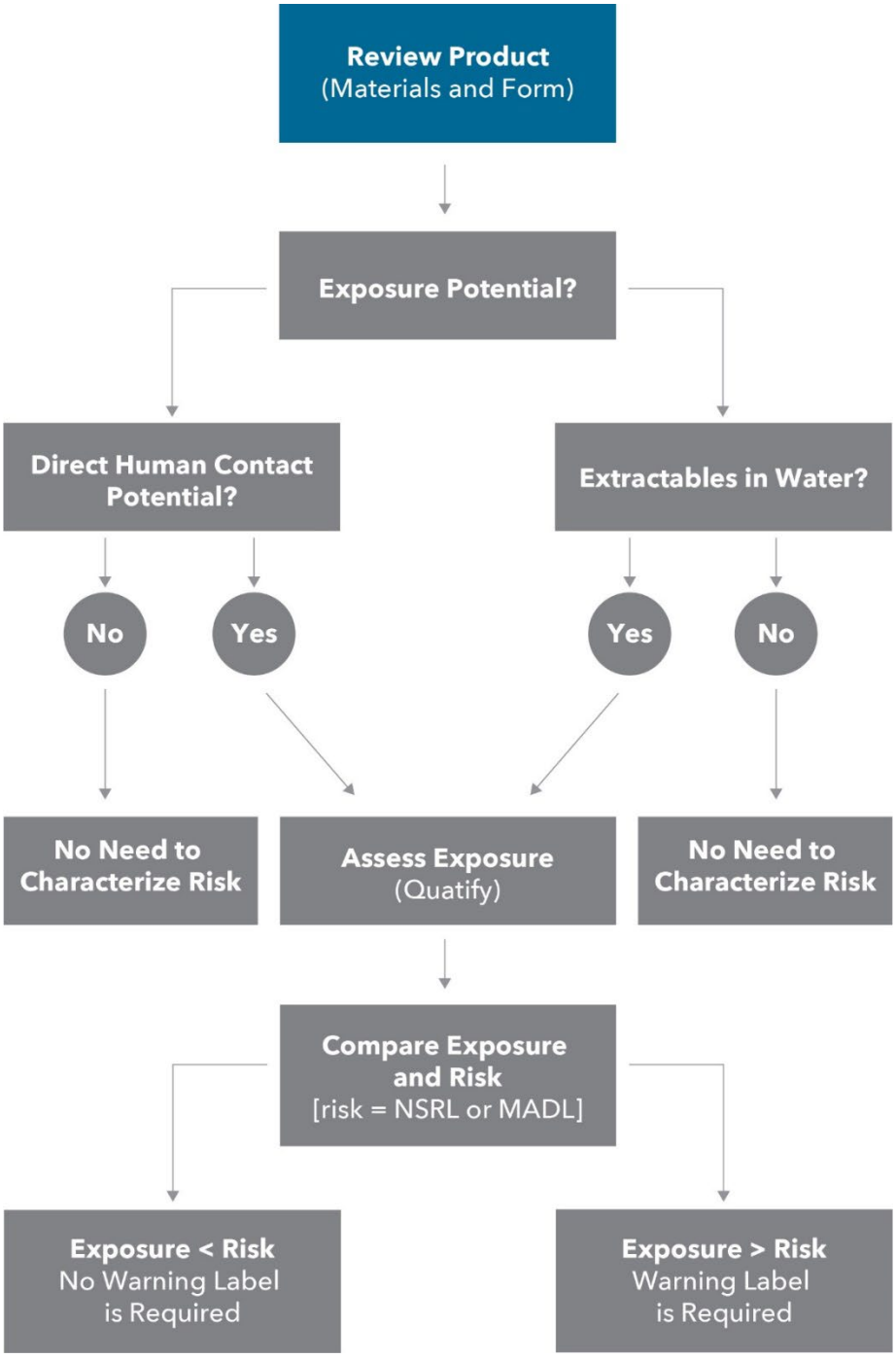
ICH — The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use

4 Determining Conformance with California Proposition 65 Requirements

4.1 Decision Tree Approach for Determining Product Compliance with California Proposition 65 Requirements

Figure 1 outlines a decision tree for a risk manager to use to determine if a product/material complies with California Proposition 65 requirements. The decision tree asks a series of questions to drive the process for product compliance determination. The first step in the decision tree is to conduct a thorough Product Review and is shown in blue. Sections 4.2 through 4.4 address the steps in the Product review process. Subsequent steps in the decision tree are shown in grey and are discussed in Sections 5 through 8.

Figure 1
Risk Management Decision Tree
(See Section 4)



The first step in the decision tree is to conduct a thorough Product Review and is shown in blue

Subsequent steps in the decision tree are shown in grey and are discussed in Sections 5 through 8

4.2 Review Product Materials

In order to determine if a product/material complies with California Proposition 65, a determination of the complete chemical makeup of a product is required. The following product information shall be obtained and reviewed to determine compliance with California Proposition 65 (please refer to Appendix A for an example questionnaire and Appendix B for an example Product Materials Information (PMI) or Bill of Materials (BOM) form used to obtain the required information):

(a) Model Number and Name of Product
  (i) If the product is used to represent other, similar products, the justification for product "bracketing" shall be included in the documentation
(b) Information about the Product manufacturer (i.e., company name, address, phone number, and point of contact)
(c) Information about the Product supplier(s) (i.e., supplier company name, address, phone number, and point of contact)
(d) Complete chemical formulation of the Product (e.g., common name for each chemical, corresponding CAS numbers, percent composition of each chemical in the product, supplier information for each material/component)
(e) Diagram/Drawing/Photograph of the Product to be evaluated, including a blown-out diagram to show all components
(f) Manufacturer Instructions
  (i) Intended Use of Product
  (ii) Intended Frequency and Duration of use of the Product
  (iii) Conditions under which the Product will be used (e.g., maximum temperature to which the product is exposed during its intended use, residential or occupational use).
(g) Information about how the Product is sold and/or given away (i.e., online, in-store, outside sales)
(h) Installation instructions (e.g., by a professional, by a consumer)
(i) Complete list of replacement part(s) for the Product
  (i) Installation instructions for replacement part(s)
(j) Information about any surface coating applied to the Product
  (i) Chemical formulation for the surface coating
  (ii) Information about how the surface coating is applied
    (1) In the field application information
    (2) In the factory application information
  (iii) If there is a surface coating, will it wear off over time, exposing the underlying surface?
(k) Any other information deemed necessary to conduct a complete Product review

4.3 Material Specific Analysis

The purpose of obtaining the documentation in Section 4.2 is to identify constituent materials that may require further assessment. Specific testing and the method for risk assessment analysis, if necessary, shall be determined by the intended use and the material chemical composition of the product provided by the manufacturer. If further assessment is recommended based on the initial Product review, the most rigorous conditions shall apply.

4.4 Proposition 65 Chemical Analysis

After the initial product review, the chemical composition of the product, shall be compared to chemicals on the most current Proposition 65 list. Chemicals considered would be those that are intentionally added to the product, those known to be present in a product. If ingredients are not on the Proposition 65 list, no further assessment is required and the product is in compliance with Proposition 65 requirements, and no warning is required. If any ingredients are determined to be on the Proposition 65 list, an exposure assessment may be conducted (see section 5).

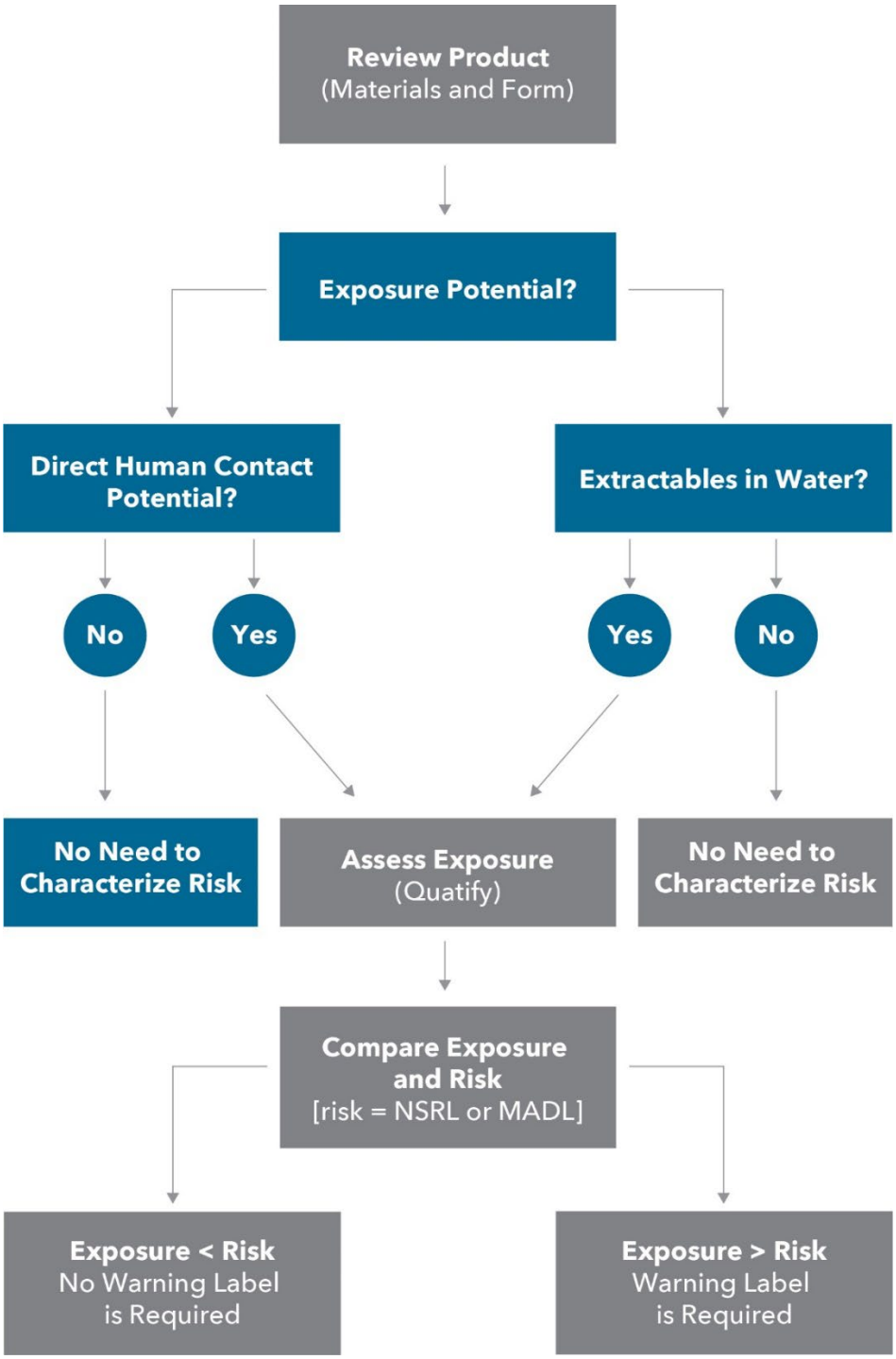
5 Exposure Assessment

After the initial product review and comparison of ingredients to chemicals on the Proposition 65 list, an exposure assessment may need to be conducted to determine if further risk analysis is needed. According to the U.S. EPA Guidelines for Human Exposure Assessment (U.S. EPA 2019), an exposure assessment is "the process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent…" with exposure defined by the California Code of Regulations as "coming into contact with a substance, for example by swallowing, breathing, or touching the skin or eyes."

If product ingredients are on the Proposition 65 list, but no human exposure potential exists, no further assessment is required, and the product is in compliance with Proposition 65 requirements. Thus, no warning is required. However, if a product's ingredients are on the Proposition 65 list and there is the potential for human exposure, an exposure assessment is warranted (see Figure 2).

With respect to this Standard, the purpose of the exposure assessment is to estimate the type and magnitude of actual/estimated exposures, the frequency and duration of the exposures, and the route by which humans may be exposed to the chemical ingredient(s) of a product/material, if product ingredient(s) are on the Proposition 65 list. All of these factors (magnitude, frequency, duration, and route of exposure) determine the potential for adverse health effects to occur (U.S. EPA 2019). The steps for conducting an exposure assessment are outlined in Sections 5.1 and 5.2. The exposure assessment steps are shown in blue on the decision tree in Figure 2. For more detailed information on exposure assessments, please refer to Guidelines for Human Exposure Assessment (U.S. EPA 2019) and the Exposure Factors Handbook (U.S. EPA 2011).

Figure 2
Exposure Assessment Steps
(See Section 5)



The exposure assessment steps are shown in blue

Subsequent steps in the decision tree are shown in grey and are discussed in Sections 5 through 8

5.1 Characterize the Exposure Setting and Determine Exposure Potential

The exposure setting, both the physical environment and the potentially exposed population must be defined by the risk manager as an initial step in the exposure assessment and are dependent upon the intended use of each product. Information obtained from the initial product review step will inform the risk manager as to the exposure setting for a specific product (e.g., a water filtration device might be used on a kitchen faucet and use of the product will expose anyone who uses water from the faucet after filtration). Exposure potential is dependent upon whether an exposure pathway is complete in a particular exposure setting, either by direct contact with a toxicant in a product or by contact with chemicals that leach from the product into water or air. Exposure may occur to a product and in some cases, product packaging. Product packaging that is not part of the product does not need to be evaluated along with the product. However, if packaging can cause a significant exposure to a listed chemical, should be considered separately from the product itself.

5.2 Identify Exposure Route(s)/Exposure Pathways

After the exposure setting has been determined, a risk manager must evaluate the setting to determine if any exposure pathways may be complete by any route of exposure. According to the California Code of Regulations:

§ 25707. Routes of Exposure

"Where scientifically valid absorption studies conducted according to generally accepted standards demonstrate that absorption of a chemical through a specific route of exposure can be reasonably anticipated to present no significant risk of cancer at levels of exposure not in excess of current regulatory levels, the lead agency may identify the chemical as presenting no significant risk by that route of exposure. Any exposure, discharge or release of a chemical so identified shall be deemed to present no significant risk to the extent that it results in exposure to humans by the identified route, and does not exceed the level established in any other applicable federal or state standard, regulation, guideline, action level, license, permit, condition, requirement or order.

The following chemicals present no significant risk of cancer by the route of ingestion:

(1) Asbestos

(2) Beryllium and beryllium compounds

(3) Cadmium and cadmium compounds

(4) Nickel and nickel compounds"

5.2.1 Mode of Contact Review

The exposure assessment should include an evaluation of the different potential modes of contact (routes of exposure), both direct and indirect to determine if any of the exposure pathways are complete. There are three basic modes of contact, and the degree or extent of exposure is determined by measuring/estimating the amount of a toxicant at the point of contact. The three basic modes of contact are ingestion, inhalation, and direct contact (dermal) and are discussed in Sections 5.2.1.1 through 5.2.1.3.

5.2.1.1 Ingestion Exposure

Ingestion exposure occurs when an individual introduces a chemical into the gastrointestinal tract, either intentionally or unintentionally. A chemical may interact with the gastrointestinal tract or may be absorbed into the bloodstream. In an exposure assessment, the ingestion of both food and non-food items must be taken into account which may include an understanding of oral exposure to vapors or air concentrations of chemicals, and chemicals in dust, soil, and other non-food items (U.S. EPA 2019).

5.2.1.2 Direct Contact (Dermal) Exposure

Direct contact exposure occurs when a chemical contacts an individual's skin (e.g., while swimming, bathing, showering, gardening). A chemical may act directly on the skin or may be absorbed through the skin to act systemically. A dermal exposure evaluation includes an assessment of what components of a product are readily handled by a consumer. This mode of contact review should consider whether a component is internal to a product, where an individual does not come in contact, or whether a component of the product is external, where direct contact can occur. Dermal contact may also be considered if a component is exposed to water when leaching or extraction may occur, and that water containing a compound can either be in direct contact with skin, or have an air vapor or air concentration, which comes into contact with skin.

5.2.1.3 Inhalation Exposure

Inhalation exposure occurs when an individual breathes a chemical. Depending on chemical properties, a chemical can cause point-of-entry effects by directly affecting the respiratory tract or the chemical may enter the bloodstream through respiratory tract tissues and potentially cause systemic effects. Due to the complex nature of the respiratory tract, estimating the inhaled dose is complicated (U.S. EPA 2019). With respect to this Standard, inhalation exposure involves the breathing of any chemicals a product may release into the air or vapor, or through water that carries a leachate/extractable that vaporizes and is then inhaled.

5.2.2 Combined Exposure

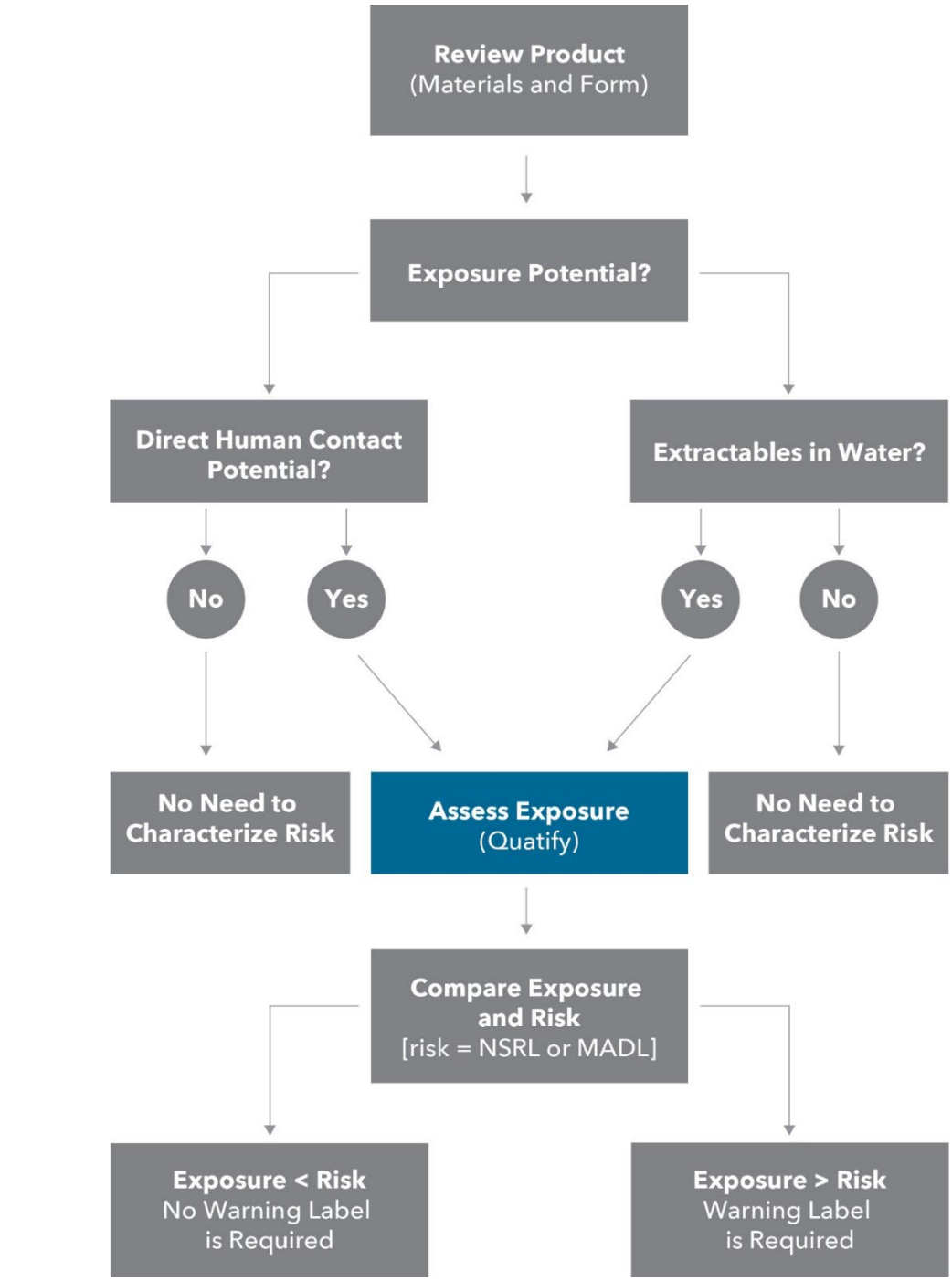
Combined exposure is the total exposure to a chemical due to ingestion, inhalation, and dermal routes of exposure and is additive and accounted for through a summation of the various exposure amounts. In some cases, a specific health effect (e.g., reproductive effects) only occur through one route of exposure (e.g., reproductive effects only occur via the ingestion route but not the dermal or inhalation routes). Proposition 65 evaluations are conducted on a chemical-by-chemical basis.

6 Laboratory Analysis/Modeling Methods Used to Quantify Exposure Concentrations

Once an initial product formulation review has been conducted, and the exposure assessment for ingredients on the Proposition 65 list has been conducted and found at least one exposure pathway to be complete, a risk manager may choose to quantify what levels of a chemical an individual may be exposed to by conducting laboratory analyses/modeling. The types of testing/modeling required will depend on the product being evaluated and the possible exposure scenarios (e.g., inhalation, dermal contact, and ingestion). The exposure quantification steps (laboratory analyses/modeling) are shown in blue on the decision tree in Figure 3.

Note: *For Proposition 65 settlements (Settlement Judgments) testing in accordance with the settlement shall be followed. For evidence of enforcement see a list of settlement judgments which are included in Appendix C*

Figure 3
Exposure Quantification Steps
(See Section 6)



The exposure quantification steps (laboratory analyses/modeling) are shown in blue

Subsequent steps in the decision tree are shown in grey and are discussed in Sections 5 through 8

6.1 Types of analytical testing available for products/materials

The type of analyses required for a product will be based on the chemicals requiring further assessment. Article 9 of Title 27, California Code of Regulations provides guidance regarding the use of specific methods of detection and analysis, where "methods of detection and analysis" defined in Article 9 is a "specific analytical testing procedure appropriate for detecting a particular chemical in a particular matrix such as air, water, soil or food that is applied for the purpose of detecting the chemical or measuring its concentration." "Matrix" is defined as "the component or substrate that contains the chemical." According to Article 9:

- The method of detection and analysis should be "conducted by a laboratory certified by the State of California or accredited by the State of California, a federal agency, the National Environmental Laboratory Accreditation Program or similar nationally recognized accrediting organization to perform the particular method of detection and analysis in question."
- The method of detection and analysis should be applied to the same matrix in which the exposure is likely to occur (e.g., air, water, soil, or food).
- The methods of detection and analysis that may be used are those that are "required or sanctioned by the federal Food and Drug Administration, the U.S. Environmental Protection Agency, the federal Consumer Product Safety Commission, the California Department of Health Services, the California Environmental Protection Agency and its constituent boards, departments or office, an Air District, a Regional Water Quality Control Board, a Certified Unified Program Agency, or other local enforcement agency in California with jurisdiction over the product…"

Please refer to Appendix D for information regarding testing methods.

6.2 Models that can be used to estimate exposure concentrations

Modeling can be used to estimate exposure concentrations, either in combination with laboratory testing or without. When used together with analytical testing, and a dose concentration in water (if relevant) data can be taken from the testing, it can be used to determine if there is significant ingestion exposure, and also if there is a relevant concentration of a chemical that can be leached or extracted and expose an individual by either

(a) direct contact with the user or consumer (dermal route of exposure), or
(b) release into water or off-gas at a concentration that an individual can inhale (inhalation route of exposure).

Models can be used without analytical testing by using indirect estimation of exposure concentrations. Indirect estimation is typically not as accurate as using analytical data to predict exposure. Whether being used alone or in combination with analytical testing, some models may be useful to use to estimate dose or concentration upon exposure, one useful tool for this can be the EPA model EpISuite. Details of the EPISuite are beyond the scope of this Standard but can be accessed to review in more detail here: https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface.

Human exposure can occur in one of three routes or in a combination of these routes: oral, inhalation, and dermal. Another great tool is the EPA Expobox which can help provide guidance on how to decide the appropriate approaches, consideration for media, and methods or models for the three routes of exposure: https://www.epa.gov/expobox.

For the practicing risk assessor, the EPA updated their guidance on human exposure assessment in 2019 and that guidance can be accessed here: https://www.epa.gov/risk/guidelines-human-exposure-assessment. Section 2.6 includes a list of exposure models that may be useful in the quantification of exposure.

These resources can include guidance on addressing uncertainty in the exposure assessment as well. EPA guidance addresses some of this, including Bayesian analysis. Another useful resource for comparison for extractables and leachates includes FDA guidance on medical devices, which relates to the ISO 10993-1 Standard. The guidance can be accessed here: https://www.fda.gov/media/85865/download.

6.3 Calculating Estimated Dose (Non – Benchmark Method)

The total combined exposure amount (concentration) from laboratory analyses/exposure modeling must be calculated to estimate the total dose.
Average daily dose: Exposure levels and estimated dose is defined in tiers or groups based on potential frequency of use (e.g., High, Mid and Low). Utilizing the highest tier as the basis for evaluation is the most conservative approach. However other tiers are considered during evaluation.

Ingestion is, for most of the products/materials within the scope of this Standard (e.g., drinking water treatment products, plumbing products, drinking water treatment chemicals) the most likely exposure pathway typically leading to the highest dose. Inhalation of water vapor and dermal absorption based on skin contact of water containing a leached or extracted chemical are secondary sources of exposure that a risk assessor can use expert judgement to determine if these routes of exposure should be included in the model. For pool and spa equipment, the most likely exposure pathway leading to the highest dose will depend on how the product/material is used.

It is important not to confuse this Estimated Dose with estimates for benchmark dosing. In this circumstance, calculating estimated dose is more specific to the concentration that will be relevant in the exposure assessment method, benchmark dose calculations may be more relevant in the risk characterization section discussed in section 7.

7 Identification and/or Derivation of Risk Values for Materials and Leachates

Once exposure pathways for products/materials have been identified and any exposure that might occur has been quantified (see Sections 5 and 6 of this Standard), the next step in the risk assessment process involves identification of an existing toxicity reference value (risk value), or derivation of a toxicity reference value or risk value for the chemical(s) in the product, or a leachate from a product. Proposition 65 is limited to consideration of two general types of toxicity, cancer and reproductive/ developmental toxicity. Thus, risk values that exist under Proposition 65, or that might need to be derived in order to comply with Proposition 65 labeling, only relate to one of those two endpoints of toxicity. The risk values associated with Proposition 65 compliance are known as "No Significant Risk Levels" (NSRLs) for carcinogens and as "Maximum Allowable Dose Levels" (MADLs) for reproductive/developmental toxicants. The California Office of Environmental Health Hazard and Assessment (OEHHA), the regulatory authority that administers Proposition 65 in California, maintains a list of chemicals that the State has identified as either carcinogens or reproductive toxicants. In some cases, OEHHA has derived NSRL or MADL levels for a listed chemical while in other cases, the chemical is listed without OEHHA defining a "safe harbor level" (*i.e.,* a risk value).[4] This Standard for certain products/materials addresses both situations that might be encountered by risk managers.

[4] Chemical get listed by OEHHA as Proposition 65 chemicals through one of two mechanisms. Either California's outside expert panels recommend a listing or an outside authoritative body (i.e., IARC, EPA, FDA) has listed the chemical as either a carcinogen or a reproductive/ developmental toxicant.

7.1 Decision Tree Approach for Identifying Risk Values

Figures 4 and 5 outline a decision tree approach for a risk manager to use when identifying risk values that can be employed during risk characterization for making Proposition 65 labeling decisions. The decision tree asks a series of questions to drive the process for risk value identification, specifically NSRLs in Figure 4 and MADLS in Figure 5. Moving through the decision tree, a risk manager will be either identifying that a NSRL or MADL exists for the chemical/leachate of interest or, if such values are not already listed by OEHHA, the risk manager will be determining if a NSRL or MADL can be derived.

Key points in the decision tree include the following:

(a) A risk manager finds that the chemical or leachate is not listed by OEHHA as a carcinogen or a reproductive/developmental toxicant (the "red" stop sign-shaped points in the decision tree) which means that no Proposition 65 labeling is needed;

(b) A risk manager identifies a chemical or leachate listed as either a carcinogen and/or a reproductive/developmental toxicant by OEHHA and also finds that OEHHA has identified a "safe harbor level" (NSRL and/or MADL) such that risk characterization must be performed to make a labeling decision for the chemical/leachate; and

(c) A risk manager identifies a chemical or leachate listed as either a carcinogen and/or a reproductive/developmental toxicant by OEHHA and finds that OEHHA has not identified a "safe harbor level" (NSRL and/or MADL), which leads to the need to derive a NSRL and/or MADL value for that chemical/leachate.

It is important to remember that for some chemicals or leachates, they have been listed by OEHHA as both carcinogens and as reproductive/ developmental toxicants. In those cases, both decision trees would apply, and a risk manager would need to perform assessments for, and make decisions about, labeling for both types of toxicity. Additionally, risk managers should only derive NSRL and MADL values on their own if they have the training and qualifications to do so (*e.g.*, toxicology, epidemiology, physiology, medicine, *etc.*). The Standard does provide a risk manager with some tools to use when assessing the quality of a NSRL or MADL assessment that either already exists, or that might be performed at their request.

Figure 4
Cancer Risk Labeling
(See Section 7.1)

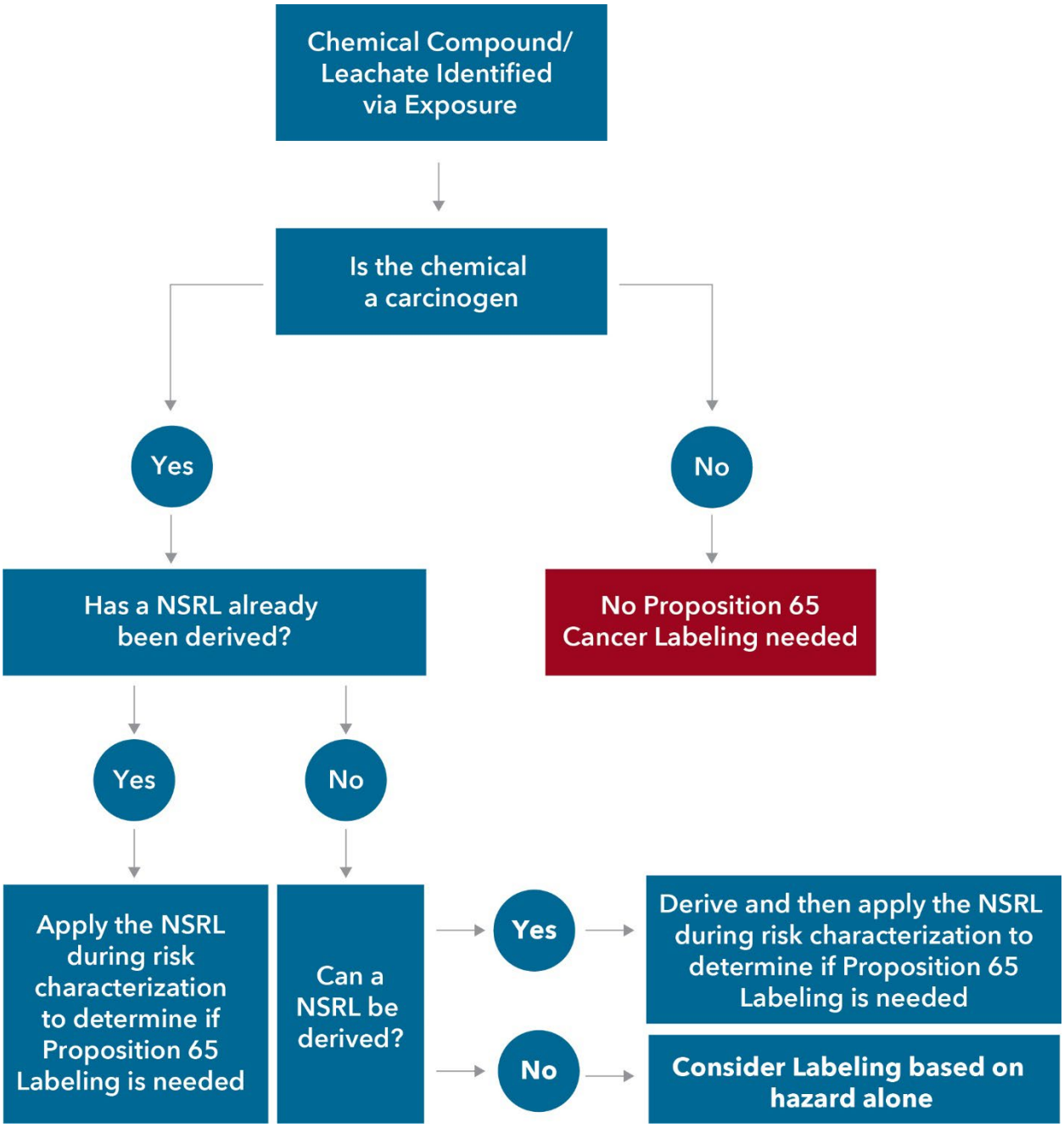
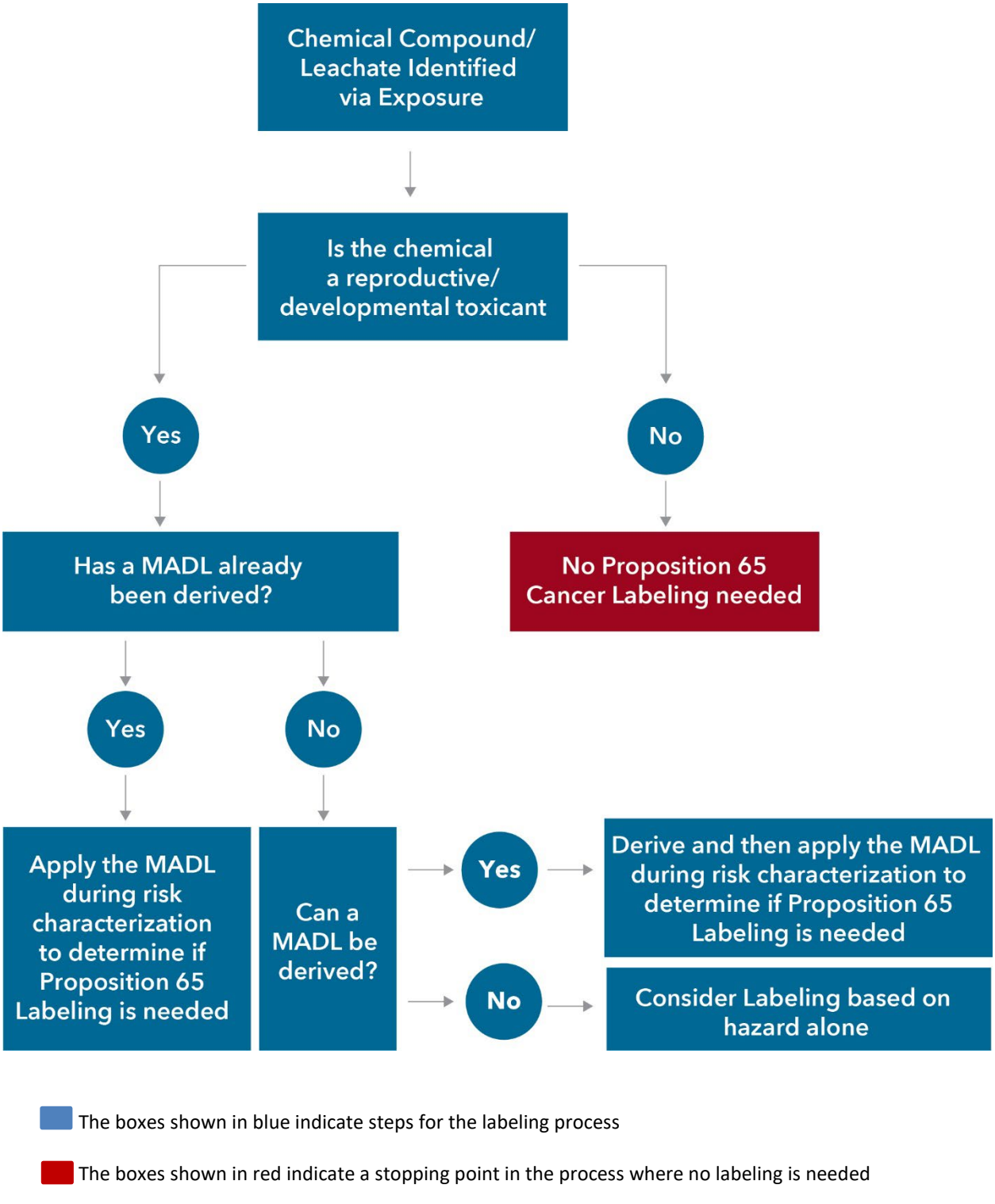


Figure 5
Reproductive/Developmental Risk Labeling
(See Section 7.1)



The boxes shown in blue indicate steps for the labeling process

The boxes shown in red indicate a stopping point in the process where no labeling is needed

7.2 NSRL Values for Carcinogens

A NSRL represents the *"levels of exposure calculated to result in no more than one excess case of cancer in an exposed population of 100,000, assuming exposure over a 70-year lifetime (10^{-5} lifetime risk of cancer)"* (OEHHA, 1989[5]). In Figure 4, the first basic question asks whether a chemical in the product or a leachate has been identified as a carcinogen and listed by OEHHA. The OEHHA list should be used to guide the decision tree finding of whether a compound is a carcinogen. It is important to remember that OEHHA's list of carcinogens is developed based on knowledge available to date and changes over time as new scientific information becomes available or as authoritative bodies perform reviews and list compounds. As a result, risk managers need to revisit the Proposition 65 listings on a routine basis to see if a chemical in their products has been newly listed or removed from existing listing.

For chemicals that are identified as carcinogens, the next point in the decision tree asks if there is a NSRL that has already been derived and made available by OEHHA. If one is available, then that NSRL would be used during risk characterization in Section 8 of the Standard. Although the Proposition 65 list includes a listing of many different NSRL values, not all carcinogens have NSRLs published by OEHHA. If the chemical of interest, or a leachate, is listed as a carcinogen without a listed NSRL, the next step in the decision tree asks if one can be derived. As already discussed, only qualified personnel should undertake NSRL derivation. The next section gives some guidance on the principles to be applied during NSRL derivation as well as some guidance for the risk manager that needs to assess the quality of work performed at their request.

7.2.1 Derivation of NSRL Values: Issues to Consider

The methodology for deriving a NSRL set forth by OEHHA (OEHHA, 2001[6]) is similar to methods used by other regulatory authorities such as the U.S. EPA (2005)[7] for developing cancer potency values. A NSRL and a cancer potency factor are both quantitative assessments of cancer risk. As already discussed, cancer risk related to a NSRL is a level that is linked with no more than 1 case of cancer being associated with exposure to the chemical within a population of 100,000 people. The U.S. EPA cancer potency factor is defined as an upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime exposure to an agent. It typically is expressed in units of proportion (of a population) affected per mg of substance/kg body weight-day. For the general population, U.S. EPA typically applies a risk no more than one excess cancer per million people in the population, a higher standard than the OEHHA standard of an excess cancer risk that exceeds 1 in 100,000.

[5] https://oehha.ca.gov/media/downloads/crnr/072911isor25703.pdf
[6] https://oehha.ca.gov/media/downloads/crnr/2001safeharborprocess.pdf
[7] https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf

Common to both OEHHA and U.S. EPA methodology is the first step of evaluating the quality of available toxicological data, which can include data collected in animals or in human populations. The available studies are used to identify the critical effect of the chemical, in this case carcinogenicity potential. In this data evaluation process, OEHHA guidance assumes that there is no threshold below which there is no risk of cancer. As a result, OEHHA derives NSRLs through use of no-threshold models (extrapolation down to no exposure in a straight line, known as low dose linear extrapolation). In the final step of cancer risk assessment (risk characterization as discussed in Section 8 of this Standard), the NSRL derived will be compared to exposure estimates for a population. If the exposure estimates are at or lower than the NSRL, then the exposure to the population is considered acceptable if it is within a margin of safety, or a risk that does not exceed a risk of greater than 1 in 100,00 (OEHHA 1989).

Evaluation of the quality of the available data is a key or critical step in the process of NSRL derivation. A weight-of-the-evidence evaluation is typically used. Evidence considered in the process typically would include data on tumor findings, or lack of such data, in humans and laboratory animals; an agent's chemical and physical properties; a chemical's structure-activity relationships (SARs) as compared with other carcinogenic agents; and studies addressing potential carcinogenic processes and mode(s) of action, either *in vivo* or *in vitro*. Although data from human studies (epidemiologic studies) are generally preferred for characterizing human cancer hazard and risk, all types of data and information could be employed as non-human data may provide insight into the possible mode(s) of action and likelihood of human cancer hazard and risk. Such an evaluation of data should only be undertaken by risk assessors that have training and/or experience in evaluating toxicological study data in animals as well as studies in human populations.

In some cases, there may be cancer risk assessments that have been performed by outside regulatory bodies (*e.g.,* EFSA, U.S. EPA, other U.S. state agencies) or even published in the peer-reviewed scientific literature. If that is the case, then risk managers within companies should evaluate those risk assessment findings based on some key data quality factors that are commonly used in evaluation of carcinogenicity datasets.

These quality factors for animal studies would include the following:

(a) the study was conducted under Good Laboratory Practice (GLP)[8] conditions;
(b) the exposure has been adequately described and it is relevant to the way that humans might be exposed;
(c) the study was conducted for the lifetime of the animal with daily dosing;
(d) study groups included both exposed and unexposed animals and the groups were of sufficient size for statistical analysis;
(e) dose-response data was collected (multiple exposure groups versus only one); and
(f) background rates of tumor formation in the animal species and strain were considered and discussed, if relevant. Because of the need to ensure that quality data are being used in any cancer risk evaluation, guidelines for toxicology study design have been developed, including designs for carcinogenicity testing in animals.[9] These guidelines for animal study

[8] GLP is a quality system concerned with the process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.
[9] https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-870-health-effects-test-guidelines

design can be used by a risk manager when evaluating the quality of study data that may have been used to derive a NSRL. Adherence with these guidelines is preferred if animal data are being used as a basis for a NSRL value.

In addition to animal studies, human epidemiological study data may have been used to derive a NSRL. If so, a similar evaluation of study quality is appropriate. The quality factors for human studies would include the following:

(a) the study clearly articulates study objectives or hypothesis;
(b) there was proper selection and characterization of comparison groups (exposed and unexposed groups or case and control groups) and exposure is relevant to the assessment being performed (oral, versus dermal versus inhalation);
(c) exposure has been adequately characterized (quantified);
(d) the study had sufficient length of follow-up for disease occurrence;
(e) ascertainment of the causes of cancer morbidity and mortality in the study was adequately described;
(f) bias and confounding factors were considered;
(g) the sample size was adequate to detect an effect (power of the study);
(h) methodology for data collection and analysis was clearly described; and
(i) the study included complete and clear documentation of results. It is unusual for human studies to have all of these characteristics, and some are more critical than others. For example, inadequate description of exposure, both amount and duration, would be a limitation that could lead a risk assessor to exclude human data for NSRL derivation.

Also of concern would be studies that are not able to separate out exposures for specific chemicals; multiple types of exposures occurred, not just exposure to one chemical. A risk manager should evaluate any NSRL derivation process based on human data with these quality factors in mind.

Although this Standard is not meant to be a comprehensive discussion of issues associated with NSRL development, it is important for risk managers to be familiar with the concept of "genotoxic potential" or "a genotoxic mode of action" for a chemical. The term "genotoxic" is defined as the ability of a chemical to interact with and damage the genetic material, DNA, of the cell. In some cases, the damage leads to a "mutation" in the DNA, where a mutation is defined as a heritable change in the structure or sequence of the DNA that carries the blueprint for the normal functioning of the cell, and which changes the cell's function. The functional change could be uncontrolled cellular proliferation (tumor formation). Chemicals that are carcinogenic can be classified as being genotoxic.

Toxicologists often perform a battery of genotoxicity studies for chemicals as a first step in defining the hazards linked to that chemical. Risk managers may encounter chemicals that have robust datasets showing that a compound is genotoxic, while other chemicals may have a robust dataset showing it is not genotoxic. A lack of genotoxicity does not mean a chemical does not pose a cancer hazard. That is because there are chemicals that cause cancer by mechanisms other than through direct interactions with DNA. The importance of discussing genotoxicity in this section of the Standard is merely to point out that OEHHA's approach to NSRL development does not allow for consideration of the mode of action of cancer development, whether a chemical is genotoxic, whereas EPA has specific guidance that separates chemicals by this characteristic, allowing for use of different methods for cancer risk assessment depending on whether a chemical is genotoxic, or not. For additional discussion of this issue, the EPA guidance documents are useful.[10]

Risk managers that follow the decision tree for carcinogens (Figure 4) will arrive at the point where they will either decide that no labeling for cancer is needed or will find they need to move to the next step in the process, risk characterization, where the NSRL values are placed in the context of exposure potential.

7.3 MADL Values for Reproductive Toxicants

In the decision tree, after considering whether or not the chemical is listed as a carcinogen, the next basic question asks whether the chemical in the product or the leachate has been identified as a reproductive toxicant and listed by OEHHA on the Proposition 65 list. The OEHHA list should be used to guide the decision tree finding of whether a compound is a reproductive toxicant.

For chemicals that are identified as reproductive and/or developmental toxicants under Proposition 65, the next point in the decision tree asks if there is a MADL that already has been derived. If one is available, then the MADL would be used during risk characterization in Section 8 of the Standard (he Proposition 65 list includes a listing of a MADL, if one has been derived). Not all reproductive toxicants have MADLs published by OEHHA. If no MADL is listed, then the risk manager needs to determine if there are data of sufficient quality for derivation of a value. As a result, for chemicals identified as reproductive toxicants but for which no MADL is available, the next decision tree point asks whether a MADL can be derived. As already discussed, derivation of a MADL value should only be undertaken by someone with the appropriate training and expertise, which may not be the risk manager.

[10] https://www3.epa.gov/airtoxics/cancer_guidelines_final_3-25-05.pdf

7.3.1 Derivation of MADL Values: Issues to Consider

OEHHA's guidance (OEHAA, 2001[11]) sets forth its methodology for deriving MADL values. The U.S. EPA also has published guidance on assessing reproductive toxicity risk (U.S. EPA 2016[12]) and developmental toxicity risk (U.S. EPA 1991[13]). The science of risk assessment for chemicals with potential reproductive toxicity and/or developmental toxicity also employs a weight-of-the-evidence approach and requires a specific type of training and expertise for scientists that undertake evaluation of this type of human and/or animal study. Animal studies are most commonly used to derive MADL values. Although U.S. EPA guidance addressed the topic of reproductive and developmental risk assessment separately, OEHHA's listing combines the two potential hazards under one warning statement, a statement that can be required based on the presence of only one of the two hazards, or both.

Common to both OEHHA and U.S. EPA methodology is the need to evaluate the quality of available toxicological data. Just as was described above for derivation of a NSRL, the available studies are used to identify the critical effect of the chemical, in this case the ability to induce birth defects (developmental toxicity) or to affect the ability of an animal to reproduce (reproductive toxicity). Since adverse effects on reproductive organs can affect fertility and the ability to reproduce, the potential of a chemical to affect both male and female reproductive organs and systems need to be evaluated. OEHHA guidance discusses the general principles to be applied in MADL development, principles that a risk manager needs to understand whether they are relying on already published MADL values or is asking an outside expert to derive a MADL on their behalf. These principles are as follows (taken from OEHHA, 2001):

(a) The determination of whether exposure to a chemical poses the risk of reproductive and/or developmental toxicity is to be based on evidence that a level of exposure has no observable effect at one thousand (1,000) times the level of exposure in question. Thus, the risk assessor must determine the maximum dose level having no observable effect in a study and dividing that level by one thousand (1,000) to arrive at the maximum allowable dose level, the MADL.
(b) Only studies directed towards endpoints of reproductive and/or developmental toxicity provide the basis for the determination that a chemical is known to the state to cause reproductive and/or developmental toxicity. In other words, the toxicity study used for derivation must be one designed where animals are exposed before mating and while pregnant.
(c) If there are multiple reproductive and/or developmental effects observed in a study chosen for use to derive a MADL, or if there are multiple studies available for review, the reproductive and/or developmental effect for which a study or studies produce the lowest No Observable Effect Level (NOEL) shall be utilized for derivation of the MADL (most sensitive endpoint).
(d) The NOEL shall be the highest dose level which results in no observable reproductive and/or developmental effect and should be expressed in milligrams of chemical per kilogram of bodyweight per day.

[11] https://oehha.ca.gov/media/downloads/crnr/2001safeharborprocess.pdf
[12] https://www.epa.gov/sites/production/files/2014-11/documents/guidelines_repro_toxicity.pdf
[13] https://www.epa.gov/sites/production/files/2014-11/documents/dev_tox.pdf

(e) The quality and suitability of available epidemiologic data shall be included in the assessment to determine whether the study is appropriate as the basis of an assessment considering such factors as the selection of the exposed and reference groups, the reliable ascertainment of exposure, and completeness of follow-up. Biases and confounding factors shall be identified and quantified.

(f) Animal studies, typically in rodents or rabbits, that are to be used for derivation of a MADL shall meet generally accepted scientific principles, including the thoroughness of experimental protocol, the degree to which dosing resembles the expected manner of human exposure, the temporal exposure pattern, the duration of study, the purity of test material, the number and size of exposed groups, and the route of exposure and the extent of occurrence of effects.

(g) The NOEL shall be based on the most sensitive study deemed to be of sufficient quality, either animal or human.

(h) The results obtained for the most sensitive study of sufficient quality for risk assessment shall be applicable to all routes of exposure for which the results are relevant. In other words, if the study is an inhalation study and humans would be expected to be exposed by inhalation, that needs to be considered when selecting a study for risk assessment purposes. If the only data available are inhalation exposure data, then anatomic, physiologic, pharmacokinetic and metabolic considerations can be taken into account.

(i) When data do not allow the determination of a NOEL, the lowest observable effect level (LOEL) can be used by applying an additional factor of 10 (dividing by 10,000 rather than 1000) when deriving the MADL. Again, the resulting value is converted to a milligram per day dose level. If the MADL process is based on an adverse reproductive effect in a male, a human body weight of 70 kg (154 lbs) shall be assumed. If the MADL process is based on an adverse reproductive effect in a female or on a developing organism (embryo, fetus), a human body weight of 58 kg (128 lbs) shall be assumed.

7.3.2 Rare but relevant topics to Risk Characterization

On occasion, a risk assessment can become complex if there is evidence that has to consider limited data and evidence or circumstances that influence a calculation beyond what is required under normal guidance, this can include factors like:

(a) sensitive subpopulations (can be relevant to rare metabolizers of endocrine disruptors, for example);

(b) animal data that is specific to a specific species or genetic strain of animals that do not have reproducible effects in other animal models or genetic strains when compared; and

(c) chemical specific factors like unique reactivity/formation of metabolites etc.. that maybe exposure route dependent as well (first pass metabolism in oral versus inhalation or dermal). Exploration of these types of scenarios as they would relate to NSRL or MADL derivation or evaluation are beyond the scope of this Standard, but it is important for the risk manager to be aware of the possibility.

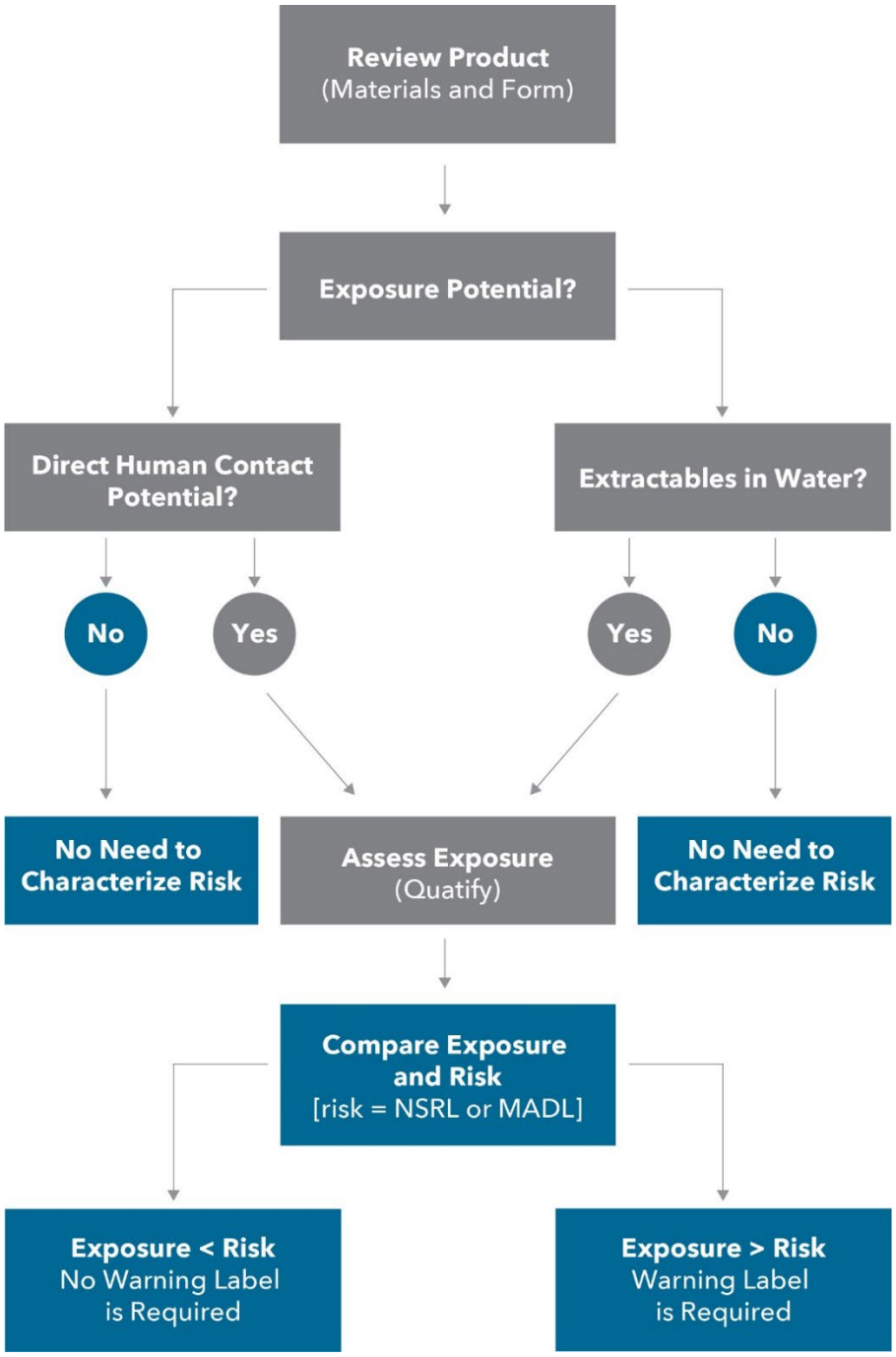
8 Risk Characterization for Product Compliance and Labeling

8.1 Risk Characterization Outcomes

The goal of risk characterization as it pertains to this Standard is to provide an understanding of the type and magnitude of an adverse effect that a particular exposure could cause under particular circumstances. This Standard focuses on characterizing any risks that have been identified for any of the known chemical constituents of products. The Standard applies a tiered approach to risk characterization. Although compliance with provisions of Proposition 65 can result in the need to label products that have been identified as either carcinogenic hazards or reproductive and developmental toxicity hazards, this Standard does not provide labeling recommendations related to Proposition 65 more specifically, whether to label a product or not label with a warning statement. Such decisions are left to companies after they have used this Standard to determine if any risks need to be addressed. The Standard does provide companies with an understanding of how to label if a decision is made to evaluate product risks under the regulations and requirements of Proposition 65.

The figure below provides an overview of the information needed for risk characterization. The part of the figure that appears in blue relates to risk characterization and is the focus of this step in the Standard. The other parts of the figure that appear in gray were discussed in Sections 4, 5 and 6 of this Standard.

Figure 6
Risk Characterization Outcome
(See Section 8)



The part of the figure that appears in blue relates to risk characterization and is the focus of this step

Subsequent steps in the decision tree are shown in grey and are discussed in Sections 5 through 8

8.2 Establishing an Approach to Risk Characterization

Risk characterization is the process of comparing exposure and risk information to determine if there is a likelihood that a product may need to comply with Proposition 65 requirements for labeling. In Figure 6, if exposure is found to be lower than risk, then labeling under Proposition 65 would not be warranted. If, however, exposure exceeds risk, then a company may need to consider the need to label according to Proposition 65.

8.3 Product Labeling Guidance for Safe Harbor Warnings

At the time this IGC was finalized, information about the California Proposition 65 warning label requirements could be found at this webpage: https://www.p65warnings.ca.gov/. This section provides guidance as to what information is required to be included on a "safe harbor" Proposition 65 warning label, and where a product/product packaging should be labelled. A "safe harbor" warning is deemed to be clear and reasonable by OEHHA and provides a safe harbor against enforcement actions for businesses that choose to use them. A business is not required to use the safe harbor warning methods and content. The safe harbor warning method is not applicable to products manufactured prior to August 1, 2018, nor is it applicable to companies covered by warning methods and content contained in a court-approved settlement. For information regarding safe harbor warnings provided on the internet and in catalogs, please refer to the Proposition 65 warnings webpage: https://www.p65warnings.ca.gov/.

8.3.1 Information Required for a Safe Harbor Warning Label

Information required for a safe harbor warning label for a consumer product includes, but is not limited to:

- A warning for consumer products must say the product "can expose you to" a Proposition 65 chemical rather than saying the product "contains" the chemical.
- A warning for a consumer product must include: The name of at least one listed chemical that prompted the warning. The chemical name as it appears on the Proposition 65 list needs to be included in the warning. If a chemical abbreviation is included as part of the full chemical name in a warning, the abbreviation alone may be used for subsequent references to the chemical name.
- A warning must give the internet address for OEHHA's Proposition 65 warnings website, www.P65Warnings.ca.gov.
- There is no minimum type or font size that must be used on a safe harbor warning (with the exception of a "short-form" warning); however, regulations require safe harbor warnings on a label to be prominently displayed with such conspicuousness as compared with other words, statements, designs, or devices on the label as to ensure the warning is likely to be seen, read, and understood under ordinary conditions of purchase or use.
- A "short-form" warning may be used in some cases. There is currently no limitation on using the "short-form" warning on smaller verses larger products. The entire warning may be in a type or font size no smaller than the largest type or font size used for other "consumer information" on the product. The font size must be no smaller than 6-point. The "short-form" warning may be affixed to or printed on a product label which includes its container or wrapper.

- A product manufacturer/supplier may need to provide a safe harbor warning in a language other than English if the consumer information on the consumer product is provided in a language other than English.
- Most warnings must include a triangular warning symbol ⚠, although there is no current ANSI Standard for warning symbols and no requirement that the warning symbol color correspond to a specific ISO number. However, regulations require the warning symbol to be yellow but there is a provision in the regulations for businesses that only print in black and white to have the ability to print the symbol in black and white. Please refer to the downloadable PDF from this webpage for more details: https://www.p65warnings.ca.gov/sites/default/files/art_6_business_qa.pdf

A sample safe harbor warning may look like this:

"⚠**WARNING**: This product can expose you to chemicals including arsenic, which is known to the State of California to cause cancer. For more information, go to www.P65Warnings.ca.gov."

8.3.2 Warning Label Placement

A product warning label should be placed in a manner to ensure that a consumer will see the warning prior to exposure. A warning label must be visible on exterior packaging if the packaging is opaque if an exposure requiring a warning can occur upon opening the packaging. A business may choose to provide a warning on both the exterior packaging and the product.

Appendix A
Example Proposition 65 Questionnaire

1. Company Name, Address, Contact Information:

2. Manufacturer Name, Address, Contact Information:

3. Please provide the following:
   (a) Diagram/Drawing/Photograph of Model
   (b) Complete chemical formulation
      (i) Include chemical names, CAS numbers, percent composition of each
      (ii) Include supplier information for each component/material in the product as it was manufactured
   (c) Laboratory toxicity test data, if available (e.g., NSF/ANSI 61 test data for a plumbing product)

4. Is the product currently certified to any Standard associated with toxicity? Yes☐ No☐
   If yes, please provide details:

5. Product Information:
   (a) Model Number and Name:
   (b) What is the intended use of the product?
   (c) How long is product intended to be used?
   (d) How/Where is it sold? Online☐ Retail☐ Outside Sales Group☐
   (e) Is it installed by a professional ☐ or a consumer ☐?
   (f) If the product has replacement parts/components, how are they intended to be installed
   (g) Does the product have a surface coating? Yes ☐ No☐ Please consider all surfaces that may come into contact with a person directly or indirectly (e.g., wetted area of a faucet or showerhead, bathtub surface, sink surface).
      If yes, please explain:
      (i) If so, how is coating applied?
         a. In the field Yes ☐ No☐
         b. In the factory Yes ☐ No☐
      (ii) Is there a possibility that the coating will wear off over time, potentially exposing an individual to the underlying surface? Yes ☐ No☐
         If yes, please explain:
   (h) If the product has a wetted surface, is there a surface treatment used? (e.g., lead wash) Yes☐ No☐
      If yes, please explain:

Appendix B
Example Product Material Information (PMI) Form

COMPANY NAME: _____
Model Number (Representative Sample): _____
Model Numbers (Bracketed Models):* _____

***Models are identical except for volume or aesthetic changes. Refer to bracketing form for additional information.**

NOTE: Shaded fields below are required only for evaluation against low lead criteria.

Complete this box if solder and flux are used in the product			
	Is it used? Yes/No	% Lead Content	Recognized Lab Findings for Lead Content
Solder			
Flux			

No.	Part Description	Part #	Quantity per assembly	Material	Supplier	Supplier Contact: Phone No. & email	External Surface (Dermal Contact Area) in^2	Aerosol Potential (Y/N)	Water Contact Area in^2	% Wetted Surface	% Lead Content in material	Weighted Lead Content	Recognized Lab Findings % Lead Content in Material
						Total:			0	0.00%	total:	0.0000	

The undersigned representative of the Company Certifies that the information provided is accurate and complete.

Signature: _____ **Date** _____
Print Name: _____ **Title:** _____
Company: _____ **Phone** _____

Appendix C
Proposition 65 Settlement Judgments

Case Documents:
Attorney General Settlements
https://oag.ca.gov/prop65/litigation

Annual Reports of Settlements
https://oag.ca.gov/prop65/annual-settlement-reports

Center for Environmental Health v. Katadyn North America, Inc
https://oag.ca.gov/system/files/prop65/judgments/2013-00237J2853.pdf

Appendix D

For chemicals of concern via the dermal route of exposure, an appropriate method of analysis will address the following:

Extraction (isolation of analytes) from product surface:
(a) Needs to be demonstrated that contaminant(s) may be removed easily and repeatably, and
(b) Needs to remove contaminant(s) efficiently (adequate recovery from surface).

Analysis:
(a) Appropriate analytical technique must be used, or one must be developed if an appropriate analytical technique is not available,
(b) Must be specific to the compound(s) in question, and
(c) Must be sufficiently sensitive.

Quality control:
(a) Demonstrate adequate detection limit,
(b) Demonstrate calibration,
(c) Recovery from the extraction matrix (matrix fortification and recovery), and
(d) Duplicate analysis.

For chemicals of concern via the ingestion exposure pathway,utilize exposure/extraction methods set in NSF/ANSI/CAN 61 and other Drinking Water Treatment Unit Standards (DWTUS) such as NSF/ANSI 42, 44, 53, 55, 58, 62, or 401. For Point-of-Entry water treatment product use NSF/ANSI/CAN 61 and for Point-of Use water treatment products use the applicable DWTUS.

For analysis of the chemicals not covered in NSF/ANSI/CAN 61 and other DWTUS use EPA or other recognized methods. Resources for methods that may be applicable:

- Standard Methods for the Examination of Water and Wastewater, 23rd Edition.
- Test Methods for Evaluating Solid Waste: Physical/Chemical Methods, EPA SW-846 Compendium
- Groundwater Testing: EPA 600/4-79-020 Series
- Methods Approved to Analyze Drinking Water Samples to Ensure Compliance with Regulations: https://www.epa.gov/dwanalyticalmethods
- Methods to screen for residual chemical contamination on surfaces (e.g., bisphenol A residue (BPA) on component with BPA as an ingredient)
- Methods to screen for volatilization of chemicals into the air (e.g., off-gassing of a chemical ingredient).

APPENDIX E
Examples of NSRL and MADL Derivations

Situation Encountered:

An exposure assessment has been performed and it is likely that humans could be exposed to Compound Alpha[14] through drinking water (oral exposure) and/or bathing (dermal exposure). Derivation of a NSRL

Step 1: Is Compound Alpha Listed in the Proposition 65 List?
The risk manager searches the current Proposition 65 to see if Compound Alpha is listed by the State of California as a Carcinogen (the Proposition 65 List) and finds Compound Alpha is listed but no NSRL has been derived by OEHHA.

Step 2: Do scientific studies and/or data exist that can be used to derive a NSRL for Compound Alpha?
The risk manager searches sites where regulatory authorities list risk values that have already been derived for Compound Alpha focusing on risk values linked to cancer as a hazard. The sites to be searched would include those considered by OEHHA as authoritative bodies (i.e., the U.S. Environmental Protection Agency (U.S. EPA), the World Health Organization's International Agency for Research on Cancer (IARC), the National Toxicology Program (NTP), the National Institute for Occupational Safety and Health (NIOSH), and the U.S. Food and Drug Administration (U.S. FDA)). Other sites that should be considered for searching would include other regulatory bodies that have Standards in place for protection of human health (e.g., Health Canada, the Australian Government's Therapeutic Goods Administration and the Food Standards agency, European Commission, etc.). The search finds that none of these sources list a risk value for Compound Alpha related to the potential for cancer with exposure to Compound Alpha.

The lack of identified risk values means that the scientific literature will need to be searched. The risk manager designs a search strategy for a search of the publicly available scientific literature using the name "Compound Alpha"/the Chemical Abstracts Service (CAS) Number linked with terms such as "cancer" and "carcinogen" and "genotoxic". The risk manager identifies both animal data and human data discussing the link of Compound Alpha to cancer and retrieves the full study reports for analysis of the data quality. Table E-1 below provides a summary of the type of studies and data that were identified.

[14] The term "Compound Alpha" is used in this appendix to represent the name of a real chemical.

TABLE E-1 Publicly Available on Compound Alpha Related to Potential Carcinogenicity of the Compound				
Study Species	**Study Type**	**Study Quality Factors**	**Key Design Characteristics**	**Statistical Analysis Performed?**
In Vitro Animal Cells	Ames assay (with and without S9) Rat micronucleus test	Peer-reviewed paper Performed under GLP	Used OECD guidelines for the tests Used a positive control compound (both assays) Positive in the Ames assay but only with S9 included (metabolic activation) Positive in the *in vitro* micronucleus assay	No
Rat	Two year feeding study	Peer-reviewed paper No mention of GLP Study performed in the 1980's Both male and female animals were included in the design with 8 rats per sex per dose group.	Designed with two dose groups and a control diet group No reporting of level of feed intake per day. No increased incidence of tumors of any type were reported.	Yes
Human	Retrospective case-control study	Peer-reviewed paper Worker population Cancer of all types (no focus on one form of cancer) Exposure to Compound Alpha was poorly defined, based solely on	Reported no increase in risk of cancer (no specific cancer type was specified)	Yes

TABLE E-1 Publicly Available on Compound Alpha Related to Potential Carcinogenicity of the Compound				
Study Species	**Study Type**	**Study Quality Factors**	**Key Design Characteristics**	**Statistical Analysis Performed?**
		whether a worker had worked for more than 5 years in a plant that made Compound Alpha.		

Step 3: Are the studies and/or data adequate for NSRL derivation?
The rat study included relevant data, looking at a large sampling of organ histopathology, in both male and female animals over two years, and reported no increased incidence of tumors as compared to the control group. The only evidence of genotoxicity was in an Ames assay with metabolic activation. Only one low quality human study was identified, and exposure groups were poorly defined, relying on length of time employed in a plant making Compound Alpha. The results in the human study were consistent with the data collected in rats, however (no increased risk of cancer reported). Due to the negative data in both animals and humans, but the low quality of the studies overall, the risk manager concludes that the data are insufficient to derive a NSRL with any certainty, even in light of the positive genotoxicity data (two studies only available publicly). This decision also would apply to consideration of dermal exposure since no dermal exposure data in animals were available. Compound Alpha is expected to be poorly absorbed through the skin, however, because of the chemical nature of the compound and data on similar compounds.

Step 4: Derive the NSRL
None will be derived.

Step 5: Compare the NSRL to the level of anticipated exposure
Since a NSRL was not derived, no comparison is possible. Due to the poor quality of data, the label for Compound Alpha would not include a cancer hazard warning.

Derivation of a MADL

Step 1: Is Compound Alpha Listed in the Proposition 65 List?
The risk manager searches the current Proposition 65 to see if Compound Alpha is listed by the State of California as a Reproductive/Developmental Toxicant (the Proposition 65 List) and finds Compound A is listed but no MADL has been derived by OEHHA.

Step 2: Do scientific studies and/or data exist that can be used to derive a MADL for Compound Alpha?
The risk manager searches sites where regulatory authorities list risk values that have already been derived for Compound Alpha focusing on risk values linked to endpoints of reproductive and/or developmental toxicity. The sites to be searched would include those considered by OEHHA as authoritative bodies (*i.e.,* the U.S. Environmental Protection Agency (EPA), the World Health Organization's International Agency for Research on Cancer (IARC), the National Toxicology Program (NTP), the National Institute for Occupational Safety and Health (NIOSH), and the U.S. Food and Drug Administration (FDA). Other sites that should be considered for searching would include other regulatory bodies that have standards in place for protection of human health (*e.g.,* Health Canada, the Australian Government's Therapeutic Goods Administration and the Food Standards agency, European Commission, *etc.*). The search finds that none of these sources list a risk value for Compound Alpha related to reproductive and/or developmental toxicity.

The lack of identified risk values means that the scientific literature will need to be searched. The risk manager designs a search strategy[15] for a search of the publicly available scientific literature using the name "Compound Alpha" linked with terms such as "reproduction" and "development" and "toxic". The risk manager identifies both animal data and human data discussing the link of Compound Alpha to adverse effects on reproduction and retrieves the full study reports for analysis of the data quality. Table E-2 below provides a summary of the type of studies and data that were identified.

TABLE E-2
Publicly Available Studies on Compound Alpha Addressing Reproductive and/or Developmental Toxicity

Study Species	Study Type	Study Quality Factors	Key Design Characteristics	Statistical Analysis Performed?
Rat	Oral 28-day study (gavage dosing)	Peer-reviewed paper No mention of GLP (academic lab)	Control group included Multiple test doses (two and a control) One sex (adult male rats only) with 5 rats/	Yes

[15] It should be noted that this part of the process requires the risk manager to have some expertise in toxicology and should not be performed by someone without such expertise.

TABLE E-2 Publicly Available Studies on Compound Alpha Addressing Reproductive and/or Developmental Toxicity				
Study Species	**Study Type**	**Study Quality Factors**	**Key Design Characteristics**	**Statistical Analysis Performed?**
			group Examined male reproductive organs as part of the study A NOAEL and a LOAEL were established.	
Rat	Two year feeding study	Peer-reviewed paper No mention of GLP Study performed in the 1980's Both male and female animals were included in the design with 5 rats per sex per dose group.	Designed with two dose groups and a control diet group No reporting of level of feed intake per day. No increased incidence of tumors of any type were reported, including in the testes of other male reproductive organs.	Yes
Human	Retrospective observational cohort study	Peer-reviewed paper No mention of GCP (academic lab)	Worker study Control group included Endpoint of concern was effects on male and female reproductive capacity Several hundred workers in each of the cohort groups	Yes
Human	Case reports (five different papers)	Peer-reviewed papers	Male infertility endpoints (low testosterone levels; low sperm count)	No

Step 3: Are the studies and/or data adequate for MADL derivation?
Although no large GLP-compliant animal study is available, the rat study included relevant data in showed statistically significant differences with Compound Alpha exposure. The animal study data, damage to testes and reduced sperm numbers, was consistent with observations in human case reports and a human observational cohort study. The risk manager concludes that the data are sufficient to derive a MADL, as long as uncertainties in the database are accounted for in the risk calculation. Although no dermal exposure data in animals were available, the oral data can be used to assess risks with dermal exposure as well. Compound Alpha is expected to be poorly absorbed through the skin because of the chemical nature of the compound and data on similar compounds.

Step 4: Derive the MADL
The rat study can be used to derive the MADL as follows:

Oral NOAEL mg Compound Alpha/kg bw/day ÷ 1000 (UF factor) = MADL

A 1000-fold Uncertainty Factor (UF) was applied to account for extrapolation from animals to humans (10X), to account for sensitive humans in the population (10X) and to account for the existence of only one animal study that was not directed to robust evaluation of reproductive toxicity and the lack of data in female animals.

Step 5: Compare the MADL to the level of anticipated exposure
The last step is to compare the MADL (mg/kg bw/day) with anticipated levels of exposure through oral intake and through dermal uptake. The comparison is to determine if the MADL > or < the exposure value (see the flow diagram).