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HAZARD COMMUNICATION

Hazard Classification Guidance

for Manufacturers, Importers, and Employers

OSHA 3844-02 2016

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Occupational Safety and Health Act of 1970

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This publication provides a general overview of a particular standards-related topic. This publication does not alter or determine compliance responsibilities which are set forth in OSHA standards, and the *Occupational Safety and Health Act.* Moreover, because interpretations and enforcement policy may change over time, for additional guidance on OSHA compliance requirements, the reader should consult current administrative interpretations and decisions by the Occupational Safety and Health Review Commission and the courts.

This guidance document is not a standard or regulation, and it creates no new legal obligations. It contains recommendations as well as descriptions of mandatory safety and health standards. The recommendations are advisory in nature, informational in content, and are intended to assist employers in providing a safe and healthful workplace. The Occupational Safety and Health Act *requires employers to comply with safety and health standards and regulations promulgated by OSHA or by a state with an OSHA-approved state plan. In addition, the Act's General Duty Clause, Section 5(a)(1), requires employers to provide their employees with a workplace free from recognized hazards likely to cause death or serious physical harm.*

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Occupational Safety and Health Administration
U.S. Department of Labor

OSHA 3844-02 2016

TABLE OF CONTENTS

OVERVIEW

In March 2012, the Occupational Safety and Health Administration (OSHA) revised its Hazard Communication Standard to align it with the United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS), Revision 3. The revision to the Hazard Communication Standard (HCS) built on the existing standard, by requiring chemical manufacturers and importers to follow specific criteria when evaluating the hazardous chemicals and when communicating the hazards through labels and safety data sheets (SDSs).

This document is designed to help manufacturers and importers of chemicals not only identify chemical hazards, but also to classify these hazards so that workers and downstream users can be informed about and better understand these hazards as required by OSHA's Hazard Communication Standard. This guidance may also be useful to employers who decide to conduct hazard classifications to assure the accuracy and completeness of information provided to them by suppliers.

Understanding the hazards is the critically important first stage in the process of establishing an effective hazard communication program. The process of hazard classification consists of four basic steps.

- Selection of chemicals to evaluate;
- Collection of data;
- Analysis of the collected data; and
- Records of the rationale behind the results obtained.

This document provides guidance on the processes involved and identifies considerations in the conduct of hazard classifications. Guidance on the allocation of the hazard communication label elements is provided in an OSHA Brief on Labels and Pictograms, located on the Hazard Communication webpage, at www.osha.gov/hazcom.

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How this Document is Organized

This guidance is organized into several chapters. Chapter I introduces the guidance. Chapter II provides an overview of the hazard classification process. Chapter III discusses how to identify the chemicals to be classified. Chapter IV explains the process of data collection. Chapter V describes the process and information needed for data analysis. Chapter VI discusses the information that may be useful to note in recording the rationale used to develop the classification of the various hazards. Chapters VII, VIII, and IX present the guidance to classify health hazards, physical hazards, and hazards not otherwise classified covered by the Hazard Communication Standard, respectively.

In addition, several appendices are provided at the end of this document:

- A glossary of terms and definitions is included in Appendix A, since much of the discussion in this document is of a technical nature.
- A list of sources is provided in Appendix B. This list is by no means exhaustive, but it contains many useful resources.
- Appendix C contains a list of chemicals for which OSHA has adopted permissible exposure limits. This is a helpful starting point for identifying chemicals that are toxic or hazardous The HCS does not contain a "floor" (list) of chemicals pre-determined to be hazardous under the standard (except for chemicals OSHA has already determined to be carcinogens); however, there are lists of hazardous chemicals compiled by authoritative sources that classifiers may find useful to consult. The chemicals listed in Appendix C are an example of one such list. Classifiers should also consult the American Conference of Governmental Industrial Hygienists' (ACGIH's) list of Threshold Limit Values (TLVs) and the items identified as carcinogens by the International Agency for Research on Cancer (IARC) *Monographs on the Evaluation of Carcinogenic Risks to Humans,* or the *Report on Carcinogens* from the National Toxicology Program (NTP). These lists are updated periodically, and users should check to determine whether there has been an update.
- A list of OSHA-designated carcinogens is provided in Appendix D. Please see Chapter VII.6, Carcinogenicity, for guidance on classification of these chemicals.

I. INTRODUCTION

OSHA's Hazard Communication Standard (HCS) is designed to protect against chemical-source injuries and illnesses by ensuring that employers and workers are provided with sufficient information to anticipate, recognize, evaluate, and control chemical hazards and take appropriate protective measures. This information is provided through safety data sheets (SDSs), labels, and employee training. In order for SDSs, labels, and training to be effective, the hazard information they convey must be complete and accurate. Thus, it is critically important to obtain comprehensive and correct information about the hazards associated with particular chemicals.

What is Hazard Classification?

Hazard classification is the process of evaluating the full range of available scientific evidence to determine if a chemical is hazardous, as well as to identify the level of severity of the hazardous effect. When complete, the evaluation identifies the hazard class(es) and associated hazard category of the chemical.

The HCS defines hazard class as the nature of a physical or health hazard, e.g., flammable solid, carcinogen, and acute toxicity. Hazard category means the division of criteria within each hazard class, e.g., acute toxicity and flammable liquids each include four hazard categories numbered from category 1 through category 4. These categories compare hazard severity within a hazard class and should not be taken as a comparison of hazard categories more generally. That is, a chemical identified as a category 2 in the acute toxicity hazard class is not necessarily less toxic than a chemical assigned a category 1 of another hazard class. The hierarchy of the categories is only specific to the hazard class. The hazard classification process provides the basis for the hazard information that is provided in SDSs, labels, and worker training.

The hazard classification process, as provided in the Hazard Communication Standard, has several steps, including:

- Identifying the chemical;
- Identifying the relevant data regarding the hazards of a chemical;
- Reviewing the relevant data to ascertain the hazards associated with the chemical;
- Determining whether the chemical will be classified as hazardous according to the definition of hazardous chemical in the standard; and
- Determining the degree of the hazard, where appropriate, by comparing the data with the criteria for health and physical hazards.

The HCS provides specific criteria for hazard classification to ensure that chemical manufacturers, importers, and other classification experts come to similar conclusions regarding the hazards of chemicals. The resulting classification is then used to determine appropriate hazard warnings. This method not only provides employers and workers with more consistent classification of hazards, but the hazard information on SDSs and labels is in a form that is more

consistent and presented in a way that facilitates the understanding of the hazards of chemicals. This hazard information can then be used when evaluating the workplace conditions to determine the hazards in the workplace, as well as to respond to exposure incidents.

The information and criteria provided in Appendix A to 29 CFR 1910.1200 are used to classify the health hazards posed by hazardous chemicals. Similarly, the information and criteria provided in Appendix B to 29 CFR 1910.1200 are used to classify the physical hazards posed by hazardous chemicals.

Hazard classification does not involve an estimation of risk. The difference between the terms hazard and risk is often poorly understood. Hazard refers to an inherent property of a substance that is capable of causing an adverse effect. Risk, on the other hand, refers to the probability that an adverse effect will occur with specific exposure conditions. Thus, a chemical will present the same hazard in all situations due to its innate chemical or physical properties and its actions on cells and tissues. However, considerable differences may exist in the risk posed by a chemical, depending on how the chemical is contained or handled, personal protective measures used, and other conditions that result in or limit exposure. This document addresses only the hazard classification process, and will not discuss risk assessment, which is not performed under the HCS.

Risk is often expressed as the simple equation: **Hazard X Exposure = Risk**.

Who Must Conduct Hazard Classifications?

Only chemical manufacturers and importers are required to perform hazard classifications on the chemicals they produce or import. Under the HCS, an employer that manufactures, processes, formulates, blends, mixes, repackages, or otherwise changes the composition of a hazardous chemical is considered a "chemical manufacturer." Distributors and employers may also choose to conduct hazard classifications if they are concerned about the adequacy of the hazard information received for the chemicals they use in their business or distribute to others.

What Resources are Needed to Conduct a Hazard Classification?

Three primary resources are required for hazard classification. First is the complete, accurate, most up-to-date literature and data concerning the hazardous chemical in question (discussed below in Chapter V, Data Analysis). Second, is the ability to properly understand and interpret the information retrieved in order to identify and document hazards. Third, is the specific criteria for each health and physical hazard class and category defined in the Hazard Communication Standard. As mentioned above, Appendix A to 29 CFR 1910.1200 provides the classification criteria for health hazards, and Appendix B to 29 CFR 1910.1200 provides the classification criteria for physical hazards.

Manufacturers and importers of hazardous chemicals are responsible for ensuring that hazard information provided to their workers and downstream users is complete and accurate. To achieve this, the person(s) assigned to conduct hazard classifications must have the ability to

conduct complete and effective literature research and data retrieval. They should also be able to effectively interpret the literature and data in order to determine the nature and extent of physical and health hazards. A lack of qualified workers does not exempt a manufacturer or importer from compliance with the HCS.

How to Use This Guidance Document

The hazard classification requirements of the HCS are specification-oriented. That is, chemical manufacturers, importers, and employers evaluating chemicals are required to follow specific criteria for evaluating and classifying hazards, and they must be able to demonstrate that they have accurately reported the hazards of the chemicals produced or imported in accordance with the criteria set forth in the HCS.

This document provides a detailed description of the criteria used to classify a hazardous chemical and guidance on how to apply them. In addition, a basic framework for hazard classification is provided, along with a description of the process that can be used to comply with the requirements of the HCS. An example using a mock chemical is also provided to illustrate the classification process of the given hazard.

The interpretation of information relating to the physical and health hazards associated with a chemical can be a highly technical undertaking, and should be conducted by trained staff such as toxicologists, industrial hygienists, and safety professionals. This document will not replace the need for such professional expertise. It is intended to serve only as useful guidance on the basic considerations and operational aspects involved in the conduct of hazard classifications.

Once hazard classification is complete, classifiers must select the appropriate label elements for the hazards identified. Appendix C to 29 CFR 1910.1200, Allocation of Label Elements, identifies the proper pictogram, signal word, hazard and precautionary statements for each hazard class and category in the HCS.

This document does not address detailed labeling requirements or SDSs. OSHA has developed QuickCards™ and OSHA Briefs on labels, pictograms, and SDSs, as well as other guidance. These materials can be found on the HCS website at: www.osha.gov/hazcom.

II. THE HAZARD CLASSIFICATION PROCESS

Introduction

The purpose of the Hazard Communication Standard is to ensure that the hazards of all chemicals produced or imported are classified, and that the information on the hazardous chemicals is transmitted to employers and workers. The standard covers only hazardous chemicals. During the classification process, the chemical manufacturer or importer must determine if the chemical being evaluated is hazardous or not. With the alignment of the HCS to the GHS, the hazard information will be consistent in format and content, making it easier for employers and workers to understand and use. This section of the guidance clarifies what is considered a hazardous chemical.

What is the HCS Definition of a "Chemical"?

The definition of a chemical in the HCS is much broader than that which is commonly used in everyday speech. The HCS definition of chemical is "any substance, or mixture of substances." Thus, virtually any product is a "chemical." These various types of chemicals are defined as follows:

- ***Substance*** - chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the product and any impurities deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.
- ***Element*** - the simplest form of matter. There are currently 118 known elements in the periodic table. Examples of elements are aluminum, carbon, chlorine, hydrogen, mercury and oxygen.
- ***Chemical compound*** - a substance consisting of two or more elements combined or bonded together so that its constituent elements are always present in the same proportions.
- ***Mixture*** - a combination or a solution composed of two or more substances in which they do not react.

Although virtually all products are considered chemicals under this definition, the HCS identifies certain categories of chemicals that are not covered by the standard. These categories are:

- Any **hazardous waste** as defined by the *Solid Waste Disposal Act,* as amended by the *Resource Conservation and Recovery Act of 1976* (42 U.S.C. 6901 et seq.), as amended, when subject to regulations issued under that Act by the Environmental Protection Agency;
- Any **hazardous substance** as defined by the *Comprehensive Environmental Response, Compensation and Liability Act* (42 U.S.C. 9601 et seq.) **when the hazardous substance is the focus of remedial or removal action** being conducted under that Act in accordance with Environmental Protection Agency regulations;

- **Tobacco or tobacco products;**
- **Wood or wood products,** including lumber which will not be processed, where the chemical manufacturer or importer can establish that the only hazard they pose to employees is the potential for flammability or combustibility (wood or wood products which have been treated with a hazardous chemical covered by this standard, and wood which may be subsequently sawed or cut, generating dust, are not exempted);
- **Articles**, defined as a manufactured item other than a fluid or particle: (i) which is formed to a specific shape or design during manufacture; (ii) which has end use function(s) dependent in whole or in part upon its shape or design during end use; and (iii) which under normal conditions of use does not release more than very small quantities, e.g., minute or trace amounts of a hazardous chemical, and does not pose a physical hazard or health risk to employees;
- **Food or alcoholic beverages** which are sold, used, or prepared in a retail establishment (such as a grocery store, restaurant, or drinking place), and foods intended for personal consumption by employees while in the workplace;
- Any **drug**, as that term is defined in the *Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 301 et seq.), when it is in solid, final form for direct administration to the patient (e.g., tablets or pills); drugs which are packaged by the chemical manufacturer for sale to consumers in a retail establishment (e.g., over-the-counter drugs); and drugs intended for personal consumption by employees while in the workplace (e.g., first-aid supplies);
- **Cosmetics** which are packaged for sale to consumers in a retail establishment, and cosmetics intended for personal consumption by employees while in the workplace;
- Any **consumer product** or **hazardous substance**, as those terms are defined in the *Consumer Product Safety Act* (15 U.S.C. 2051 et seq.) and the *Federal Hazardous Substances Act* (15 U.S.C. 1261 et seq.), respectively, where the employer can show that it is used in the workplace for the purpose intended by the chemical manufacturer or importer of the product, and the use results in **a duration and frequency of exposure which is not greater than the range of exposures that could reasonably be experienced by consumers when used for the purpose intended;**
- **Nuisance particulates** where the chemical manufacturer or importer can establish that they do not pose any physical or health hazard covered under this section;
- **Ionizing and nonionizing radiation**; and
- **Biological hazards**.

The HCS also does not require labeling for certain chemicals, but hazard classification is still needed for these chemicals to provide the required safety data sheet. The chemicals include:

- Any pesticide as such term is defined in the *Federal Insecticide, Fungicide, and Rodenticide Act* (7 U.S.C. 136 et seq.), when subject to the labeling requirements of that Act and labeling regulations issued under that Act by the Environmental Protection Agency;

- Any chemical substance or mixture as such terms are defined in the *Toxic Substances Control Act* (15 U.S.C. 2601 et seq.), when subject to the labeling requirements of that Act and labeling regulations issued under that Act by the Environmental Protection Agency;
- Any food, food additive, color additive, drug, cosmetic, or medical or veterinary device or product, including materials intended for use as ingredients in such products (e.g. flavors and fragrances), as such terms are defined in the *Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 301 et seq.) or the *Virus-Serum-Toxin Act of 1913* (21 U.S.C. 151 et seq.), and regulations issued under those Acts, when they are subject to the labeling requirements under those Acts by either the Food and Drug Administration or the Department of Agriculture;
- Any distilled spirits (alcoholic beverages), wine, or malt beverage intended for nonindustrial use, as such terms are defined in the *Federal Alcohol Administration Act* (27 U.S.C. 201 et seq.) and regulations issued under that Act, when subject to the labeling requirements of that Act and labeling regulations issued under that Act by the Bureau of Alcohol, Tobacco, Firearms and Explosives;
- Any consumer product or hazardous substance as those terms are defined in the *Consumer Product Safety Act* (15 U.S.C. 2051 et seq.) and the *Federal Hazardous Substances Act* (15 U.S.C. 1261 et seq.) respectively, when subject to a consumer product safety standard or labeling requirement of those Acts, or regulations issued under those Acts by the Consumer Product Safety Commission; and,
- Agricultural or vegetable seed treated with pesticides and labeled in accordance with the *Federal Seed Act* (7 U.S.C. 1551 et seq.) and the labeling regulations issued under that Act by the Department of Agriculture.

How to Determine if a Chemical is "Hazardous"

Under the HCS, any chemical that is classified as a physical hazard, a health hazard, a simple asphyxiant, combustible dust, pyrophoric gas, or hazard not otherwise classified is considered a hazardous chemical. The HCS definitions for physical hazard and health hazard are:

- ***Physical hazard*** means a chemical that is classified as posing one of the following hazardous effects: explosive; flammable (gases, aerosols, liquids, or solids); oxidizer (liquid, solid or gas); self-reactive; pyrophoric (liquid or solid); self-heating; organic peroxide; corrosive to metal; gas under pressure; or in contact with water emits flammable gas. The criteria for determining whether a chemical is classified as a physical hazard are detailed in Appendix B to 29 CFR 1910.1200 – Physical Hazard Criteria.
- ***Health hazard*** means a chemical that is classified as posing one of the following hazardous effects: acute toxicity (any route of exposure); skin corrosion or irritation; serious eye damage or eye irritation; respiratory or skin sensitization; germ cell mutagenicity; carcinogenicity; reproductive toxicity; specific target organ toxicity (single or repeated exposure); or aspiration hazard. The criteria for determining whether a chemical is classified as a health hazard are detailed in Appendix A to 29 CFR 1910.1200 – Health Hazard Criteria.

The definitions for each of the specific physical and health hazards identified above are the same as those found in the GHS, Rev. 3. To maintain the coverage of those hazards that were included in the 1994 Hazard Communication Standard, OSHA included hazard communication elements for the following hazards that are not found in GHS Rev. 3: combustible dusts, pyrophoric gases, and simple asphyxiants. OSHA has also created "hazards not otherwise classified", a hazard class to capture hazards for which criteria have not yet been created.

Each of these hazards are included in this guidance document. Guidance on classification of simple asphyxiants is presented in Chapter VII, Classification of Health Hazards. Guidance on classification of pyrophoric gases and combustible dusts is presented in Chapter VIII, Classification of Physical Hazards. Guidance on classification of hazards not otherwise classified is presented in Chapter IX, Classification of Hazards not Otherwise Classified.

Table II.1 lists the different health hazard classes and categories identified in the HCS. Similarly, Table II.2 lists the different physical hazard classes and categories found in the HCS. Those hazard classes listed in italicized font in these two tables are the hazard classes not identified in GHS Rev.3, but are included in the HCS to maintain workplace coverage. Explanations of the classification process for each of these hazard classes and their associated hazard categories are presented in Chapters VII and VIII of this document, respectively.

Table II.1. Health Hazard Classes and Categories.

Hazard Class	**Hazard Category**			
Acute Toxicity	1	2	3	4
Skin Corrosion/Irritation	1A	1B	1C	2
Serious Eye Damage/ Eye Irritation	1	2A	2B	
Respiratory or Skin Sensitization	1A	1B		
Germ Cell Mutagenicity	1A	1B	2	
Carcinogenicity	1A	1B	2	
Reproductive Toxicity	1A	1B	2	Lactation
STOT – Single Exposure	1	2	3	
STOT – Repeated Exposure	1	2		
Aspiration	1			
Simple Asphyxiants	Single Category			

Table II.2. Physical Hazard Classes and Categories.

Hazard Class	Hazard Category						
Explosives	Unstable Explosives	Div 1.1	Div 1.2	Div 1.3	Div 1.4	Div 1.5	Div 1.6
Flammable Gases	1	2					
Flammable Aerosols	1	2					
Oxidizing Gases	1						
Gases under Pressure Compressed Gases Liquefied Gases Refrigerated Liquefied Gases Dissolved Gases	1						
Flammable Liquids	1	2	3	4			
Flammable Solids	1	2					
Self-Reactive Chemicals	Type A	Type B	Type C	Type D	Type E	Type F	Type G
Pyrophoric Liquids	1						
Pyrophoric Solid	1						
Pyrophoric Gases	Single category						
Self-heating Chemicals	1	2					
Chemicals, which in contact with water, emit flammable gases	1	2	3				
Oxidizing Liquids	1	2	3				
Oxidizing Solids	1	2	3				
Organic Peroxides	Type A	Type B	Type C	Type D	Type E	Type F	Type G
Corrosive to Metals	1						
Combustible Dusts	Single category						

For a hazard classification process to be complete, one must consider all possible hazards, and should document any hazards that are identified. In conducting the hazard classification, one should be cognizant of all types of physical and health hazards to properly identify the nature and severity of the chemical's hazards.

OSHA regulates a number of chemicals as toxic and hazardous substances, which are contained in Subpart Z of 29 CFR 1910. The classifier must refer to the regulations of these substances for specific hazard classification requirements. For example, the Lead standard requires that at least the hazards of reproductive/developmental toxicity, central nervous system effects, kidney effects, blood effects, and acute toxicity effects be addressed in classification (See 29 CFR 1910.1025(m)(ii)). In addition, there are certain lists that can help the classifier identify chemicals that have been deemed hazardous by nationally and internationally recognized organizations, such as the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limits (RELs), National Toxicology Program (NTP) *Report on Carcinogens* (RoC), and International Agency for Research on Cancer (IARC). Appendix C of this document contains a list of those materials regulated by OSHA as toxic and hazardous substances. Appendix D of this document contains a list of OSHA-designated carcinogens.

The classifier must evaluate all the evidence and data available for the given chemical and use the specific criteria spelled out for each health and physical hazard to classify the chemical in appropriate hazard classes and categories. In some cases, available data provides enough information to classify a chemical. In other cases, classification is determined on the basis of the total weight of evidence using expert judgment. This means that all available information bearing on the classification of the hazard must be considered together. In the case of health hazards, for example, this includes the results of valid *in vitro* tests, relevant animal data, and human experience, such as epidemiological and clinical studies, and well-documented case reports and observations.

If OSHA has designated a chemical as a carcinogen, then the chemical must be classified as a carcinogen. There are also organizations that evaluate chemicals for carcinogenicity. These organizations, such as the International Agency for Research on Cancer (IARC) and the National Toxicology Program (NTP), publish lists of hazardous chemicals that they have determined, with varying degrees of certainty, to be carcinogens. OSHA has provided a crosswalk table to aid classifiers in translating the classification from NTP or IARC into the HCS classification scheme in Chapter VII.6 of this document. The discussion on carcinogens in this guidance provides more detail on the classification of carcinogens.

The definition for hazardous chemical in the standard is thus very broad. The standard does not require the testing of chemicals - only the collection and analysis of currently available data. Nevertheless, if no data is available or it is questionable, testing should be considered when hazardous properties are suspected.

Is Hazard Classification the Same for Mixtures as for Individual Chemicals?

Generally speaking, the chemical and physical properties and hazards of pure elements and chemical compounds are precise and constant. For example, benzene has explicit boiling and flashpoints of 176 °F and 12 °F (at sea level), respectively. In contrast, the properties of the complex mixture, Stoddard Solvent, can vary considerably depending on the manufacturer and lot received, with ranges for boiling and flashpoints of 309-396 °F and 102-110 °F, respectively.

The process for evaluating mixtures may require steps in addition to those required for single chemical agents. The HCS has designated specific classification requirements for mixtures, which depend upon the availability of test data. Please see Chapter V, Data Analysis, for a detailed discussion on classification of mixtures. In addition, the chapters for the individual hazard classes discuss the specifics necessary for classification of mixtures.

What is Involved in Conducting a Hazard Classification?

All possible physical or health hazards that might be associated with a chemical's use must be considered. The hazard classification process consists of four main steps:

- Selection of chemicals to evaluate;
- Collection of data;
- Analysis of the collected data using the criteria provided in the HCS; and
- Documentation of the hazard classification process and the results obtained[1].

The Hazard Communication Standard provides the specific criteria upon which the hazard classification for a given chemical is based, ensuring that all those evaluating data and performing hazard classification are following the same process, resulting in similar classification conclusions. If no hazards are found, the manufacturer, importer, or employer is not required to take further action pertaining to the evaluated chemical. Documentation of the results of the analysis used in the classification process may be useful for future reference.

For many chemicals, hazard information has been compiled in readily available and reliable sources (see Appendix B of this document). The specific classification criteria for each health or physical hazard class identified in the HCS enables manufacturers, importers, and others performing hazard classification to collect and evaluate the available data to determine if the chemical is hazardous and identify the associated level of severity.

In some cases, a chemical may present a single hazard. In other cases, several hazards may be associated with exposure to a chemical. The severity of the hazardous effect can range from mild to severe. In the HCS, for example, identified health hazards for acetic acid, as normally

[1] Note that documentation of the hazard classification process and the results obtained is not required by the HCS; however OSHA recommends it. See Chapter VI, Recording the Rationale Behind the Results Obtained, of this document.

used in industry, are skin irritation/corrosion and respiratory sensitization. In contrast, exposure to lead may involve a multitude of hazards, including reproductive/developmental toxicity, central nervous system effects, kidney effects, and acute toxicity effects.

Hazard evaluation is a process that relies heavily on the professional judgment of the evaluator, particularly in the area of chronic health hazards. The specification approach of the HCS requires the chemical manufacturer, importer or employer to conduct a thorough evaluation, examining the full range of available data and producing a scientifically defensible evaluation of the chemical hazards.

III. IDENTIFYING HAZARDOUS CHEMICALS

The ultimate goal in the hazard classification process is to know and document the hazards of all covered chemicals you manufacture or import. In order to achieve this, you must first determine which chemicals require a hazard classification. The logical way to do this is to first prepare an inventory of all the chemicals you manufacture or import, as well as a list of the ingredients in the mixtures produced. To create the list of ingredients from the mixtures produced, consider information found in the chemical formula, on order receipts, batch sheets, and so on.

While a single SDS must be created for the mixtures produced, you may rely upon the information provided on the SDSs and labels for ingredients obtained from the chemical manufacturer or importer, unless you have reason to believe the information is incorrect. However, you may choose to conduct a hazard classification for those ingredients if there is concern about the adequacy of the hazard information received.

All employers are required to have a list of hazardous chemicals known to be present in the workplace under 29 CFR 1910.1200(e)(1)(i). If a chemical inventory is not already in place, a good start would be to review purchase orders and receipts to create an initial inventory. Next, take time to inspect the workplace to identify any additional chemicals present. It would be ideal to note the location and quantity of each chemical found. Chemical inventories are often maintained as computer files for ease and efficiency in keeping them current. With knowledge of the chemicals in your possession, you can use this information to perform hazard classifications for chemicals that you manufacture or import.

On a related safety note, the chemical inventory or survey can also be used to decide which chemicals to dispose of, as well as to identify potentially unsafe storage areas and techniques. Some chemicals should not be stored near each other due to incompatibilities and potential reactions.

IV. DATA COLLECTION

The second step in the hazard classification process is data collection. There are two main questions to be answered: (1) what type of data should be searched for and collected; and (2) how do I go about finding sources that might contain the desired data? You should recognize that the hazard classification process involves the identification of all of the hazards associated with a chemical, not just some of them. OSHA expects classifiers to use reasonable efforts in their search for available data for all hazard classes (see Chapter V, Data Analysis), for a discussion on the use of available data). Specific types of data used for classification of a given hazard are discussed in the individual hazard chapters of this document. Any hazard that exists for the chemical must be identified and communicated to downstream employers and workers.

To complete the hazard identification, information is needed in three categories:

- chemical identity;
- physical and chemical properties; and
- health effects.

There are numerous sources that could be searched for this information. A list of commonly used data sources is provided in Appendix B of this document, although other sources exist and new sources continue to appear online and in print. For new or less commonly used chemicals, there may not be much data available from any of these sources. While the HCS does not require testing, you may choose to test chemicals to determine chemical and physical properties and identify hazards.

In the sections that follow, a discussion of data needs for the three categories of information is provided. Also, a few recommended key references for the various types of data are listed. Complete and reliable data must be entered on SDSs and labels to meet the HCS requirements. Before the search for hazard data can begin, the exact chemical composition of the chemical(s) or products manufactured or imported must be identified. This chemical search includes the name of each chemical (whether it is a substance or a mixture), including active ingredients, inactive ingredients, impurities, and stabilizing additives.

Chemical Identity

The specific chemical identity of all chemicals on your chemical inventory should be carefully and completely compiled. The specific chemical identity includes:

- the chemical name along with common name and synonyms;
- the Chemical Abstracts Services (CAS) Registry Number (if available); and
- any other information that reveals the precise chemical designation and composition of the substance, such as impurities and stabilizers.

Correct identification of chemicals is critical for data retrieval. Use the precise chemical name, where available, and Chemical Abstract Service (CAS) number when searching for information. A problem with the use of common names or abbreviations is that they may be used for more than one molecular entity. To avoid confusion, literature is often indexed using the CAS number or the primary chemical name. For example, TCE is commonly used as an acronym for trichloroethylene (CAS 79-01-6), but sometimes this same acronym is used to refer to tetrachloroethylene (CAS 127-18-4).

***CAS numbers** are assigned by the Chemical Abstract Service of the American Chemical Society.*

Additionally, the use of trade names could cause difficulty in finding information. An example of the type of chemical identification data that is needed is presented for Perclene®, a widely used industrial solvent. Perclene® is a trade name for perchloroethylene or Perc (common name), or more specifically tetrachloroethylene (CAS Number 127-18-4). Several databases exist that can only be searched using the CAS number or chemical name. Thus, the most effective search of computerized databases is conducted using both the precise chemical name (tetrachloroethylene) and the CAS number (CAS Number 127-18-4). Searches using the trade or common name(s) or abbreviation(s) may not return information for that chemical.

The percent composition (or exact percentage) should be available in-house for all chemicals manufactured or imported. The chemical composition information may be based on an analysis of the final or technical grade product or product formulation. A technical grade product is not usually a pure substance and often contains other chemicals such as stabilizers, solvents, carriers, "inert" ingredients, or impurities. For the purposes of hazard classification, these other chemicals must also be considered since they may have their own unique hazards and may contribute to the hazards of the chemical.

Thus, one of the initial steps is to collect as much data as possible pertaining to the physical and chemical properties and toxicity data for chemicals on your chemical inventory.

Key sources of information related to chemical identification are:

- Company records;
- SDSs and product safety bulletins from manufacturers or suppliers;
- OSHA Chemical Sampling Information pages;
- The Merck Index;
- ChemID; and
- Trade associations.

Physical and Chemical Properties

The physical and chemical properties of a hazardous chemical are the empirical data of the substance or mixture. That is, this data has been gathered from observation or by tests performed on the chemical. For many hazardous chemicals, this data has been compiled and is readily available.

Key sources of information related to physical and chemical properties include:

- Fire Protection Guide to Hazardous Materials;
- Department of Transportation Emergency Response Guidebook, most recent version (phmsa.dot.gov/hazmat/library/erg);
- OSHA's Occupational Chemical Database (www.osha.gov/chemicaldata);
- Hazardous Substances Data Bank (HSDB) (toxnet.nlm.nih.gov);
- Product safety bulletins from manufacturers or suppliers;
- National Institute for Occupational Safety and Health (NIOSH) documents (www.cdc.gov/niosh/topics/chemical.html);
- NIOSH Pocket Guide to Chemical Hazards (www.cdc.gov/niosh/npg);
- International Chemical Safety Cards (www.cdc.gov/niosh/ipcs);
- OECD eChemPortal (www.oecd.org/env/ehs/risk-assessment/echemportalglobalportaltoinformationonchemicalsubstances.htm);
- The Merck Index;
- CRC Handbook of Chemistry and Physics;
- Sax's Dangerous Properties of Industrial Materials, latest edition;
- Bretherick's Handbook of Reactive Chemicals Hazards, latest edition; and
- Trade associations.

The HCS includes classification criteria for 17 physical hazard classes (see Table II.2) and are discussed in detail in Chapter VIII. These physical hazard classes should not be confused with the physical and chemical properties of a chemical.

Health Effects

The HCS includes the classification criteria for 11 health hazard classes (see Table II.1) and are discussed in detail in Chapter VII. In many cases, a chemical may pose more than one type of health hazard. If your company is manufacturing a new chemical you may be required to submit pre-manufacturing health effects data to the U.S. Environmental Protection Agency (EPA) to comply with the *Toxic Substances Control Act* (TSCA). Data submitted to EPA by other companies may be available to you by contacting EPA. This data may be used to assist with hazard classification and the preparation of SDSs and labels. The company also should seek toxicity data from the literature, government, or private sources. Some recommended reference sources are listed below.

- Company-sponsored research, if available;
- SDSs and product safety bulletins from manufacturers, suppliers, or Internet sites;
- OSHA's Occupational Chemical Database (www.osha.gov/chemicaldata);
- Hazardous Substances Data Bank (HSDB) (toxnet.nlm.nih.gov);
- National Institute of Occupational Safety and Health (NIOSH) documents (www.cdc.gov/niosh/topics/chemical.html);
- NIOSH Pocket Guide to Chemical Hazards (www.cdc.gov/niosh/npg);
- Center for Disease Control's (CDC) Agency for Toxic Substances and Disease Registry (ATSDR), www.atsdr.cdc.gov/toxprofiles/index.asp
- International Chemical Safety Cards (www.cdc.gov/niosh/ipcs);
- NIOSH Registry of Toxic Effects of Chemical Substances (RTECS®) (www.cdc.gov/niosh/rtecs/RTECSaccess.html);
- OSHA Chemical Sampling Information pages;
- IARC Monographs on the Evaluation of Carcinogenic Risks to Humans (monographs.iarc.fr);
- NTP Annual Report on Carcinogens (ntp.niehs.nih.gov/pubhealth/roc);
- TLVs and BEIs (ACGIH) (www.acgih.org/tlv-bei-guidelines/policies-procedures-presentations/overview);
- OECD eChemPortal (www.oecd.org/env/ehs/risk-assessment/echemportalglobalportaltoinformationonchemicalsubstances.htm);
- Hawley's Condensed Chemical Dictionary, latest edition;
- Sax's Dangerous Properties of Industrial Materials, latest edition;
- Published literature; and
- Trade associations.

V. DATA ANALYSIS

The third step in the hazard classification process is data analysis. This step is the most demanding in terms of technical expertise. The HCS requires that chemical manufacturers and importers conduct a hazard classification to determine whether physical hazards or health hazards exist.

For both health and physical hazards, explicit classification criteria are provided in the HCS. For example, criteria are given for classifying a chemical as a flammable liquid, an organic peroxide, and for designating a chemical as acutely toxic or a carcinogen.

In some cases, the HCS establishes the criteria to be followed. For example, if a liquid has a flashpoint of less than or equal to 93°C (199.4°F), it is by definition a "flammable liquid." To determine into what category of flammable liquid the chemical is classified, you also will need to identify its initial boiling point. This involves a simple data analysis. You can rely on the flashpoint and boiling point listed in a standard reference. In the event that your company is manufacturing or importing a chemical for which there is no information on the flashpoint and boiling point, you may choose to determine the flashpoint by laboratory testing. See *Use of available data, test methods and test data quality* below for a more detailed discussion.

The following discusses the general considerations for analyzing data to complete the classification process as defined in the Hazard Communication Standard.

Hazard Classification

In the Hazard Communication Standard, the term "hazard classification" is used to indicate that only the intrinsic hazardous properties of chemicals are considered. Hazard classification incorporates three steps:

a) Identification of relevant data regarding the hazards of a chemical;

b) Subsequent review of those data to ascertain the hazards associated with the chemical;

c) Determination of whether the chemical should be classified as hazardous and the degree of hazard, where applicable.

For many hazard classes, the criteria are semi-quantitative or qualitative and expert judgment is required to interpret the data for classification purposes.

Use of available data, test methods and test data quality

The criteria for determining health hazards are test-method neutral. That is, they do not specify particular test methods, as long as the methods are scientifically validated. The term "scientifically validated" refers to the process by which the reliability and the relevance of a procedure are established for a particular purpose. Any test that determines hazardous properties, which is conducted according to recognized scientific principles, can be used for purposes of a hazard determination for health hazards. Test conditions need to be standardized so that the results are reproducible for a given chemical, and the standardized test yields "valid" data for defining the hazard class of concern. OSHA allows the use of existing test data for classifying chemicals, although expert judgment also may be needed for classification purposes.

The effect of a chemical on biological systems is influenced by the physical and chemical properties of the substance and/or ingredients of the mixture and the way in which ingredient substances are biologically available. A chemical need not be classified when it can be shown by conclusive experimental data from scientifically validated test methods that the chemical is not biologically available.

For classification purposes, epidemiological data and experience on the effects of chemicals on humans (e.g., occupational data, data from accident databases) must be considered in the evaluation of the chemical's human health hazards.[2]

Testing is not required by the HCS. Therefore, if existing data is not available, you have the option to state this on the safety data sheet. However, if you decide to test the chemical, use the test methods specified in the appropriate health or physical hazard appendices to the HCS to gather the data (see the Classification Procedure and Guidance section for each health hazard class and for each physical hazard class of this guidance, and Appendix A and Appendix B to 29 CFR 1910.1200). Appropriate test methods for each physical hazard class are identified in the standard and discussed in each physical hazard section of this guidance.

Classification based on weight of evidence (WoE)

For some hazard classes, classification results directly when the data satisfy the criteria. This is the case for most physical hazard classes. For others, classification of a chemical may be determined on the basis of the total weight of evidence using expert judgment. Under the GHS, weight of evidence (WoE) means that all available information bearing on the classification of a hazard is considered together, including the results of valid *in vitro* tests, relevant animal data, and human experience, such as epidemiological and clinical studies and well-documented case reports and observations. There are several reasons to utilize a WoE approach. First, WoE makes use of all available information. This is important especially when there is conflicting information between studies. Second, less reliable studies can be pooled to draw a conclusion on the relevant endpoint. Finally, WoE allows for use of different but adequate information that is available (e.g., data on other species, or routes of exposure).

[2] As human experience can also provide information on the hazards of a chemical, occupational data and data from accident databases are examples of where you can get such information.

OSHA has provided general criteria on how to perform an analysis based on weight of evidence in Appendix A.0.3 to 29 CFR 1910.1200, as well as specific criteria in the individual health chapters where weight of evidence is used (skin corrosion/irritation, serious eye damage/eye irritation, respirator or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, specific target organ toxicity - single exposure (STOT-SE), and STOT-repeated or prolonged exposure). See Appendices A.2-A.9 to 29 CFR 1910.1200.

When performing a WoE assessment to determine the classification of a chemical, the classifier must determine which data or study results have the most utility and validity to support the resulting hazard classification of the chemical. These considerations include four basic elements: data adequacy, data reliability, data relevance, and quantity of evidence. It is also necessary to understand how to apply this information to the data in order to make hazard classification decisions. Information on chemicals related to the material being classified must also be considered, as appropriate, along with site of action and mechanism or mode of action study results. In addition, both positive and negative results must be considered together in a single weight-of-evidence determination.

Most toxicity and epidemiology reports provide an analysis of the data and conclude whether the results were positive or negative, or describe the adverse effects observed at specific dose levels. Positive results mean that the exposed humans or animals were more likely to develop toxic effects than the non-exposed population.

Positive effects which are consistent with the criteria for classification, whether seen in humans or animals, normally justify classification. Where evidence is available from both humans and animals and there is a conflict between the findings, the quality and reliability of the evidence from both sources must be evaluated in order to resolve the question of classification. Reliable, good quality human data generally has precedence over other data. However, even well-designed and conducted epidemiological studies may lack a sufficient number of subjects to detect relatively rare but still significant effects, or to assess potentially confounding factors. Therefore, positive results from well-conducted animal studies are not necessarily negated by the lack of positive human experience, but require an assessment of the robustness, quality and statistical power of both the human and animal data.

Route of exposure, mechanistic information, and metabolism studies are used in determining the relevance of a health effect in humans. When such information raises doubt about relevance in humans, a lower classification may be warranted. When there is scientific evidence demonstrating that the mechanism or mode of action is not relevant to humans, the data may not justify classification.

Both positive and negative results are considered together in the weight of evidence determination. However, a single positive study performed according to established scientific principles and with statistically and biologically significant positive results may justify classification.

Statistical significance is a mathematical determination of the confidence in the outcome of a test. The usual criterion for establishing statistical significance is the p-value (probability value). A statistically significant difference in results is generally indicated by $p<0.05$, meaning there is less than a 5% probability that the toxic effects observed were due to chance and were not caused by the chemical. Another way of looking at it is that there is a 95% probability that the effect is real, i.e., the effect seen was the result of the chemical exposure.

The other major measure of statistical significance is the 95% confidence level for a specific data point. Most reports of toxicity testing will include some information on the confidence in the data. For example, a study with a stated confidence level of 95% and an LD_{50}[3] with a listed value of 9.5 ± 1.2 indicates that if the same study were to be repeated many times, the LD_{50} would be expected to be within the range of 8.3 - 10.7 on 95 out of every 100 times.

Hazard evaluation relies on professional judgment, particularly in the area of chronic hazards. The specific and detailed orientation of the HCS does not diminish the duty of the chemical manufacturer, importer or employer to conduct a thorough evaluation, examining all relevant data and producing a scientifically defensible classification.

Considerations for the classification of mixtures

Classification of mixtures is based on the following sequence for most hazard classes:

1. If the mixture **has been tested as a whole and test data are available for the complete mixture**, these results are used to classify the mixture.
2. If a mixture **has not been tested as a whole or test data are not available for the complete mixture**, the bridging principles designated in each health hazard chapter of Appendix A of the Hazard Communication Standard are used to classify the mixture.
3. If **test data are not available for the mixture itself, and the available information is not sufficient** to allow application of the above-mentioned bridging principles, then the method(s) described in each chapter for estimating the hazards based on the information known will be applied to classify the mixture (e.g., application of cut-off values/ concentration limits).

An exception to the above order of precedence is made for Carcinogenicity, Germ Cell Mutagenicity, and Reproductive Toxicity (CMR). For these three hazard classes, mixtures are classified based upon information on the ingredient substances, unless on a case-by-case basis, justification can be provided for classifying based upon the mixture as a whole. Mixture rules for these three hazard classes are presented in Chapters VII.5, VII.6, and VII.7 of this document. See also chapters A.5, A.6, and A.7 in the Hazard Communication Standard for further information.

[3] LD_{50} (Lethal Dose 50) is the amount of a chemical, given all at once, which causes the death of 50% (one half) of a group of test animals.

Bridging principles for the classification of mixtures where test data are not available for the complete mixture

Where the mixture itself has not been tested to determine its toxicity, but there are sufficient data on **both the individual ingredients and similar tested mixtures** to adequately characterize the hazards of the mixture, the following bridging principles are used, subject to any specific provisions for mixtures for each hazard class. These principles ensure that the classification process uses the available data to the greatest extent possible in characterizing the hazards of the mixture.

Dilution

For mixtures classified in accordance with all the health hazard classes of the HCS (see Appendices A.1 through A.10 to 29 CFR 1910.1200), if a tested mixture is diluted with a diluent that has an equivalent or lower toxicity classification than the least toxic original ingredient, and which is not expected to affect the toxicity of other ingredients, then:

(a) The new diluted mixture is classified as equivalent to the original tested mixture; or

(b) For classification of acute toxicity, the additivity formula must be applied (see A.1.3.6 in Appendix A to 29 CFR 1910.1200).

Batching

The toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same mixture, when produced by or under the control of the ***same chemical manufacturer***, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary. The batching approach is used for mixtures classified in accordance with all the health hazard classes of the HCS (see Appendices A.1 through A.10 to 29 CFR 1910.1200).

Concentration of mixtures

The concentration of ingredients may be used to classify mixtures for the following hazard classes: acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, specific target organ toxicity - single exposure (STOT-SE), STOT-repeated or prolonged exposure, or aspiration (see Appendices A.1, A.2, A.3, A.8, A.9, or A.10 to 29 CFR 1910.1200). In these cases, if a tested mixture is classified in Category 1, and the concentration of the ingredients of the tested mixture that are in Category 1 is increased, the resulting untested mixture is classified in Category 1.

Interpolation within one toxicity category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same toxicity category, and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has concentrations of toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B. This approach to interpolating data

within one toxicity category is used for mixtures classified in accordance with the classification criteria for the following hazard classes in the HCS: acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, specific target organ toxicity - single exposure (STOT-SE), STOT-repeated or prolonged exposure, or aspiration (see Appendices A.1, A.2, A.3, A.8, A.9, or A.10 to 29 CFR 1910.1200).

Substantially similar mixtures

For mixtures classified in accordance with all health hazard categories of the HCS (see Appendices A.1 through A.10 to 29 CFR 1910.1200), given the following set of conditions:

(a) Where there are two mixtures:

(i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) And data on toxicity for A and C are available and substantially equivalent; i.e., they are in the same hazard category and are not expected to affect the toxicity of B; then

If mixture (i) or (ii) is already classified based on test data, the other mixture can be assigned the same hazard category.

Aerosols

For mixtures classified in accordance with the classification criteria for acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, specific target organ toxicity - single exposure (STOT-SE), or STOT-repeated or prolonged exposure (see Appendices A.1, A.2, A.3, A.4, A.8, or A.9 to 29 CFR 1910.1200), an aerosol form of a mixture is classified in the same hazard category as the tested, non-aerosolized form of the mixture, provided the added propellant does not affect the toxicity of the mixture when spraying.

Use of cut-off values/concentration limits

When classifying an untested mixture based on the hazards of its ingredients, cut-off values/concentration limits[4] for the classified ingredients of the mixture are used for several hazard classes. While the adopted cut-off values/concentration limits adequately identify the hazard for most mixtures, there may be some that contain hazardous ingredients at lower concentrations than the specified cut-off values/concentration limits that still pose an identifiable hazard. There may also be cases where the cut-off value/concentration limit is considerably lower than the established non-hazardous level for an ingredient.

[4] For the purposes of the HCS, the terms “cut-off values” and “concentration limits” mean the same thing.

If the chemical manufacturer, importer or other hazard classifier has information that the hazard of an ingredient will be evident (i.e., it presents a health risk) below the specified cut-off value/concentration limit, the mixture containing that ingredient must be classified accordingly.

In exceptional cases, conclusive data may demonstrate that the hazard of an ingredient will not be evident (i.e., it does not present a health risk) when present at a level above the specified cut-off value/concentration limit(s). In these cases the mixture may be classified according to those data. The data must exclude the possibility that the ingredient will behave in the mixture in a manner that would increase the hazard over that of the pure substance. Furthermore, the mixture must not contain ingredients that would affect that determination.

The HCS has established specific cut-off values for different health hazards. Table V.1 presents these cut-off values. When a substance in a specified hazard class is present in a mixture at or above the cut-off level, the mixture must be classified in that hazard class.

Table V.1. Cut-off Values for Health Hazards

Hazard class	Label Cut-Off Values	SDS Cut-Off Values
Respiratory/Skin sensitization	≥ 0.1%	≥ 0.1%
Germ cell mutagenicity (Category 1)	≥ 0.1%	≥ 0.1%
Germ cell mutagenicity (Category 2)	≥ 1.0%	≥ 1.0%
Carcinogenicity	≥ 0.1%	≥ 0.1%
Reproductive toxicity	≥ 0.1%	≥ 0.1%
Specific target organ toxicity (single exposure)	≥ 1.0%	≥ 1.0%
Specific target organ toxicity (repeated exposure)	≥ 1.0%	≥ 1.0%
Specific target organ toxicity Category 3	≥20%	≥20%

Synergistic or antagonistic effects

When performing an assessment in accordance with the requirements of the Hazard Communication Standard, the evaluator must take into account all available information about the potential occurrence of synergistic effects among the ingredients of the mixture. Lowering the classification of a mixture to a less hazardous category on the basis of antagonistic effects may be done only if the determination is supported by sufficient data.
Synergistic effects result when the overall effect of the ingredients is greater than the sum of any of the individual effects, while antagonistic effects result from the contrasting actions or negative effect from two (or more) ingredients, so that the overall effect is less than the sum of any of the individual effects.

Hazard Classification of Petroleum Streams

To classify the health hazards of petroleum streams, follow the guidance presented below in conjunction with the general guidance found in Appendix A.0.1-A.0.3 to 29 CFR 1910.1200, and the classification criteria provided for the health hazards presented in Appendix A to 29 CFR 1910.1200.

1. For hazard classes other than carcinogenicity, germ cell mutagenicity, and reproductive toxicity ("CMR"), classify a petroleum stream as follows:
   a) Where test data are available for the petroleum stream, the classification of the stream will always be based on those data.
   b) Where test data are not available for the stream itself, the classification may be based on a toxicologically appropriate read across from test results of a substantially similar stream. A substantially similar stream is one that has a similar starting material, production process, and range of physico-chemical properties (e.g., boiling point and carbon number) and similar constituent compositions.
   c) If test data are not available either for the stream itself or a substantially similar stream, then apply the method(s) described in each chapter of Appendix A to 29 CFR 1910.1200 for estimating the hazards based on the information known to classify the stream (i.e., application of cut-off values/concentration limits).
2. For the CMR hazard classes:
   a) When reliable and good quality data are available to classify a petroleum stream, based on testing of the stream or the toxicologically appropriate read-across to a substantially similar stream, a weight of evidence analysis supported by that data may be relied upon for classification regardless of whether a CMR constituent is present in the stream. A substantially similar stream is one that has a similar starting material, production process, and range of physico-chemical properties (e.g., boiling point and carbon number) and similar constituent compositions.
   b) To be reliable and good quality test data, the data must be from one or more tests that reflect appropriate study design and performance. The study or studies must appropriately take into account dose and other factors such as duration, observations, and analysis (e.g., statistical analysis, test sensitivity) so as to conclusively exclude the possibility that the lack of effect(s) is due to a poor study design, e.g., insufficient dose or number of subjects. A study (or studies) is conclusive in this sense if, when viewed in conjunction with all relevant information about the chemical, its results are consistent with the relevant information and allow a strong inference that the lack of effects is not due to a poor study design.
   c) Where reliable and good quality data are not available on the stream or a substantially similar stream, then apply the method(s) described in each chapter of Appendix A of 29 CFR 1910.1200 for estimating the hazards based on the information known to classify the stream (i.e., application of cut-off values/concentration limits).

Interface Between the HCS and U.S. Department of Transportation (DOT) labeling

As mentioned earlier, the purpose of the HCS is to ensure that the hazards of all chemicals produced or imported are classified, and that information concerning the hazards is transmitted to employers and workers. This information is transmitted by means of a comprehensive hazard communication program, which includes container labeling and other forms of warning, safety data sheets, and worker training.

With the alignment of the HCS to the GHS, one will find that there is generally a correlation between the DOT packing group and the HCS physical hazard class category. If the chemical being classified is the same chemical that has previously undergone classification to meet DOT's Hazardous Materials Regulations, you may use this data to classify the physical hazards of the chemical to meet the requirements of OSHA's Hazard Communication Standard. You may find the information contained in DOT's Hazardous Materials Regulations is another useful reference, in particular the Hazardous Materials Table, located in 49 CFR 172.101.

DOT labeling (referred to as placarding) applies to chemicals that are transported by means of rail car, aircraft, motor vehicle, and vessel. These placards must follow certain size and color requirements. The labels for the transport of dangerous goods are those prescribed by DOT's Hazardous Materials Regulations (49 CFR Parts 100-185). The classification criteria and testing procedures found in the DOT Hazardous Materials Regulations are aligned with the *UN Recommendations on the Transport of Dangerous Goods – Model Regulations*.

VI. RECORDING THE RATIONALE BEHIND THE RESULTS OBTAINED

The fourth and final step in the hazard classification process is also important. All the other steps will be wasted if findings are not recorded carefully. If a chemical is found to be hazardous, OSHA recommends that the findings and the rationale used to arrive at these findings be documented.

The HCS no longer requires documentation of the procedures used to determine the hazards of a chemical since this is now provided through the classification procedures specified in Appendices A and B of the HCS, and all those performing hazard classification must follow the same process. However, OSHA still recommends the data, the rationale used, and other results gathered during the classification process be maintained for future reference and use.

To assist in this, OSHA recommends that a structured approach to data retrieval and compilation be adopted. This structured approach also applies to the preparation of SDSs and labels. If you decide to take such an approach, this section provides some guidelines you may wish to consider.

Compilations of three types of data are considered essential:

- Initial chemical inventory;
- Specific data retrieved for each chemical; and
- List of hazardous chemicals.

Chemical Inventory

The **chemical inventory**[5] should consist of all chemicals that are imported or produced by the company, and those chemicals that are ingredients used in a mixture produced by the company. Classifiers may find it helpful if the chemical inventory includes the following information for future reference:

- chemical name;
- CAS Number;
- common name;
- synonyms;
- product/mixture name (if applicable); and
- percentage of ingredients in product/mixture (if applicable).

[5] The chemical inventory is different than the list of hazardous chemicals required under paragraph (e) of the HCS (29 CFR 1910.1200). The chemicals listed on the chemical inventory would be required to appear on the list of hazardous chemicals required under paragraph (e) of the HCS if they are present in the workplace.

As discussed in Chapter III, Identifying Hazardous Chemicals, it is recommended that this chemical inventory be computerized for future sorting, additions, deletions, and status reports.

Specific Data Retrieved for Each Chemical

OSHA recommends that the data retrieved be organized to facilitate the preparation of SDSs and labels. Listing all the hazard classes and categories, and the relevant data obtained for each hazard will also facilitate the gathering of data to document the effectiveness and completeness of the classification process. When data are not located for a specific type of hazard or when a specific hazard would not occur due to the chemical or physical form of the chemical, this should be indicated.

The data retrieved should be listed in the basic format of the SDS to facilitate preparation of SDSs and labels, as well as to allow for future updating as the need arises. As you would expect, OSHA recommends that the data be computerized and archived in a secure location for future use. A commonly used phrase for hazard data compilations for specific chemicals is **hazards profile**. A suggested organization for the documentation is provided in Table VI.1.

Table VI.1. LIST OF DATA RECOMMENDED FOR INCLUSION IN THE HAZARDS PROFILE FOR A CHEMICAL

(Reference source should be included for each item, where appropriate. In the event that no information on an item is known or it is not applicable, this should be so indicated.)

TYPE OF INFORMATION	DATA
Company Information	▪ Company Name, address, and telephone number ▪ Name of Responsible Company Official ▪ Date Prepared
Hazards Identification	▪ Hazard classification (list appropriate health and physical hazards, including the classification rationale)
Hazardous Ingredients/Identity Information	▪ Chemical Name ▪ Common Name and Synonyms ▪ CAS Number or other unique identifiers ▪ Impurities and stabilizing additives ▪ Product/Mixture Name (If Applicable) ▪ Percentage of Ingredients in Product/Mixture (If Applicable)
Description of Controls and Protective Measures	▪ First-aid measures ▪ Fire-fighting measures ▪ Accidental release measures ▪ Handling and storage ▪ Exposures control and personal protection

TYPE OF INFORMATION	DATA
Physical/Chemical Characteristics	▪ Appearance (physical state, color, etc.) ▪ Odor ▪ Odor threshold ▪ pH ▪ Melting point/freezing point ▪ Initial boiling point and boiling range ▪ Flash point ▪ Evaporation rate ▪ Flammability (solid, gas) ▪ Upper/lower flammability or explosive limits ▪ Vapor pressure ▪ Vapor density ▪ Relative density ▪ Solubility(ies) ▪ Partition coefficient: n-octanol/water ▪ Auto-ignition temperature ▪ Decomposition temperature ▪ Viscosity
Reactivity Data	▪ Reactivity ▪ Chemical stability ▪ Possibility of hazardous reactions ▪ Conditions to avoid (e.g., static discharge, shock, or vibration) ▪ Incompatible materials ▪ Hazardous decomposition or byproducts
Health Hazard Data	▪ Description of the various toxicological (health) effects and the available data used to identify those effects, including: ✓ Information on the likely routes of exposure (inhalation, ingestion, skin and eye contact); ✓ Symptoms related to the physical, chemical and toxicological characteristics; ✓ Delayed and immediate effects and also chronic effects from short- and long-term exposure; ✓ Numerical measures of toxicity (such as acute toxicity estimates); and

TYPE OF INFORMATION	DATA
	✓ Whether the hazardous chemical is listed as a carcinogen or potential carcinogen by o National Toxicology Program (NTP) Report on Carcinogens (latest edition), or o International Agency for Research on Cancer (IARC) Monographs (latest edition), or OSHA.
Other Miscellaneous Information	

List of Hazardous Chemicals

The Hazard Communication Standard requires employers to maintain a list of hazardous chemicals present in the workplace as a part of the Written Hazard Communication Program (29 CFR 1910.1200(e)). The purpose of having a list of hazardous chemicals at your facility is to document those chemicals used or stored at the facility. Not only will the list facilitate the identification of the hazards presented by the hazardous chemicals at the facility or in a given work area, a complete list of chemicals also may help identify the information you already have on the chemicals or other ingredients used in production of the final product. Since safety data sheets are required for the chemicals you receive, this may be a good place to start the list. The hazards profile developed for each chemical (discussed above) also may be useful to determine which of the chemicals in the facility or work area are considered hazardous.

If a chemical meets the definition of hazardous chemical, as defined by the Hazard Communication Standard, and the hazardous chemical is one that requires classification, then it must be included on the hazardous chemicals list. OSHA recommends that the list be alphabetized to ease retrieval, stored so that it may be accessed easily, and archived in a secure location for future use.

VII. CLASSIFICATION OF HEALTH HAZARDS

Introduction

Health hazards presented by chemicals can harm human health through a variety of routes. Workers can be exposed to hazards by inhaling vapors, mists, or dusts from the chemical; by ingesting the chemical; or by getting it on their skin. Symptoms from exposure can be acute or chronic. The hazards include those that affect eyes, skin, reproductivity, and specific target organs. In addition, some chemicals can be toxic, corrosive, or carcinogenic.

Classification of health hazards is based on data found in available literature, as a result of a calculation, or through the use of other criteria specific to the health hazard itself. The Hazard Communication Standard does not require the testing of chemicals -- only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, the test methods used must be scientifically validated. OSHA has provided scientifically validated test methods in the appropriate health hazard chapters to ensure proper classification under the HCS.

Selection of Hazard Classes

Once the chemical manufacturer, importer, or classifier has collected the data, that information is compared to the classification criteria for each hazard class. The decision logic included in this guidance for each health hazard can be used to identify the appropriate hazard class and category of the chemical. As mentioned throughout this guidance document, many hazardous chemicals have more than one physical hazard and/or health hazard. Each hazard must be presented on the label, 29 CFR 1910.1200(f)(2), and SDS, 29 CFR 1910.1200(g)(2) as specified in HCS Appendix C, Allocation of Label Elements, and HCS Appendix D, Minimum Information for an SDS.

Classification examples:

In addition to the classification examples provided at the end of each chapter in this section, the United Nations Sub-Committee of Experts on the GHS has developed several classification examples and posted them as guidance on their website. The examples are at the following location: www.unece.org/trans/danger/publi/ghs/guidance.html.

VII.1 Acute Toxicity

Introduction

The HCS 2012 classifies chemical agents as acutely toxic based on the number of deaths that occur following brief (acute) exposure of test animals. The difference in the categories is strictly the dose at which the toxicity (death) occurs. Exposure is by the three major workplace exposure routes, mouth (oral), skin (dermal), or breathing (inhalation). The analysis is based on the LD50 (median lethal dose by oral or dermal exposure) and LC50 (median lethal inhalation concentration) for a four-hour exposure. The LD50 and LC50 represent the dose or concentration, respectively, at which 50 percent of the test animals (and, presumptively, humans) will be expected to die.

While these criteria are based on laboratory animals that are quite different from humans, the relative response between animals and humans is generally comparable on a per body weight basis. Thus, the LD_{50} is expressed in terms of kilogram of body weight in order to determine potential human effects based on animal research results. For example, if a chemical has a 50 mg/kg $LD_{50,}$ it would be expected to be lethal to approximately 50 percent of humans weighing 150 pounds at a dose of 3.4 grams or approximately about three quarters of a teaspoon.[6] On the other hand, the LC_{50} value is expressed as weight of test substance per standard volume of air (mg/1) for vapors, dust, and mists, or as volume parts per million (ppmV) for gases.

Classification for acute toxicity can also be based on human evidence which shows lethality following human exposure.

Definition and General Considerations

Acute toxicity refers to those adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.

The *Acute Toxicity Estimate* (ATE) for the classification of a substance is derived using the LD_{50}/LC_{50} where available. The ATE for the classification of a substance or ingredient in a mixture is derived using:

(i) the LD_{50}/LC_{50} where available. Otherwise,
(ii) the appropriate conversion value from Table VII.1.6 that relates to the results of a range test, or
(iii) the appropriate conversion value from Table VII.1.6 that relates to a classification category.

Classification Criteria for Substances

Substances can be allocated to one of four toxicity categories based on acute toxicity by the oral, dermal or inhalation route according to the numeric cut-off criteria shown in Tables VII.1.1 through VII.1.5. Acute toxicity values are expressed as (approximate) LD_{50} (oral, dermal) or LC_{50} (inhalation) values or as acute toxicity estimates (ATE).

Acute Oral Toxicity Categories and Classification Criteria

There are four classification categories for acute oral toxicity. The category is assigned according to the HCS 2012 classification criteria for acute oral toxicity, as follows:

[6] 150 lb. x 0.454 kg/lb.= 68.1 kg;
68.1 kg x 50mg/kg = 3405 mg;
3.5 g ÷ 454 g/lb. = 7.5 x 10^{-3} lbs.;
7.5 x 10^{-3}lbs. = 0.12 oz.;
0.12 oz. = 0.72 tsp.

Table VII.1.1. Acute Oral Toxicity Categories and Classification Criteria

Classification Criteria	Category 1	Category 2	Category 3	Category 4
Oral LD_{50}	≤ 5 mg/kg bodyweight	>5 and ≤ 50 mg/kg bodyweight	>50 and ≤ 300 mg/kg bodyweight	>300 and ≤ 2000 mg/kg bodyweight

Acute Dermal Toxicity Categories and Classification Criteria

There are four classification categories for acute dermal toxicity. The category is assigned according to the HCS 2012 classification criteria for acute dermal toxicity, as follows:

Table VII.1.2. Acute Dermal Toxicity Categories and Classification Criteria

Classification Criteria	Category 1	Category 2	Category 3	Category 4
Dermal LD_{50}	≤ 50 mg/kg bodyweight	>50 and ≤ 200 mg/kg bodyweight	>200 and ≤ 1000 mg/kg bodyweight	>1000 and ≤ 2000 mg/kg bodyweight

Acute Inhalation Toxicity Categories and Classification Criteria

There are four classification categories for acute inhalation toxicity. The category is assigned according to the HCS 2012 classification criteria for acute inhalation toxicity.

Values for inhalation toxicity are based on 4-hour tests in laboratory animals. When experimental values are taken from tests using a 1-hour exposure, to avoid the need to retest, they can be converted to a 4-hour equivalent as explained below. Units for inhalation toxicity are a function of the form of the inhaled material. Values for vapors, dusts, and mists are expressed in mg/l. Values for gases are expressed in ppmV. The equation for converting mg/L to ppm where ppm is parts per million and MW is molecular weight is:

$$mg/_L = \frac{ppm \times MW}{24{,}450}$$

Gases

Gas means a substance which (i) at 50 °C (122 °C)has a vapor pressure greater than 300 kPa; or (ii) is completely gaseous at 20 °C (68 °F) at a standard pressure of 101.3 kPa.

Inhalation cut-off values are based on 4-hour testing exposures. Conversion of existing inhalation toxicity data which has been generated according to 1-hour exposure is achieved by dividing by a factor of 2 for gases. For gases, LC_{50} (4-hr.) is equivalent to LC_{50} (1-hr.) divided by a factor of 2.

Table VII.1.3. Gases: Acute Inhalation Toxicity Categories and Classification Criteria

Classification Criteria	Category 1	Category 2	Category 3	Category 4
Inhalation LC_{50} (4-hr.)	≤ 100 ppmV	>100 and ≤ 500 ppmV	>500 and ≤ 2500 ppmV	>2500 and ≤ 20000 ppmV

Vapors

Vapor means the gaseous form of a substance or mixture released from its liquid or solid state.

Inhalation cut-off values are based on 4-hour testing exposures. Conversion of existing inhalation toxicity data which has been generated according to 1-hour exposure is achieved by dividing by a factor of 2 for vapors. For vapors, LC_{50} (4-hr.) is equivalent to LC_{50} (1-hr.) divided by a factor of 2.

For some substances, the test atmosphere will be a combination of liquid and gaseous phases. For other substances, the test atmosphere may be nearly all the gaseous phase. For those test atmospheres which are near the gaseous phase, classification should be based on the cutoff values for gases in units of ppmV (refer to table for gases, above).

Table VII.1.4. Vapors: Acute Inhalation Toxicity Categories and Classification Criteria

Classification Criteria	Category 1	Category 2	Category 3	Category 4
Inhalation LC_{50} (4-hr.)	≤ 0.5 mg/L	>0.5 and ≤ 2.0 mg/L	>2.0 and ≤ 10.0 mg/L	>10.0 and ≤ 20.0 mg/L

Dusts and Mists

Dust means solid particles of a substance or mixture suspended in a gas (usually air). Dust is generally formed by mechanical processes.

Mist means liquid droplets of a substance or mixture suspended in a gas (usually air). Mist is generally formed by condensation of supersaturated vapors or by physical shearing of liquids.

Dusts and mists generally have sizes ranging from less than 1 to about 100 µm.

Inhalation cut-off values are based on 4-hour testing exposures. Conversion of existing inhalation toxicity data which has been generated according to 1-hour exposure is achieved by dividing by a factor of 4 for dusts and mists. For dusts and mists, LC_{50} (4-hr.) is equivalent to LC_{50} (1-hr.) divided by a factor of 4.

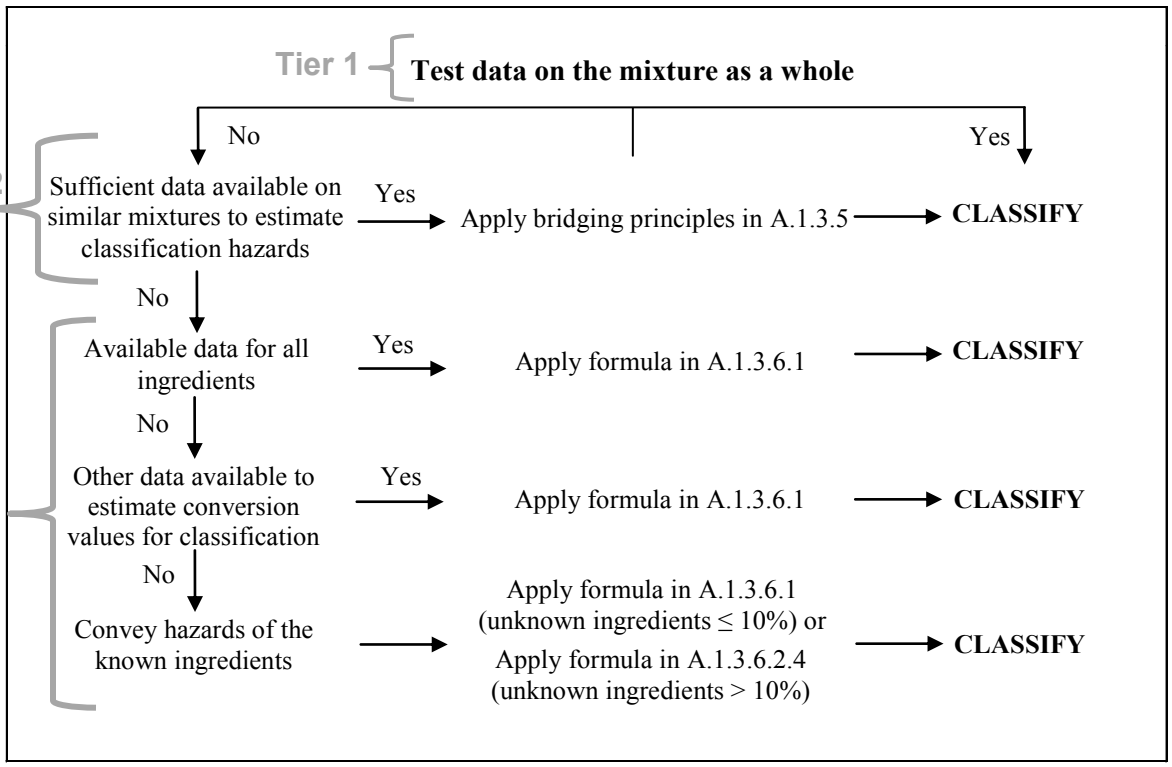
Table VII.1.5. Dusts and Mists: Acute Inhalation Toxicity Categories and Classification Criteria

Classification Criteria	Category 1	Category 2	Category 3	Category 4
Inhalation LC_{50} (4-hr.)	≤ 0.05 mg/L	>0.05 and ≤ 0.5 mg/L	>0.5 and ≤ 1.0 mg/L	>1.0 and ≤ 5.0 mg/L

Classification criteria for mixtures

For mixtures, it is necessary to obtain or derive information that allows the criteria to be applied to the mixture for the purpose of classification. The approach to classifying mixtures for acute toxicity is tiered, and is dependent upon the amount of information available for the mixture itself and for its ingredients. The flowchart below outlines the process to be followed:

Figure VII.1.1. Tiered approach to classification of mixtures for acute toxicity



It should be noted that the classification criteria for acute toxicity includes a tiered scheme in which test data available on the complete mixture are considered as the first tier in the evaluation, followed by the applicable bridging principles, and lastly, use of additivity formulas.

Tier 1: Classification of mixtures when data are available for the complete mixture

When acute toxicity test data on the mixture as a whole is available, it must be used to classify the mixture using the same criteria as those specified for substances. If acute toxicity test data for the mixtures is not available, then the classifier can consider the application of the bridging principle criteria in Tier 2, if appropriate, or use the classification resulting from the application of criteria in Tier 3.

Tier 2: Classification of mixtures when data are not available for the complete mixture – bridging principles

Where the mixture itself has not been tested to determine its acute toxicity, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the bridging principles, below.

All six bridging principles are applicable to the acute toxicity hazard class:

- Dilution
- Batching
- Concentration of mixtures
- Interpolation within one toxicity category
- Substantially similar mixtures, and
- Aerosols.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential acute toxicity hazard.

Dilution

If a tested mixture is diluted with a diluent that has an equivalent or lower toxicity classification than the least toxic original ingredient, and which is not expected to affect the toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture. Alternatively, the additivity formula explained below and in A.1.3.6.1 could be applied.

Batching

The toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product, when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures
If a tested mixture is classified in Category 1, and the concentration of the ingredients of the tested mixture that are in Category 1 is increased, the resulting untested mixture should be classified in Category 1 without additional testing.

Interpolation within one toxicity category
For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same toxicity category, and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has concentrations of toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same toxicity category as A and B.

Substantially similar mixtures
Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e., they are in the same hazard category and are not expected to affect the acute toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Aerosols
An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolized form of the mixture for oral and dermal toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolized mixtures for inhalation toxicity should be considered separately.

If appropriate data is not available to apply the above bridging principles, then the classifier applies the criteria in Tier 3.

Tier 3: Classification of mixtures based on ingredients of the mixture (additivity formula)

The basic approach to estimating a mixture's acute toxicity in Tier 3 is to calculate an Acute Toxicity Estimate for the mixture ($ATE_{mixture}$) which represents the expected LD_{50}/LC_{50} of the mixture. This is accomplished by collecting the LD_{50}/LC_{50} for each ingredient if it is known or a point estimate of an ingredient's LD_{50}/LC_{50} if either a classification or an acute toxicity range from a limit dose test is known.

The rules for applying the additivity formula are dependent on whether acute toxicity information is available for all the ingredients of a mixture. This accommodation was made because the mathematics involved in applying the additivity formula implicitly assumes that any ingredient not included in the calculation has a dilution effect on the calculated $ATE_{mixture}$. The two acute toxicity additivity formulas and rules for their use are discussed below.

Data available for all ingredients

Rules on when to include or ignore ingredients in the $ATE_{mixture}$ calculation are provided to ensure consistent application of the additivity formula.

Include:

(a) Ingredients with a known acute toxicity, which fall into any of the acute toxicity categories, or have an oral or dermal LD_{50} greater than 2000 but less than or equal to 5000 mg/kg body weight (or the equivalent dose for inhalation). This includes GHS Acute Toxicity Category 5 in the $ATE_{mixture}$ calculation.[7]

Ignore:

(a) Ingredients with a known acute toxicity outside the level specified above can be ignored in the calculation. For example, an ingredient with an Oral LD_{50} (rat) of > 5,000 mg/kg could be ignored.

(b) Ingredients that are presumed not acutely toxic (e.g., water, sugar);

Application of this rule requires expert judgment to determine if an ingredient meets the intent of the requirement. Ingredients that are not biologically available could be considered "presumed not acutely toxic".

[7] The criteria for GHS Category 5 are:
(i) The chemical is classified in category 5 if reliable evidence is available that indicates (1) the oral/dermal LD_{50} is in the range of >2000 and ≤5000 mg/kg bodyweight and the LC_{50} is in the equivalent range of the oral and dermal LD_{50} (i.e., >2000 and ≤ 5000 mg/kg bodyweight) or (2) other animal studies or toxic effects in humans indicate a concern for human health of an acute nature.
(ii) The chemical is classified in category 5, through extrapolation, estimation or measurement of data, if assignment to a more hazardous category is not warranted, and:
- reliable information is available indicating significant toxic effects in humans; or
- any mortality is observed when tested up to Category 4 values by the oral, inhalation, or dermal routes; or
- where expert judgment confirms significant clinical signs of toxicity, when tested up to Category 4 values, except for diarrhea, piloerection or an ungroomed appearance; or
- where expert judgment confirms reliable information indicating the potential for significant acute effects from other animal studies.
The HCS does not require classification in this category.

(c) Ingredients for which the data available are from a limit dose test[8] (at the upper threshold for Category 4 for the appropriate route of exposure, e.g., oral LD_{50} = 2000) and do not show acute toxicity.

The ATE of the mixture is determined by calculation from the LD_{50}-LC_{50}-ATE values for all relevant ingredients according to the following formulas for oral, dermal or inhalation toxicity. More information on relevant ingredients can be found below under "important considerations."

Formula 1A:

$$\frac{100}{ATE_{mix}} = \sum_{n} \frac{C_i}{ATE_i}$$

Where:

C_i = concentration of ingredient I
n ingredients and i is running from 1 to n
ATE_i = Acute Toxicity Estimate of ingredient i
ATE_{mix}= Acute Toxicity Estimate of mixture

Formula 1B is a different way of expressing Formula 1A that may be easier to understand. The formula is essentially calculating the $ATE_{mixture}$ or LD_{50}/LC_{50} of the mixture. C is the concentration of the ingredients expressed as a percentage. The math is addition, multiplication and division.

Formula 1B:

$$\frac{100\ (\%)}{ATE_{mix}} = \frac{C_1}{LD_{50\ (1)}} + \frac{C_2}{LD_{50(2)}} + \frac{C_3}{LD_{50(3)}} + \frac{C_4}{LD_{50(4)}} + \cdots\cdots\cdots \frac{C_{etc}}{LD_{50(etc)}}$$

or

$$ATE_{mix} = \frac{100\ (\%)}{\frac{C_1}{LD_{50\ (1)}} + \frac{C_2}{LD_{50(2)}} + \frac{C_3}{LD_{50(3)}} + \frac{C_4}{LD_{50(4)}} + \cdots\cdots\cdots \frac{C_{etc}}{LD_{50(etc)}}}$$

Data are not available for one or more ingredients

If the total concentration of the relevant ingredient(s) with unknown acute toxicity is **≤ 10%** then Formula 1A or 1B as shown above must be used.

[8] Limit dose test – the preferred test when toxicity is expected to be low and lethality is unlikely at the limit dose. The limit dose must be adequate for assessment purposes, and it is usually 2000 mg/kg body-weight.

However, if the total concentration of ingredient(s) with unknown toxicity is **> 10%** then the "corrected" additivity formula which adjusts for the total percentage of unknown ingredient(s) must be used. The "corrected" additivity formula corrects the left hand side of the ATE formula by subtracting the total percent of unknowns, if they exceed 10%, from 100.

Formula 2A:

$$\frac{100-(\sum \mathrm{C}_{\text{unknown}} \text{if} > 10\%\ )}{ATE_{mix}} = \sum_{n} \frac{Ci}{ATEi}$$

Formula 2B is a different way of expressing Formula 2A that may be easier to understand. C is the concentration of the ingredients expressed as a percentage. The math is addition, multiplication and division.

Formula 2B:

$$= \frac{C_1}{LD_{50\ (1)}} + \frac{C_2}{LD_{50(2)}} + \frac{C_3}{LD_{50(3)}} + \frac{C_4}{LD_{50(4)}} + \cdots\cdots\cdots \frac{C_{etc}}{LD_{50(etc)}}$$

$$\frac{100\ (\%) - (\sum C_{unk}\ if > 10\%)}{ATE_{mix}}$$

or

$$ATE_{mix} = \frac{100\ (\%) - (\sum C_{unk}\ if > 10\%)}{\frac{C_1}{LD_{50\ (1)}} + \frac{C_2}{LD_{50(2)}} + \frac{C_3}{LD_{50(3)}} + \frac{C_4}{LD_{50(4)}} + \cdots\cdots\cdots \frac{C_{etc}}{LD_{50(etc)}}}$$

Important considerations

An important consideration when applying the additivity formula is recognition that the additivity formula is applied to each route of exposure separately. In other words, $ATE_{mixture}$ is calculated for a specific route (e.g., oral, dermal, and inhalation) and the ingredient LD_{50}/LC_{50} values and point estimates used in a calculation must correspond to the specific route (and physical state for inhalation) for which the $ATE_{mixture}$ is being calculated.

Consistent application of the additivity formula

In order to ensure consistent application of the additivity formula guidance is provided on:

- When ingredients should be included in the ATE calculation,
- When ingredients can be ignored in the ATE calculation, and
- How to convert an acute toxicity range estimate from a limit dose test or hazard classification into a point estimate for use in the $ATE_{mixture}$ calculation.

The following guidance needs to be considered when calculating the $ATE_{mixture}$:

- **"Relevant Ingredient" Concept**
  For the purpose of the $ATE_{mixture}$ calculation, only "relevant ingredients" need to be included when applying the additivity formula. The general rule is to only include ingredients at a concentration of ≥ 1% in the calculation. However, an ingredient could still be considered relevant and included in the calculation at a concentration of < 1% if the classifier suspects that the ingredient could be relevant for classifying the mixture. The relevant ingredient criteria particularly point out that consideration should be given to include Category 1 and Category 2 ingredients at concentrations <1%. In these cases, the classifier must use expert judgment to determine at what concentration below 1% Category 1 or 2 ingredients should be included in the calculation. Important points to consider when making the decision are:

    - The lower the $LD_{50}/LC_{50,}$ the more significant its impact is on the calculation since the additivity formula is a proportional calculation which places a greater weight on more toxic ingredients in the calculation. The decision to exclude an ingredient could result in underestimating the acute toxicity of the mixture.
    - As the total number of Category 1 and/or Category 2 ingredients increases in a mixture, a decision not to include them in the $ATE_{mixture}$ calculation with concentrations below 1% may result in underestimating the acute toxicity of the mixture since the additivity formula places greater weight on more toxic ingredients and the additivity effect of multiple ingredients would not be considered in the $ATE_{mixture}$ calculation.

- **Unknown acute toxicity**
  In the event that an ingredient with unknown acute toxicity is used in a mixture at a concentration ≥ 1%, and the mixture has **not** been classified based on testing of the mixture as a whole, the mixture cannot be attributed a definitive acute toxicity estimate. In this situation, the mixture is classified based on the known ingredients only. A statement that "X percent of the mixture consists of ingredient(s) of unknown acute toxicity" is required on the label and safety data sheet in such cases. See 29 CFR 1910.1200 Appendix C, Allocation of Label Elements and Appendix D, Safety Data Sheets.

  The unknown acute toxicity statement is only required on the label and the SDS where the chemical mixture is already classified as acutely toxic for a particular route of exposure, and there are one or more other "relevant ingredients" (as defined above) of unknown acute toxicity for that particular route.

  Classifiers may present the unknown acute toxicity information on ingredients either as a single statement or as multiple statements, where routes are differentiated. If there is acute toxicity by more than one route of exposure and the classifier chooses to provide one statement, then the route with the highest total percentage unknown toxicity from one or more relevant ingredients will be used in the statement.

The single statement on the label would read:

Y% of the mixture consists of ingredients of unknown acute toxicity.

Because it is possible to have ingredients with unknown toxicity for more than one route (e.g., oral, dermal, inhalation), differentiating the unknown toxicity statement by route is recommended. As such, classifiers may also communicate the information as:

X% of the mixture consist of ingredient(s) of unknown acute oral toxicity
X% of the mixture consists of ingredient(s) of unknown acute dermal toxicity
X% of the mixture consists of ingredient(s) of unknown acute inhalation toxicity

The GHS clarified the classification criteria with regard to the unknown toxicity statement in Revision 4 to indicate that the statement of unknown toxicity should be differentiated by route. The HCS adopted Revision 3 of the GHS and thus does not require the unknown toxicity statement to be differentiated by route. However, OSHA's recommendation is that classifiers follow the guidance provided in Revision 4 of the GHS (see GHS Rev. 4 paragraphs 3.1.3.6.2.2 and 3.1.4.2).

Example 1:

Mixture A: Relevant routes of exposure are Oral and Dermal

Ingredient	Wt%	Ingredient with unknown Acute toxicity		
		Oral Route	Dermal Route	Inhalation Route
X	10			Yes
Y	30	Yes		
Z	60		Yes	Yes

Using the data for Mixture A above it would be appropriate to have:

1. The statements on the SDS would read:
   70% of the mixture consists of ingredients of unknown acute inhalation toxicity
   60% of the mixture consists of an ingredient of unknown acute dermal toxicity
   30% of the mixture consists of an ingredient of unknown acute oral toxicity

2. The single statement on the label would read:
   70% of the mixture consists of ingredients of unknown acute toxicity

- **Mixtures containing other mixtures**
  When a mixture (i.e., Mixture A) is used as an ingredient of another mixture either an actual LD_{50}/LC_{50} value or the calculated toxicity estimate (ATE) for Mixture A may be used in the $ATE_{mixture}$ calculation for the new mixture instead of using the LD_{50}/LC_{50} values or point estimates for each ingredient of Mixture A.

- **Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for use in the formulas for the classification of mixtures**
  The additivity formula requires a single numeric value for each ingredient included in the $ATE_{mixture}$ calculation. If an LD_{50}/LC_{50} is available it should be used in the ATE Calculation. In those cases where the only known information about an ingredient is its hazard category, Table VII.1.6 can be used to look up the converted acute toxicity point estimate.

  Additionally, in those cases where a limit dose test was used to establish a LD_{50}/LC_{50} range, the range may also be converted to a acute toxicity point estimate using Table VII.1.6. Limit dose data generated prior to the creation/adoption of the GHS acute toxicity substance criteria will not always match the ranges specified in Table VII.1.6 since GHS criteria represent a change in ranges for many existing regulatory systems. In those cases where existing limit dose data do not exactly match the ranges in Table VII.1.6, expert judgment will be necessary to determine what point estimate to use in the $ATE_{mixture}$ calculation.

  As you can see below, the converted acute toxicity point estimate is conservative and where there is a lack of data it would tend to classify the mixture into a more hazardous subcategory. OSHA would expect a similar approach if using alternate ranges.

Table VII.1.6. Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for use in the formulas for the classification of mixtures

Exposure routes	Classification category or experimentally obtained acute toxicity range estimate	Converted acute toxicity point estimate
Oral (mg/kg bodyweight)	0 < Category 1 ≤ 5	0.5
	5 < Category 2 ≤ 50	5
	50 < Category 3 ≤ 300	100
	300 < Category 4 ≤ 2000	500
Dermal (mg/kg bodyweight)	0 < Category 1 ≤ 50	5
	50 < Category 2 ≤ 200	50
	200 < Category 3 ≤ 1000	300
	1000 < Category 4 ≤ 2000	1100

Exposure routes	Classification category or experimentally obtained acute toxicity range estimate	Converted acute toxicity point estimate
Gases (ppmV)	0 < Category 1 ≤ 100	10
	100 < Category 2 ≤ 500	100
	500 < Category 3 ≤ 2500	700
	2500 < Category 4 ≤ 20000	4500
Vapours (mg/l)	0 < Category 1 ≤ 0.5	0.05
	0.5 < Category 2 ≤ 2.0	0.5
	2.0 < Category 3 ≤ 10.0	3
	10.0 < Category 4 ≤ 20.0	11
Dust/mist (mg/l)	0 < Category 1 ≤ 0.05	0.005
	0.05 < Category 2 ≤ 0.5	0.05
	0.5 < Category 3 ≤ 1.0	0.5
	1.0 < Category 4 ≤ 5.0	1.5

Note: Gas concentrations are expressed in parts per million per volume (ppmV)

There is an example at the end of this chapter which illustrates the application of the type of expert judgment that can be used when considering how to use existing range data that do not match the ranges presented in Table VII.1.6.

- **Data are not available for one or more ingredients of the mixture**
  In some cases an ingredient's LD_{50}-LC_{50}-ATE is not available but other information is available that allows for a derived or estimated acute toxicity estimate.

  This approach generally requires substantial supplemental technical information which needs to be interpreted by highly trained and experienced experts. The types of information that may be considered to derive or estimate an ingredient ATE is provided below.

  (a) Route-to-route extrapolation between oral, dermal and inhalation acute toxicity estimates. Such an evaluation requires appropriate pharmacodynamic and pharmacokinetic data.

  (b) Evidence from human exposure that indicates toxic effects but does not provide lethal dose data. Human evidence can be used to derive an ATE.

  (c) Information from other types of toxicity tests/studies can sometimes be useful in deriving an acute toxicity classification. These studies will not usually provide an LD_{50}-LC_{50}-ATE value that can be used directly for classification, but they may provide information to allow an estimate of acute toxicity.

(d) Data from closely analogous substances using structure activity relationships (SAR) may be used to estimate an ATE.

In cases where such information is not available, then the criteria provided in 29 CFR 1910.1200 paragraph A.1.3.6.2.4 must be reviewed to determine if the modified additivity formula should be used for the $ATE_{mixture}$ calculation.

$$\frac{100-(\sum \mathrm{C}_{\text{unknown}} \text{if} > 10\%\ )}{ATE_{mix}} = \sum_{n} \frac{Ci}{ATEi}$$

Relevant routes of exposure

The $ATE_{mixture}$ calculation is not automatically required for all routes of exposure. The calculation need be done for only one route of exposure as long as all the ingredients have actual LD_{50}/LC_{50} values or a converted acute toxicity point estimate for use in that route's $ATE_{mixture}$ calculation. However, if there is relevant evidence suggesting acute toxicity by multiple routes of exposure then the $ATE_{mixture}$ should be calculated for all the appropriate routes of exposure.

The use of expert judgment will be necessary to evaluate each ingredient's acute toxicity information, across all routes of exposure, and determine if that data support calculating the $ATE_{mixture}$ across multiple routes of exposure. There is an example at the end of this chapter which illustrates the concept of evaluating the relevant substance data to determine which route(s) need to be calculated.

An additional important point to consider when deciding which route(s) to calculate is an understanding of how the HCS is structured. The HCS applies to any chemical which is known to be present in the workplace in such a manner that employees may be exposed to hazards under normal conditions of use or in a foreseeable emergency. Consideration of a "foreseeable emergency" or "misuse" of chemicals may be needed in addition to considering the normal use of chemicals. It is possible that such considerations may influence the decision on which route(s) are needed for $ATE_{mixture}$ calculations.

Classification Procedure and Guidance

Test Data

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS only requires classifiers to collect and evaluate the best available existing evidence on the hazards of each chemical. For classification purposes, epidemiological data and experience on the effects of chemicals on humans (e.g., occupational data, data from accident databases) must be taken into account in the evaluation of human health hazards of a chemical.

Data generated in accordance with recognized scientific principles are acceptable under HCS 2012. If valid data on acute toxicity of a substance or mixture are available (LD_{50}/LC_{50}), these data must be used in the classification.

Examples of scientifically validated test methods
There are a number of test methods that use recognized scientific principles for investigation of acute toxicity:

Acute Oral Toxicity:

- OECD Test Guideline 401: Acute Oral Toxicity. This test method was deleted in December 2002 because of animal welfare concerns. Classical acute toxicity studies are based on lethality, e.g., LD_{50} values.
- OECD Test Guideline 420: Acute Oral Toxicity – Fixed Dose Procedure provides a range estimate of the oral LD_{50}. Contemporary test methods use clinical signs of nonlethal toxicity (evident toxicity).
- OECD Test Guideline 423: Acute Oral Toxicity – Acute Toxic Class Method provides a range estimate of the oral LD_{50}.
- OECD Test Guideline 425: Acute Oral Toxicity – Up-and-Down-Procedure (UPD) provides a point-estimate of the LD_{50} value with confidence intervals.
- USEPA OTS code: 798.1175;
- USEPA OPP code: 81-1;
- USEPA OPPTS code: 870.1100;
- EEC Directive 92/32/EEC (B.1 bis & B.1 tris).

Acute Dermal Toxicity:

- OECD Test Guideline 402: Acute Dermal Toxicity. The preferred test species are rats, rabbits, or guinea pigs.
- USEPA OTS code: 798.1100;
- USEPA OPP code: 81-2;
- USEPA OPPTS code: 870.1200;
- EEC Directive 92/32/EEC (B.3).

Acute Inhalation Toxicity:

- OECD Test Guideline 403: Acute Inhalation Toxicity. The test exposure period is usually 4 hours. The preferred test species is the rat.
- USEPA OTS code: 798.1150;
- USEPA OPP code: 81-3;
- USEPA OPPTS code: 870.1300 & 870.1350;
- EEC Directive 92/32/EEC (B.2).

There are currently no internationally recognized *in vitro* tests for acute toxicity.

See the above guidance on using Table VII.1.6 to convert a LD_{50}/LC_{50} range from a limit dose test to an acute toxicity point estimate. Where an existing LD_{50}/LC_{50} range does not exactly match the ranges in Table VII.1.6, expert judgment will be necessary to determine what point estimate to use in the $ATE_{mixture}$ calculation.

Test species
The preferred test species for evaluation of acute toxicity by the oral and inhalation routes is the rat, while the rat or rabbit are preferred for evaluation of acute dermal toxicity. Test data already generated for the classification of chemicals under existing systems should be accepted when reclassifying these chemicals under HCS 2012. When experimental data for acute toxicity are available in several animal species, scientific judgment should be used in selecting the most appropriate LD_{50} value from among scientifically validated tests.

Although the HCS provides specific classification criteria, including the appropriate test methods and species to use for evaluation, the HCS also indicates that information pertaining to other species and test methods is also relevant. In determining hazards, you need to search for and analyze all data pertaining to toxicity and make judgments as to whether the tests were conducted using recognized scientific principles. If the studies are acceptable, the data should be used as appropriate to determine whether the chemical is acutely toxic, or belongs to another health hazard category (e.g., hepatotoxicity or irritant).

The ATE is usually obtained from animal studies but in principle suitable human data can also be used if available. Where human data are available they should be used to estimate the ATE which can be used directly for classification as described above.

Corrosivity
In addition to classification for inhalation toxicity, if data are available that indicates that the mechanism of toxicity was corrosivity of the substance or mixture, the classifier should consider if the chemical is corrosive to the respiratory tract. Corrosion of the respiratory tract is defined as destruction of the respiratory tract tissue after a single, limited period of exposure analogous to skin corrosion; this includes destruction of the mucosa. The corrosivity evaluation could be based on expert judgment using such evidence as: human and animal experience, existing (in vitro) data, pH values, information from similar substances or any other pertinent data.

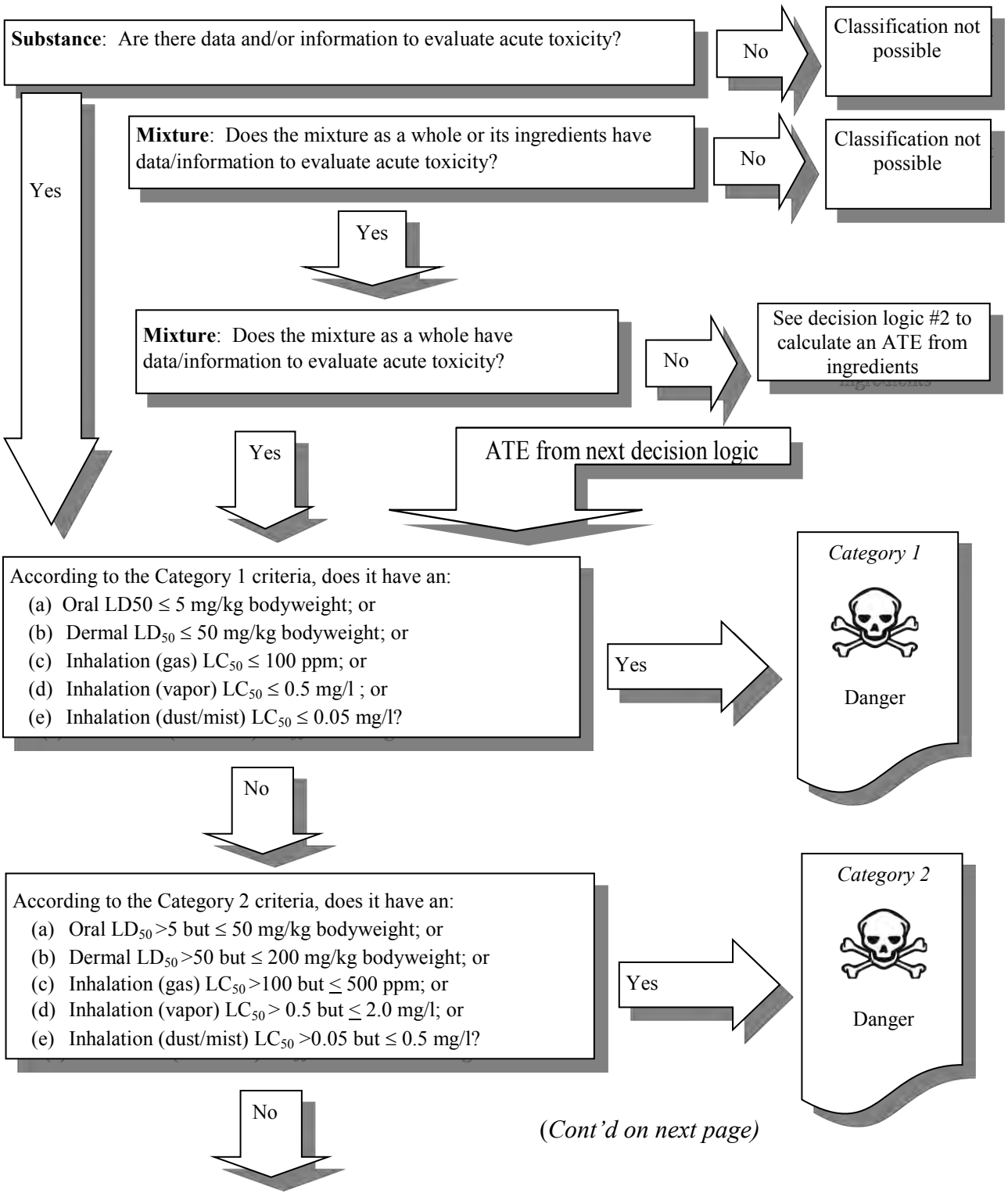
If data are available that indicates acute inhalation toxicity with corrosion of the respiratory tract that leads to lethality, the chemical may be labeled ‘corrosive to the respiratory tract’. The corrosion pictogram (used for skin and eye corrosivity) may be added together with the hazard statement ‘corrosive to the respiratory tract’.

If data are available that indicates acute inhalation toxicity with corrosion of the respiratory tract and the effect **does not** lead to lethality, then the hazard may be addressed in the Specific Target Organ Toxicity hazard classes as explained in Sections VII.8 and VII.9 of this document.

Decision Logic
Two decision logics for classifying *acute toxicity* are provided. The first decision logic is for substances and mixtures where there is test data for the mixture as a whole. The second decision logic is for classifying mixtures according to the bridging principles and classification based on ingredients of the mixture. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

These decision logics are essentially flow charts for classifying substances and mixtures regarding acute toxicity. They present questions in a sequence that walks you through the classification steps and criteria for classifying acute toxicity. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic #1 for acute toxicity



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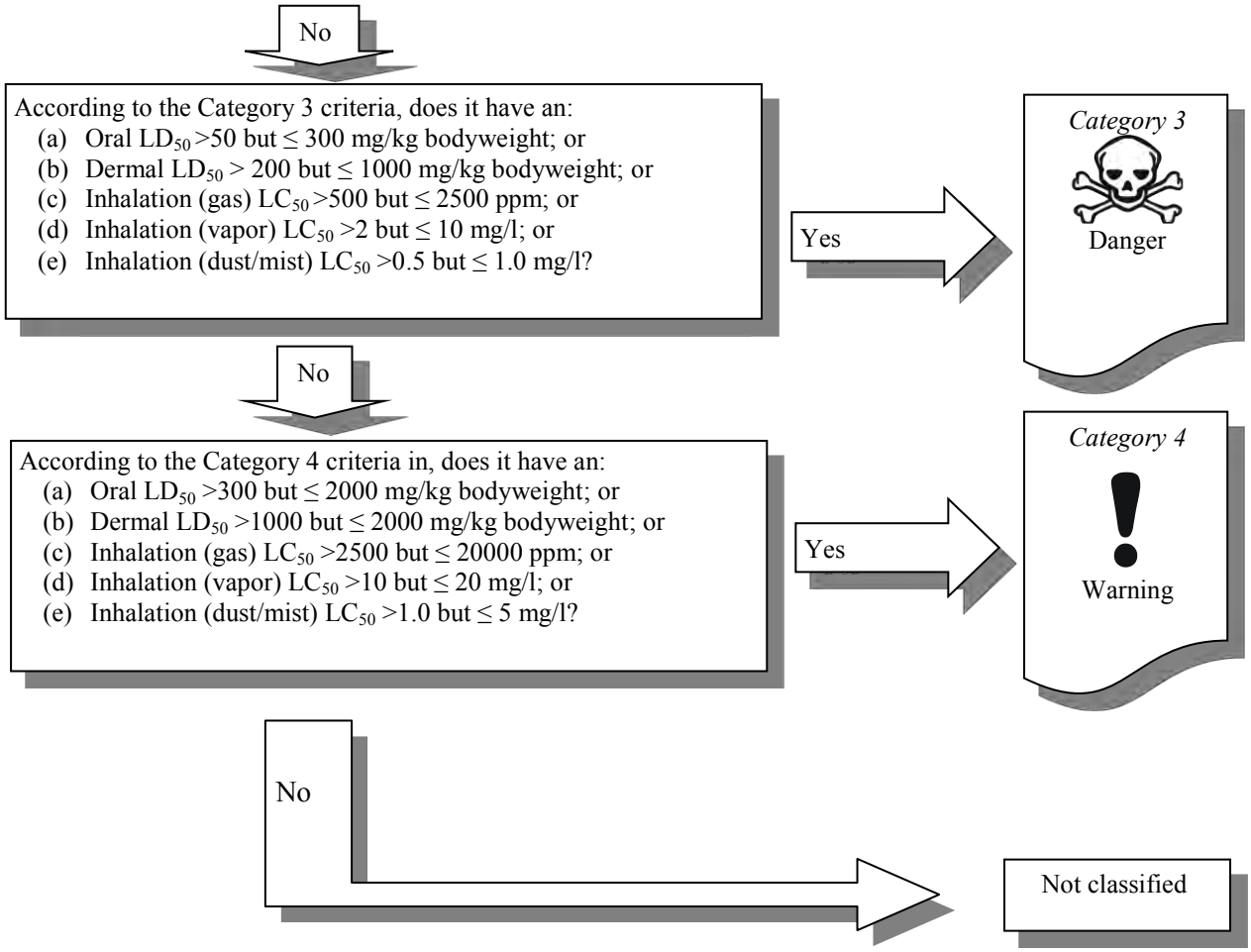

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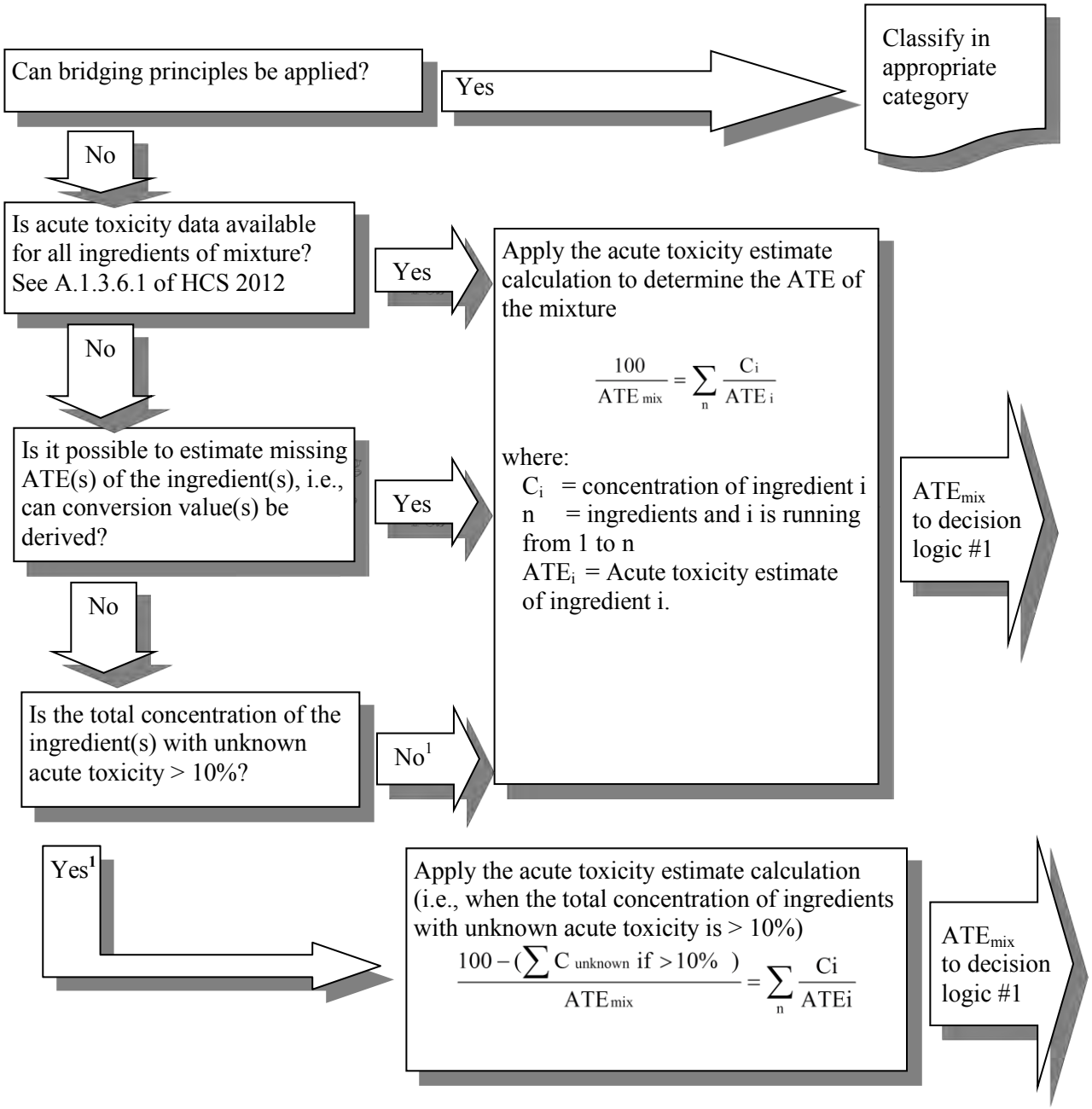
Decision logic #2 for acute toxicity *(see criteria in A.1.3.5 and A.1.3.6 of the HCS (29 CFR 1910.1200))*



[1] In the event that an ingredient without any useable information is used in a mixture at a concentration ≥ 1%, the classification should be based on the ingredients with the known acute toxicity only, and additional statement(s) should identify the fact that x % of the mixture consists of ingredient(s) of unknown acute (oral/dermal/inhalation) toxicity. See the discussion above for additional guidance on presenting information about unknown toxicity. The additional statement(s) must be communicated on the label and in SDS Section 2.

Acute Toxicity Classification Examples

The following examples are provided to demonstrate the acute toxicity calculation and classification process.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 **Acute Toxicity - Corrosive Substance**		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity data: In a GLP-compliant acute toxicity study in rats the following results were observed: At a test dose of 200 mg/kg bw: no mortality, only transient symptoms and no necropsy findings At a test dose of 500 mg/kg: 100% mortality, symptoms: poor general state; necropsy findings: hyperemia in stomach (due to local irritation/corrosivity), no other organs affected	Acute Toxicity Oral Category 4	Since at a dose of 200 mg/kg bw no mortality and only slight transient symptoms without necropsy findings were observed, and at 500 mg/kg bw the high amount/concentration of the corrosive substance caused serious effect only at the site of action and mortality, based on expert judgment it can be assumed that the likely LD_{50} is > 300 mg/kg bw. Therefore, the Acute Toxicity Estimate (ATE) value for classification purpose is between 300 and 500 mg/kg bw, corresponding to Category 4 classification for acute toxicity.

Substance Example #2 **Acute Toxicity Use of Human Data**		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity Data: Animal test data: LD_{50} (rat) > 5,000 mg/kg bw (several values) Human experience: lethal in relatively low dose range (ca. 300-1,000 mg/kg)	Acute Toxicity Oral Category 3	Valid human data from a large data base (case studies) have precedence over animal data; the rat in this case is not the appropriate test species.

Substance Example #3 Acute Toxicity - Dermal		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity Data: Aromatic Amine Animal test data: LD_{50} (rat) > 2,000 mg/kg bw Human experience: many lethal intoxications at relatively low doses after dermal exposure (dose range of 200 to 1000 mg/kg bw)	Acute Toxicity Dermal Category 3	Human experience (valid) has precedence over experimental data; the rat is not an appropriate species for this substance class.

Substance Example #4 Acute Toxicity - Dermal		
Test Data	**HCS 2012 Classification**	**Rationale**
Animal data: A study to evaluate the acute dermal toxicity was performed in rabbits. The following test data results were reported: - At the dose level of 50 mg/kg bw: no mortality was observed - At 200 mg/kg bw: 100% mortality Therefore, LD_{50} was estimated to be between 50 mg/kg bw and 200 mg/kg bw	Acute Toxicity Dermal Category 2	Since the dermal LD_{50} is above 50 mg/kg bw and less than 200 mg/kg bw, Category 2 classification is warranted.

Substance Example #5 Acute Toxicity – Inhalation/dust		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity Data: The acute inhalation toxicity was studied in rats in a GLP-compliant study performed according to OECD test guideline 403. The LC_{50} (1-hr.) = 3 mg/l.	Acute Toxicity Inhalation Category 3	The classification criteria for acute inhalation toxicity refer to a 4-hour exposure time. Therefore to classify a substance, existing inhalation toxicity data generated from 1-hour exposure should be converted accordingly: LC_{50} values with 1hour have to be converted by dividing by 4. The LC_{50} (4-hr.) = 0.75 mg/l which is Category 3.

Substance Example #6 Acute Toxicity – Inhalation/gas		
Test Data	**HCS 2012 Classification**	**Rationale**
Animal data: A GLP-compliant test for acute inhalation toxicity (gaseous form) was performed in accordance with OECD test guideline 403 in rats. The LC_{50} was 4500 ppm/4h.	Acute Toxicity Inhalation Category 4	LC_{50} = 4500 ppm is considered an Acute Toxicity Estimate (ATE) for classification purposes. According to the classification criteria for acute inhalation toxicity for gases, this value corresponds to Category 4.

Substance Example #7 Acute Toxicity – Oral		
Test Data	**HCS 2012 Classification**	**Rationale**
Oral LD_{50} : 300 mg/kg bw (observed in a GLP-compliant study in rats)	Acute Toxicity Oral Category 3	LD_{50} = 300 mg/kg bw is considered an Acute Toxicity Estimate (ATE) for classification purposes; according to the classification criteria for acute oral toxicity, 300 mg/kg bw is the upper value for Category 3. Therefore, it is assigned Category 3 Acute Oral Toxicity classification.

Examples of substances not fulfilling the criteria for classification:

Substance Example #8 Acute Toxicity – Inhalation/Vapors		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity Data: Three values for acute inhalation toxicity of TS10 (vapor form) in rats were described. Two studies were performed in accordance with OECD test guideline 403. One study was determined not to be scientifically valid. The LC_{50} values were reported as follows: LC 50 (4-h): 19 mg/l (not scientifically valid) LC 50 (4-h): 23 mg/l (TG 403) LC 50 (4-h): 28 mg/l (TG 403)	HCS- No Acute Toxicity Classification	With 3 different available LC_{50} values, a validity check proved that the 1st study with 19 mg/l is not scientifically valid in contrast to the two others; thus, with an **ATE> 20 mg/l** the criteria for Category 4 are not fulfilled.

Substance Example #9 Acute Toxicity – Oral		
Test Data	**HCS 2012 Classification**	**Rationale**
Tested in rats in accordance with OECD Test Guideline 423. In a limit test at a value of 2000 mg/kg bw no mortality or signs of toxicity were observed.	No Acute Toxicity classification	There was no mortality nor signs of toxic effects at the outer limit of category 4. Therefore there is no acute toxicity classification.

Substance Example #10 Acute Toxicity – Oral		
Test Data	**HCS 2012 Classification**	**Rationale**
Oral LD_{50} > 2,000 mg/kg (no further details available) Further information from SDS: NOAEL (No Adverse Effect Level) in a 90 day oral study > 3,000 mg/kg bw	No Acute Toxicity classification	Does not fulfill criteria for classification: – Oral LD_{50} > 2,000 mg/kg – At 3,000 mg/kg after daily administration (90 times) of 3,000 mg/kg no adverse health effects (i.e., no toxicity) were observed.

Example of a mixture fulfilling the criteria for classification

Mixture Example #1 **Acute Toxicity – Dermal**		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 5%, Dermal LD_{50} = 40 mg/kg Component 2: 44%, Dermal LD_{50} > 200 < 1,000 Component 3: 48%, Dermal LD_{50} = 90 mg/kg Component 4: 3%, Acute Dermal Toxicity Category 4	Acute Toxicity Dermal Category 2	The LD_{50} data for Components 1 and 3 are used in the $ATE_{mixture}$ calculation since data are available. For Components 1 and 2, apply the guidance in Note (b) to Table A.1.1: – The Dermal LD_{50} > 200 < 1,000 range estimate for Component 2 is converted to the acute toxicity point estimate of 300 mg/kg using Table A.1.2. of the HCS. – The classification category for Component 4 is converted to the acute toxicity point estimate of 1,100 using Table A.1.2. $$\frac{100}{ATE_{mixture}} = \sum_{n} \frac{Ci}{ATEi}$$ $$\frac{100}{ATE_{mixture}} = \frac{5}{40} + \frac{44}{300} + \frac{48}{90} + \frac{3}{1{,}100}$$ Dermal $ATE_{mixture}$ = 123 mg/kg, Category 2

Mixture Example #2 Acute Toxicity – Oral		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 16%, oral LD_{50} = 1,600 mg/kg Component 2: 4%, oral LD_{50} > 200 < 2,000 Component 3: 80%, oral LD_{50} = 3,450 mg/kg	Acute Oral Toxicity Category 4	Per A.1.3.6.1 (a) include ingredients with a known acute toxicity, which fall into any of the acute toxicity categories, or have an oral LD_{50} > 2000 ≤5000 mg/kg body weight. The LD_{50} data for Components 1 and 3 are used in the $ATE_{mixture}$ calculation since data are available. For Component 2, apply the guidance in Note (b) to Table A.1.1: The use of expert judgment is needed to determine what value to use in the $ATE_{mixture}$ calculation for Component 2. The oral LD_{50} > 200 < 2,000 range for Component 2 does not match up with the ranges provided in Table A.1.2. The lower end of the range falls within the Category 3 range of 50 – 300 mg/kg and the converted acute toxicity point estimate for an Oral Category 3 ingredient is 100. Given that the converted point estimate is lower than the experimentally determined value of > 200 mg/kg it does not make sense to use the converted point estimate. In this case, one should apply the known information, and 200 mg/kg should be used in the $ATE_{mixture}$ calculation. $$\frac{100}{ATE_{mixture}} = \sum_{n} \frac{Ci}{ATEi}$$ $$\frac{100}{ATE_{mixture}} = \frac{16}{1{,}600} + \frac{4}{200} + \frac{80}{3{,}450}$$ Oral $ATE_{mixture}$ = 1,880 mg/kg, Category 4

Mixture Example #3 Acute Toxicity – Oral		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 4%, oral LD_{50} = 125 mg/kg Component 2: 92%, No data available Component 3: 3%, oral LD_{50} = 1500 mg/kg Component 4: 0.9%, No data available Component 5: 0.1%, oral LD50 = 10 mg/kg, Oral Category 2	Acute Oral Toxicity Category 3	Components 1 and 3 are included in the $ATE_{mixture}$ calculation because they have data that fall within an acute toxicity category. The total concentration of relevant ingredients with unknown acute toxicity (i.e., Component 2) is 92%. Therefore, the $ATE_{mixture}$ equation that corrects for ingredients with unknown acute toxicity above 10% of the mixture must be used. Component 2 does not have any useable information for the oral route $ATE_{mixture}$ calculation and is in the mixture at a concentration ≥ 1% so an additional statement is included on the label and SDS. The "relevant ingredients" concept means that Component 4 could be excluded from both the $ATE_{mixture}$ calculations. This same reasoning could also apply to Component 5, as it is below the "relevant ingredients" threshold; however, the use of expert judgment is necessary to make this decision for Component 5 as it is classified in Category 2. For this example, since the percentage of this ingredient is well below the 1% threshold (i.e., 0.1%) and the ingredient is classified in Category 2 rather than Category 1, it may be excluded from the ATE calculation. $\frac{100-\left(\sum C_{unknown} if\ >10\%\right)}{ATE_{mixture}}=\sum_{n}\frac{C_i}{ATE_i}$ $\frac{100-(92)}{ATE_{mixture}}=\frac{4}{125}+\frac{3}{1500}$ $ATE_{mixture}$ = 235 mg/kg, Category 3 "92% of the mixture consists of an ingredient of unknown acute oral toxicity."

Mixture Example #4 Acute Toxicity – Multiple Routes				
		Acute toxicity test data		
Components	**Wt%**	**Oral**	**Dermal**	**Inhalation Vapors**
Component 1	26	LD_{50}: 2,737 mg/kg	LD_{50}: 6,480 mg/kg	LC_{50}: 11 mg/l
Component 2	23	LD_{50}: 4,500 mg/kg	LD_{50}:> 6,000 mg/kg	LC_{50}: 19 mg/l
Component 3	11	$LD_{50:}$ > 5,000 mg/kg	No data available	No data available
Component 4	40	LD_{50}: 400 mg/kg	Dermal limit dose > 2,000 mg/kg (No signs of toxicity)	LC_{50}: 4 mg/l

Oral route

$$\frac{100}{ATE_{mixture}} = \sum_{n} \frac{Ci}{ATEi}$$

$$\frac{100}{ATE_{mixture}} = \frac{26}{2{,}737} + \frac{23}{4{,}500} + \frac{40}{400}$$

$ATE_{mixture}$ = 873 mg/kg, Acute Oral Toxicity Category 4

Inhalation route

$$\frac{100 - \left(\sum C_{unknown} \text{ if } > 10\%\right)}{ATE_{mixture}} = \sum_{n} \frac{C_i}{ATE_i}$$

$$\frac{100 - (11)}{ATE_{mixture}} = \frac{26}{11} + \frac{23}{19} + \frac{40}{4}$$

$ATE_{mixture}$ = 6.6 mg/l, Acute inhalation toxicity Category 3 and "11% of the mixture consists of an ingredient of unknown acute inhalation toxicity"

HCS 2012 Classification	Rationale
Acute Oral Toxicity Category 4 Acute Inhalation Toxicity Category 3	Review of the component test data show there is relevant evidence to suggest acute toxicity via the oral and inhalation routes so the $ATE_{mixture}$ calculation was applied to the oral and inhalation routes **Oral route** – Data is available for all ingredients via the oral route – Components 1 and 4 are included in the $ATE_{mixture}$ calculation because they have data that fall within an acute toxicity category – Component 2: per A.1.3.6.1(a) include ingredients with a known acute toxicity, which fall into any of the acute toxicity categories, or have an oral LD_{50} > 2000 ≤5000 mg/kg body weight. – Component 3 is excluded because it does not fall within acute toxicity categories 1-4 and its LD_{50} > 5000 mg/kg. – Apply the guidance in Note (a) to Table A.1.1 for Components 1, 2 and 4 in the $ATE_{mixture}$ calculation since LD_{50} data is available. **Inhalation route** – The total concentration of ingredients with unknown inhalation acute toxicity (i.e., Component 3) is 11%. Therefore, the $ATE_{mixture}$ equation that corrects for ingredients with unknown acute toxicity above 10% of the mixture must be used for the inhalation route. – Components 1, 2 and 4 are included in the $ATE_{mixture}$ calculation because they have data that fall within an acute toxicity category. – Apply the guidance in Note (a) to Table A.1.1 for Components 1, 2 and 4 in the $ATE_{mixture}$ calculation since LD_{50} data is available. – Component 3 does not have any useable information for the inhalation route $ATE_{mixture}$ calculation and is in the mixture at a concentration ≥ 1% so an additional statement is included. **Dermal route** None of the ingredient test data for the dermal route show a LD_{50} < 5000 mg/kg bodyweight and so a dermal $ATE_{mixture}$ calculation was not performed. See A.1.3.6.1(a).

References

29 CFR 1910.1200, Hazard Communication, Appendix A.1 Acute Toxicity.

29 CFR 1910.1200, Hazard Communication. Appendix C, Allocation of Label Elements.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

The Organization for Economic Co-operation and Development (OECD) Guidelines for the Testing of Chemicals.

United States Environmental Protection Agency (EPA) Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Health Effects Test Guidelines.

VII.2 Skin Corrosion/Irritation

Introduction

Changes at the site of first contact (e.g., skin, eye) can be caused regardless of whether a chemical can become systemically available. These changes are considered local effects. Chemicals causing local effects after a single exposure can be further distinguished as irritant or corrosive chemicals, depending on the reversibility of the effects observed.

Corrosive chemicals are those which can destroy living tissues with which they come into contact. In toxicology, the term ”corrosive” normally means causing visible destruction of the skin, eyes, or the lining of the respiratory tract or the gastrointestinal tract on contact. Corrosion is manifested by ulcers, cell death, and scar formation. Generally speaking, corrosive materials have a very low pH (acids) or a very high pH (bases). Strong bases are usually more corrosive than acids. Examples of corrosive materials are sodium hydroxide (lye) and sulfuric acid.

Irritant chemicals are non-corrosive chemicals which, through immediate contact with the tissue under consideration, may cause inflammation. Dermal irritation is a skin reaction resulting from a single or multiple exposures to a physical or chemical entity at the same site, characterized by the presence of inflammation.

The difference between an irritant and a corrosive is the ability of the body to repair the tissue reaction. With irritants, the inflammatory reaction can be reversed, whereas with corrosive damage it is permanent and irreparable.

Appendix A.2 of the HCS addresses the classification of those chemicals which present a corrosion or irritation hazard to the skin.

General Considerations

Classification for skin corrosion/irritation should be conducted using a tiered weight-of-evidence approach. In the tiered approach, emphasis should be placed upon existing human data, followed by existing animal data, followed by *in vitro* data, and then other sources of information. Classification results directly when the data satisfy the criteria. However, in some cases, classification of a substance or a mixture is made on the basis of the weight of evidence within a tier. If no decision can be made about classification after following the tiered approach, then a total weight-of-evidence approach to classification should be used. In a total weight-of-evidence approach all available information bearing on the determination of skin corrosion/irritation is considered together, including the results of appropriate validated *in vitro* tests, relevant animal data, and human data, such as epidemiological and clinical studies and well-documented case reports and observations.

Classification Criteria for Substances

There are two categories assigned for skin effects in the HCS. In addition, the category for skin corrosion is subdivided into three subcategories according to specific criteria outlined below.

(a) Category 1 (skin corrosion)
This category is further divided into three sub-categories (1A, 1B and 1C)

(b) Category 2 (skin irritation)

Classification criteria for substances using animal test data

Skin Corrosion (Category 1)

Skin corrosion is the production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test substance for up to 4 hours. Corrosive reactions are typified by ulcers, bleeding, bloody scabs, and, by the end of observation at 14 days, by discoloration due to blanching of the skin, complete areas of alopecia, and scars. Histopathology should be considered to evaluate questionable lesions.

A substance is classified as corrosive to skin when it produces destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least one tested animal after exposure for up to 4 hours.

Table VII.2.1. Skin corrosion category and sub-categories

Category	Criteria
Category 1	Destruction of skin tissue, namely, visible necrosis through the epidermis and into the dermis, in at least one tested animal after exposure ≤ 4 hours
Sub-category 1A	Corrosive responses in at least one animal following exposure ≤ 3 minutes during an observation period ≤ 1 hour
Sub-category 1B	Corrosive responses in at least one animal following exposure > 3 minutes and ≤ 1 hour and observations ≤ 14 days
Sub-category 1C	Corrosive responses in at least one animal after exposures > 1 hour and ≤ 4 hours and observations ≤ 14 days

Skin Irritation (Category 2)

Skin irritation is the production of reversible damage to the skin following the application of a test substance for up to 4 hours.

Animal irritant responses within a test can be variable, as they are with corrosion. A separate irritant criterion accommodates cases where there is a significant irritant response but less than the mean score criterion for a positive test. For example, a test material might be designated as

an irritant if at least 1 of 3 tested animals shows a very elevated mean score throughout the study, including lesions persisting at the end of an observation period (normally 14 days). Other responses could also fulfill this criterion. However, it should be ascertained that the responses are the result of chemical exposure. Addition of this criterion increases the sensitivity of the classification system.

Reversibility of skin lesions is another consideration in evaluating irritant responses. When inflammation persists to the end of the observation period in two or more test animals, taking into consideration alopecia (limited area), hyperkeratosis, hyperplasia, and scaling, then a chemical should be considered to be an irritant.

The classification criteria for skin irritation (Category 2) are presented in Table VII.2.2. The major criterion for the irritation category is that at least 2 of 3 tested animals have a mean score of ≥ 2.3 and ≤ 4.0.

Table VII.2.2. Skin irritation categories [a, b]

Categories	Criteria
Irritation (Category 2)	(1) Mean score of ≥ 2.3 and ≤ 4.0 for erythema/eschar or for edema in at least 2 of 3 tested animals from gradings at 24, 48 and 72 hours after patch removal or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions; or (2) Inflammation that persists to the end of the observation period (normally 14 days) in at least 2 animals, particularly taking into account alopecia (limited area), hyperkeratosis, hyperplasia, and scaling; or (3) In some cases where there is pronounced variability of response among animals, with very definite positive effects related to chemical exposure in a single animal but less than the criteria above.

[a] Grading criteria correspond to those described in OECD Test Guideline 404.
[b] Criteria for evaluation of a 4, 5 or 6-animal study are provided below under the heading "Guidance on evaluation of data from studies with more than three animals."

Classification in a tiered approach

A *tiered approach* to the evaluation of initial information should be considered, where applicable (Figure VII.2.1), recognizing that not all elements in the approach may be relevant.

The tiered approach explains how to organize existing information on a substance and to make a weight-of-evidence decision about hazard assessment and hazard classification (ideally without conducting new animal tests). Although information might be gained from the evaluation of single parameters within a tier, consideration should be given to the totality of existing information and making an overall weight-of-evidence determination. This is especially true when there is information available on some but not all parameters. Emphasis should be placed

upon existing human experience and data, followed by animal experience and data, followed by other sources of information, but case-by-case determinations are necessary.

Existing human and animal data including information from single or repeated exposure is the first line of evaluation, as they give information directly relevant to effects on the skin.

Acute dermal toxicity data must be considered for classification if available. If a substance is highly toxic by the dermal route, a skin corrosion/irritation study may not be practicable since the amount of test substance to be applied would considerably exceed the toxic dose and, consequently, would result in the death of the animals. When observations are made of skin corrosion/irritation in acute toxicity studies and are observed up through the limit dose, these data must be used for classification provided that the dilutions used and species tested are equivalent. Solid substances (powders) may become corrosive or irritant when moistened or in contact with moist skin or mucous membranes.

In vitro alternatives that have been validated and accepted must be used to make classification decisions.

Likewise, pH extremes such as ≤ 2 and ≥ 11.5 may indicate skin effects, especially when associated with significant acid/alkaline reserve (buffering capacity).[9] Generally, such substances are expected to produce significant effects on the skin. In the absence of any other information, a substance is considered corrosive (Skin Category 1) if it has a pH ≤ 2 or ≥ 11.5. However, if consideration of acid/alkaline reserve suggests the substance may not be corrosive despite the low or high pH value, this needs to be confirmed by other data, preferably by data from an appropriate validated *in vitro* test.

In some cases sufficient information may be available from structurally related substances to make classification decisions.

[9] For further information concerning acid/alkaline reserve, see (1) Young et al, 1988, "Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without test on animals," *Toxicology in Vitro* 2, 19-26 and (2) Young and How, 1994, "Product classification as corrosive or irritant by measuring pH and acid / alkali reserve," *Alternative Methods in Toxicology vol. 10 - In Vitro Skin Toxicology: Irritation, Phototoxicity, Sensitization,* 23-27.

Figure VII.2.1:

Tiered evaluation for skin corrosion and irritation			
Step	**Parameter**	**Finding**	**Conclusion**
1a:	Existing human or animal skin corrosion/irritation data [a] → ↓ Not corrosive/No data ↓	Skin corrosive →	**Category 1** [b]
1b:	Existing human or animal skin corrosion/irritation data [a] → ↓ Not irritant/No data ↓	Skin irritant →	**Category 2** [b]
1c:	Existing human or animal skin corrosion/irritation data [a] → ↓ No/Insufficient data ↓	Not a skin corrosive or skin irritant →	**Not classified**
2:	Other, existing skin data in animals [c] → ↓ No/Insufficient data ↓	Yes; other existing data showing that substance may cause skin corrosion or skin irritation →	**Category 1** [b] or **Category 2** [b]
3:	Existing *ex vivo/in vitro* data [d] → ↓ No/Insufficient data/Negative response ↓	Positive: Skin corrosive → ↘ Positive: Skin irritant →	**Category 1** [b] **Category 2** [b]
4:	pH-Based assessment (with consideration of acid/alkaline reserve of the chemical) [e] → ↓ Not pH extreme, no pH data or extreme pH with data showing low/no acid/alkaline reserve ↓	pH ≤ 2 or ≥ 11.5 with high acid/alkaline reserve or no data for acid/alkaline reserve →	**Category 1**
5:	Validated Structure Activity Relationship (SAR) methods → ↓ No/Insufficient data ↓	Skin corrosive → ↘ Skin irritant →	**Category 1** [b] **Category 2** [b]

Tiered evaluation for skin corrosion and irritation			
Step	**Parameter**	**Finding**	**Conclusion**
6:	Consideration of the total weight-of-evidence [f] →	Skin corrosive →	**Category 1** [b]
	↓ ↘	Skin irritant →	**Category 2** [b]
7:	**Not classified**		

[a] Existing human or animal data could be derived from single or repeated exposure(s), for example in occupational, consumer, transport, or emergency response scenarios; from ethically conducted human clinical studies; or from purposely generated data from animal studies conducted according to validated and internationally accepted test methods. Although human data from accident or poison center databases can provide evidence for classification, absence of incidents is not itself evidence for no classification.

[b] Classify in the appropriate category/sub-category, as shown in Tables VII.2.1 and VII.2.2.

[c] All existing animal data should be carefully reviewed to determine if sufficient skin corrosion/irritation evidence is available. In evaluating such data, however, the reviewer should bear in mind that the reporting of dermal lesions may be incomplete, testing and observations may be made on a species other than the rabbit, and species may differ in sensitivity in their responses.

[d] Evidence from studies using scientifically validated protocols with isolated human/animal tissues or other, non-tissue-based, though scientifically validated, protocols should be assessed. Examples of scientifically validated test methods for skin corrosion include OECD Test Guidelines 430 (Transcutaneous Electrical Resistance Test), 431 (Human Skin Model Test), and 435 (Membrane Barrier Test Method). An example of a scientifically validated *in vitro* test method for skin irritation is OECD Test Guideline 439 (Reconstructed Human Epidermis Test Method).

[e] Measurement of pH alone may be adequate, but assessment of acid or alkali reserve (buffering capacity) would be preferable. Presently, there is no scientifically validated and internationally accepted method for assessing this parameter.

[f] All information that is available should be considered and an overall determination made on the total weight of evidence. This is especially true when there is conflict in information available on some parameters. Professional judgment should be exercised prior to making such a determination. Negative results from applicable validated skin corrosion/irritation *in vitro* tests are considered in the total weight of evidence evaluation.

Classification criteria for mixtures

It should be noted that the classification criteria for the health hazards of mixtures usually include a tiered scheme (i.e., stepwise procedure based on a hierarchy principle) in which test data available on the complete mixture are considered as the first tier in the evaluation, followed by the applicable bridging principles, and lastly, cut-off values/concentration limits or additivity.

Tier 1: Classification of mixtures when data are available for the complete mixture

When skin corrosion/irritation test data on the mixture itself is available, this data should be used to classify the mixture using the criteria for substances, taking into account the tiered weight-of-evidence illustrated in Figure VII.2.1.

When considering testing of the mixture, classifiers should use a tiered weight-of-evidence approach as included in the criteria for classification of substances for skin corrosion and irritation to help ensure an accurate classification. In the absence of any other information, a mixture is considered corrosive (Skin Category 1) if it has a pH ≤ 2 or a pH ≥ 11.5. However, if

consideration of acid/alkaline reserve suggests the mixture may not be corrosive despite the low or high pH value, then further evaluation may be necessary.

If appropriate test data for the mixture is not available, then the classifier must consider the application of the Bridging Principle criteria in Tier 2, if appropriate, or use the classification resulting from the application of criteria in Tier 3.

Tier 2: Classification of mixtures when data are not available for the complete mixture – bridging principles

Where the mixture itself has not been tested to determine its skin corrosion/irritation potential, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data are used in accordance with the below bridging principles.

The bridging principles applicable to the skin corrosion/irritation hazard class include:

- Dilution,
- Batching,
- Concentration of mixtures,
- Interpolation within one toxicity category,
- Substantially similar mixtures,
- Aerosols.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential skin corrosion/irritation hazard.

Dilution

If a tested mixture is diluted with a diluent which has an equivalent or lower skin corrosivity/irritancy classification than the least corrosive/irritant original ingredient and which is not expected to affect the corrosivity/irritancy of other ingredients, then the new diluted mixture must be classified as equivalent to the original tested mixture.

Batching

The skin corrosion/irritation potential of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the skin corrosion/irritation potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures

If a tested mixture classified in the highest sub-category for skin corrosion is concentrated, the more concentrated untested mixture must be classified in the highest corrosion sub-category without additional testing. If a tested mixture classified for skin irritation

(Category 2) is concentrated and does not contain skin corrosive ingredients, the more concentrated untested mixture should be classified for skin irritation (Category 2) without additional testing.

Interpolation within one hazard category
For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same skin corrosion/irritation hazard category, and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has concentrations of toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same skin corrosion/irritation category as A and B.

Substantially similar mixtures
Given the following:

(a) Two mixtures: (i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on skin corrosion/irritation for A and C are available and substantially equivalent, i.e., they are in the same hazard category and are not expected to affect the skin corrosion/irritation potential of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Aerosols

An aerosol form of a mixture must be classified in the same hazard category as the tested non-aerosolized form of the mixture provided that the added propellant does not affect the skin corrosion/irritation properties of the mixture upon spraying.

If appropriate data is not available to apply the above bridging principles then the classifier applies the criteria in Tier 3.

Tier 3: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

Cut-off values/concentration limits: Additivity

In general, the approach to classifying a mixture for skin corrosion/irritation in Tier 3 is based on the theory of additivity where each corrosive or irritant ingredient is considered to contribute to the overall corrosive or irritant properties of the mixture. The ingredients are summed in proportion to their concentration and potency (i.e., corrosives carry more weight in the irritation calculations).

Table VII.2.3 provides the cut-off value/concentration limits to be used to determine if the mixture is considered to be corrosive or irritant to the skin. Three potential additivity calculations are given in the first column. Each equation has specific concentration cut-offs that will trigger the classification specified in columns 2 and 3, which correspond to Category 1 and Category 2, respectively.

To better illustrate the order in which the calculations should be evaluated, an arrow has been added to the table. Following the arrow, the first calculation that exceeds the percentage cut-off trigger determines which classification is assigned to the mixture. If none of the sums exceed the cut-off triggers, then the mixture is not classified.

Table VII.2.3. Concentration of ingredients of a mixture classified as skin Category 1 or 2 that would trigger classification of the mixture as hazardous to skin (Category 1 or 2)

	Concentration triggering classification of a mixture as:	
	Skin corrosive	**Skin irritant**
Sum of ingredients classified as:	**Category 1** (see note below)	**Category 2**
Skin Category 1	≥ 5%	≥ 1% but < 5%
Skin Category 2		≥ 10%
(10 × Skin Category 1) + Skin Category 2		≥ 10%

The Four Skin Corrosion/Irritation Mixture Additivity Calculations

There are four possible calculations that may need to be performed to determine if the mixture should be classified.

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
	Skin corrosive	**Skin irritant**
	Category 1	**Category 2**
Skin Category 1	≥ 5% (1)	≥ 1% but < 5% (2)
Skin Category 2		≥ 10% (3)
(10 × Skin Category 1) + Skin Category 2		≥ 10% (4)

Skin corrosion Category 1 classification calculation:

(1) Add the percentages of all ingredients classified as Skin Category 1.
If the sum is ≥ 5% the mixture is classified as Category 1 Skin Corrosion.
∑ % Skin Category 1 ingredients ≥ 5%

Skin irritation Category 2 classification calculations:

For Category 1 ingredients:
(2) Add the percentages of all ingredients classified as Skin Category 1.
If the sum is ≥ 1% but < 5%, the mixture is classified as Category 2 Skin Irritation.
∑ % Skin Category 1 ingredients ≥ 1% but < 5%

For Category 2 ingredients:
(3) Add the percentages of all ingredients classified as Skin Category 2.
If the sum is ≥ 10%, the mixture is classified as Category 2 Skin Irritation.
∑ % Skin Category 2 ingredients ≥ 10%

For Category 1 & 2 ingredients:
(4) First add the percentages of all ingredients classified as Skin Category 1 and multiply that number by the weighting factor of 10.

Then add the percentages of all ingredients classified as Skin Category 2.

Add these two numbers together. If the sum is ≥ 10%, the mixture is classified as Category 2 Skin Irritation.

(10 × (∑ % Skin Cat 1 ingredients)) + ∑ % Skin Cat 2 ingredients ≥ 10%

Shortcut Skin Corrosion/Irritation Mixture Additivity Calculations

Shortcut
For those doing the calculations manually, a shortcut that leads to the same classification is to only do the worst-case calculations for the Corrosive Category 1 classification and the Skin Irritation Category 2 classification. In the shortcut there are only two calculations. The first sum that exceeds the percentage cut-off trigger determines which classification is assigned to the mixture. If neither exceeds the cut-off triggers then the mixture is not classified.

	Concentration triggering classification of a mixture as:	
	Skin corrosive	**Skin irritant**
Sum of ingredients classified as:	**Category 1**	**Category 2**
Skin Category 1	≥ 5%	≥ 1% but < 5%
Skin Category 2		≥ 10%
(10 × Skin Category 1) + Skin Category 2		≥ 10%

Skin corrosion Category 1 classification calculation:

(1) Add the percentages of all ingredients classified as of Skin Category 1.
If the sum is ≥ 5% the mixture is classified as Category 1 Skin Corrosion.
∑ % Skin Category 1 ingredients ≥ 5%

Shortcut Skin irritation Category 2 classification calculation:

For Category 1 & 2 ingredients:

(4) Add the percentages of all ingredients classified as of Skin Category 1 and multiply that sum by the weighting factor of 10.

Then add the percentages of all ingredients classified as of Skin Category 2.

Add these two numbers together. If the sum is ≥ 10%, the mixture is classified as Category 2 Skin Irritation.

(10 × (∑ % Skin Cat 1 ingredients)) + ∑ % Skin Cat 2 ingredients ≥ 10%

Cut-off values/concentration limits: when the additivity approach does not apply
Particular care must be taken when classifying certain types of chemicals such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants. The additivity approach might not work because many such substances are corrosive or irritant at concentrations < 1%, and the additivity approach may underestimate the overall corrosive or irritant properties of the mixture.

For mixtures containing strong acids or bases, the pH should be used as the classification criterion since pH will be a better indicator of corrosion than the concentration limits in Table VII.2.3. A mixture containing corrosive or irritant ingredients that cannot be classified based on the additivity approach shown in Table VII.2.3, due to chemical characteristics that make this approach unworkable, should be classified using the more conservative cut-off/concentration limit approach summarized below:

- Mixture is Skin Category 1 if it contains ≥ 1% of a corrosive Category 1 ingredient, and
- Mixture is Skin Category 2 if it contains ≥ 3% of an irritant ingredient.

The cut-off value/concentration limits approach is summarized in HCS Table A.2.4.

Table VII.2.4. Concentration of ingredients of a mixture when the additivity approach does not apply, that would trigger classification of the mixture as hazardous to skin

Ingredient:	Concentration	Mixture classified as: Skin
Acid with pH ≤ 2	≥ 1%	Category 1
Base with pH ≥ 11.5	≥ 1%	Category 1
Other corrosive (Category 1) ingredients for which additivity does not apply	≥ 1%	Category 1
Other irritant (Category 2) ingredients for which additivity does not apply, including acids and bases	≥ 3%	Category 2

Cut-off values/concentration limits: Important Points to Consider
To ensure consistent application of both the additivity and cut-off/concentration limit approaches for purposes of classifying the skin corrosion/irritation hazards of mixtures, the following principles need to be applied where appropriate:

- **Classification Above or Below Cut-Off Values/Concentration Limits**
  On occasion, reliable data may show that the skin corrosion/irritation of an ingredient will not be evident when present at a level above the concentration limits/cut-off values mentioned in Tables VII.2.3 and VII.2.4. In these cases, the mixture could be classified according to those data (see also 29 CFR 1910.1200 A.0.4.3). On occasion, when it is expected that the skin corrosion/irritation of an ingredient will not be evident when present at a level above the concentration cut-off values mentioned in Tables VII.2.3 and VII.2.4, testing of the mixture may be considered. If testing is not performed, the tiered weight-of-evidence approach for skin corrosion/irritation should be used.

  If there are data showing that (an) ingredient(s) may be corrosive or irritant to skin at a concentration of < 1% (corrosive) or < 3% (irritant), the mixture should be classified accordingly.

- **“Relevant Ingredient” Concept**
  For the purpose of applying the cut-off values in Tables VII.2.3 and VII.2.4, only “relevant ingredients” need to be included in the calculation.

  The “relevant ingredients” of a mixture are those which are present in concentrations ≥ 1% (w/w for solids, liquids, dusts, mists, and vapors and v/v for gases), unless there is a presumption (e.g., in the case of corrosive ingredients) that an ingredient present at a concentration < 1% can still be relevant for classifying the mixture for skin corrosion/irritation. If the classifier suspects that the ingredient could be relevant for classifying the mixture at < 1%, then the classifier must use expert judgment to determine at what concentration below 1% the corrosive Category 1 ingredient(s) should be included in the calculation.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

In classification the data are compared to the skin corrosion/irritation classification criteria. If valid data on skin irritation/corrosion of a substance or mixture are available, these data should be used for classification. To find the necessary data, a classifier is advised to try the following:

- ask the manufacturer or supplier for the skin irritation/corrosion data for the product; or
- check if the skin irritation/corrosion data is available in the SDS or any other documentation accompanying the product; or
- find the data available in the open literature, if the chemical identity of the product is known (for a single-component chemical).

Data that are generated in accordance with recognized scientific principles are acceptable under the HCS.

Examples of scientifically validated test methods
Methods that use recognized scientific principles for investigation of skin corrosion/irritation effects include:

- OECD Test Guideline 404: Acute Dermal Irritation/Corrosion
- OECD Test Guideline 430: *In Vitro* Skin Corrosion: Transcutaneous Electrical Resistance Test (TER)
- OECD Test Guideline 431: *In Vitro* Skin Corrosion: Human Skin Model Test
- OECD Test Guideline 435: *In Vitro* Skin Corrosion: Membrane Barrier Test Method
- OECD Test Guideline 439: *In Vitro* Skin Irritation: Reconstructed Human Epidermis Test Method
- USEPA OTS code: 798.4470;
- USEPA OPP code: 81-5;
- USEPA OPPTS code: 870.2500;
- EEC Directive 92/32/EEC (B.4).

In the *in vivo* test, the substance is applied in a single dose to the skin of an experimental animal (usually a healthy young albino rabbit) while untreated skin areas of the test animal serve as the control. In the *in vitro* test, the assessment of corrosivity is not carried out in live animals. Transcutaneous Electrical Resistance (TER) is a measure of the electrical impedance of the skin, as a resistance value in kilo Ohms. In the *In Vitro* Human Skin Model Test, the test material is applied topically to a three-dimensional human skin model, comprising at least a reconstructed epidermis with a functional stratum corneum.

Guidance on evaluation of data from studies with more than three animals
The classification criteria for skin corrosion/irritation are given in terms of a 3-animal test. Some older test methods may have used up to 6 animals. However, the skin corrosion/irritation criteria do not specify how to classify based on existing data from tests with more than 3 animals.

Criteria for evaluation of a 4, 5 or 6-animal study are provided in the paragraphs below, depending on the number of animals tested. Scoring for erythema/eschar and edema is performed at 24, 48 and 72 hours after exposure or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions.

In the case of a study with 6 animals the following principles apply:

(a) The substance or mixture is classified as skin corrosion Category 1 if destruction of skin tissue (that is, visible necrosis through the epidermis and into the dermis) occurs in at least one animal after exposure up to 4 hours in duration;

(b) The substance or mixture is classified as skin irritation Category 2 if at least 4 out of 6 animals show a mean score per animal of $\geq$ 2.3 and $\leq$ 4.0 for erythema/eschar or for edema.

In the case of a study with 5 animals the following principles apply:

(a) The substance or mixture is classified as skin corrosion Category 1 if destruction of skin tissue (that is, visible necrosis through the epidermis and into the dermis) occurs in at least one animal after exposure up to 4 hours in duration;

(b) The substance or mixture is classified as skin irritation Category 2 if at least 3 out of 5 animals show a mean score per animal of $\geq$ 2.3 and $\leq$ 4.0 for erythema/eschar or for edema.

In the case of a study with 4 animals the following principles apply:

(a) The substance or mixture is classified as skin corrosion Category 1 if destruction of skin tissue (that is, visible necrosis through the epidermis and into the dermis) occurs in at least one animal after exposure up to 4 hours in duration;

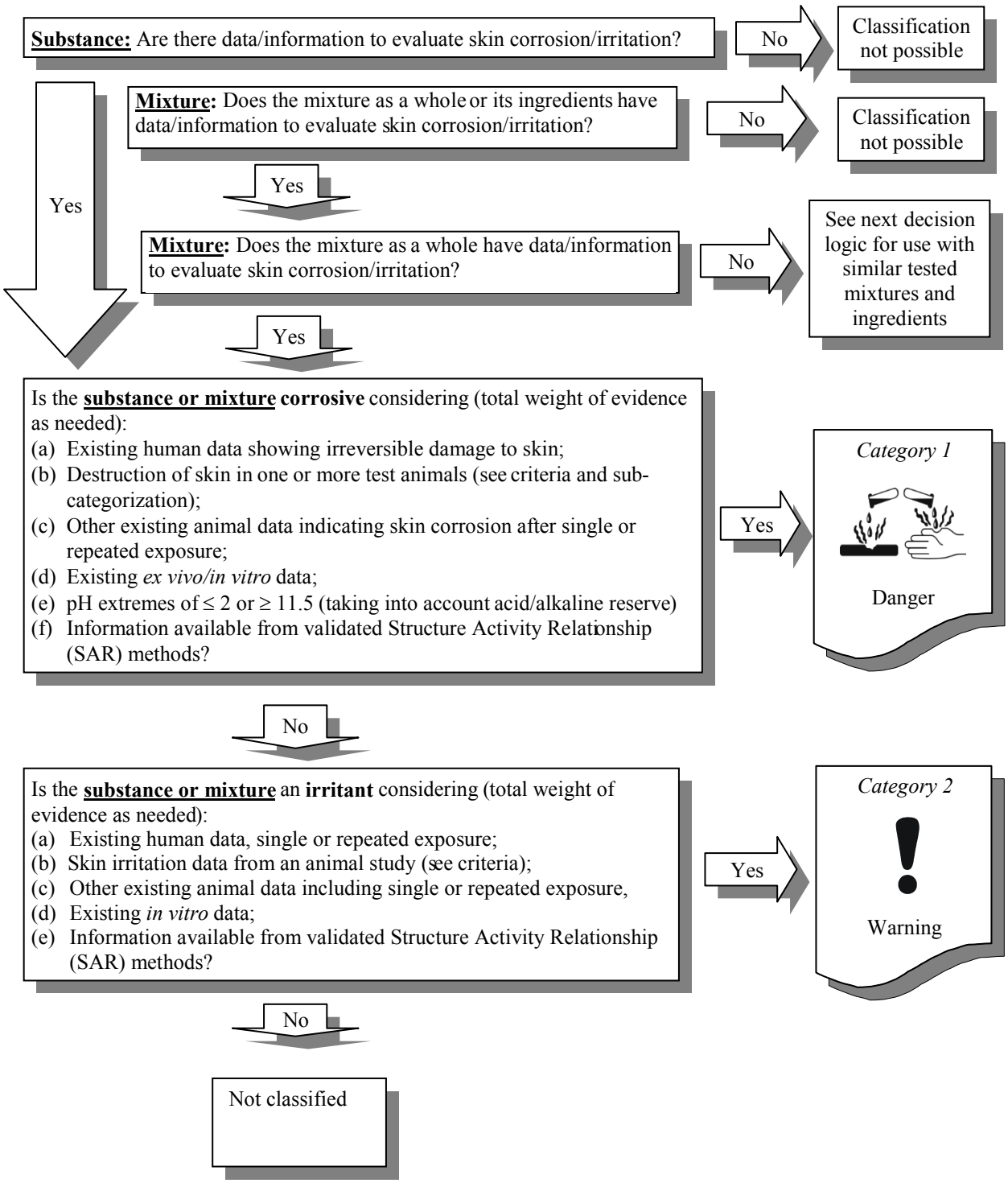
(b) The substance or mixture is classified as skin irritation Category 2 if at least 3 out of 4 animals show a mean score per animal of ≥ 2.3 and ≤ 4.0 for erythema/eschar or for edema.

Decision logic

Two decision logics for classifying *Skin Corrosion/Irritation* are provided. The first decision logic is for substances and for mixtures with data on the mixture as a whole. Use the second decision logic for classifying mixtures on the basis of information/data on similar tested mixtures and/or ingredients. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

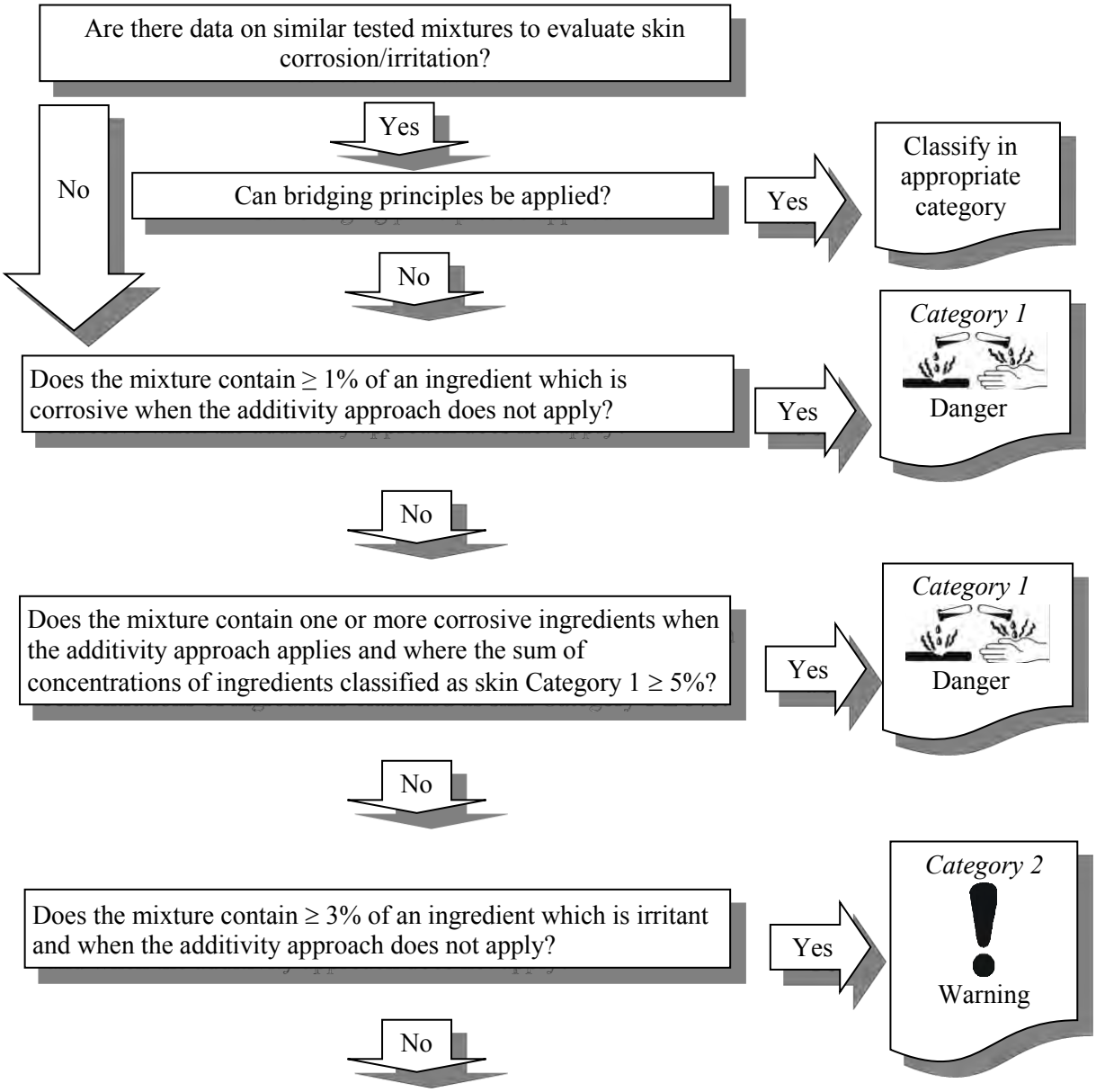
These decision logics are essentially flow charts for classifying substances and mixtures regarding skin corrosion/irritation. They present questions in a sequence that walks you through the classification steps and criteria for classifying skin corrosion/irritation. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic for skin corrosion/irritation



Mixtures decision logic for skin corrosion/irritation

Classification of mixtures on the basis of information/data on similar tested mixtures and/or ingredients



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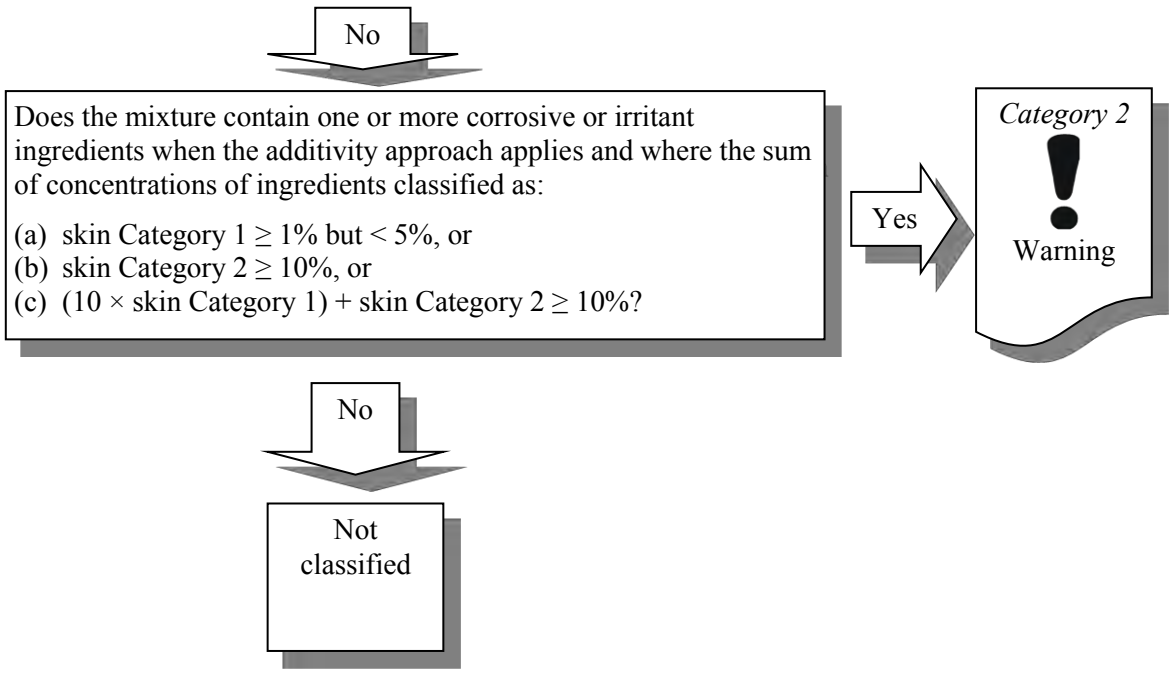


Skin Corrosion/Irritation Classification Examples

The following examples are provided to walk you through the skin corrosion/irritation calculation and classification processes.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 Skin Irritation		
Test Data	**HCS 2012 Classification**	**Rationale**
According to OECD Test Guideline 404 test substance was applied for 1 hour and three minutes. No scars or other irreversible effects were found. The scoring results obtained after 4 hours application time are – Erythema/Eschar: 2.7, 3, 0.66 – Edema: 1.7, 2, 1	Skin Irritant Category 2	Fulfills criteria – The classification is made on the basis of 2 of 3 animals exceeding a 2.3 mean score for erythema.

Substance Example #2 Skin Corrosion		
Test Data	**HCS 2012 Classification**	**Rationale**
In OECD Test 404 full necrosis/irreversible skin damage after 4-hour exposure within 14 days were observed in one animal	Skin Corrosion Category 1C	Fulfills criteria – According to the classification criteria the production of irreversible damage to the skin after 4-hour exposure in at least one animal warrants classification in Category 1C.

Substance Example #3 Skin Corrosion		
Test Data	**HCS 2012 Classification**	**Rationale**
The material is a new aliphatic tertiary amine. No data is available. The test substance has Structure Activity Relationships (SAR) to substances with similar structure known to be corrosive.	Skin Corrosion Category 1	Using expert judgment and SAR information the classifier of this mixture concluded that Category 1 is justified, since there is much information indicating that aliphatic amines are corrosive. According to the criteria, the classifier of this mixture concluded that classification as corrosive Category 1 is warranted.

Substance Example #4 Skin Irritation		
Test Data	**HCS 2012 Classification**	**Rationale**
OECD Test Guidelines 404 test results: – Erythema/Eschar: mean value 2.2 (in 2 of 3 animals) – Edema: 2.4 (in all animals)	Skin Irritation Category 2	Fulfills criteria – The criteria for Category 2 classification are fulfilled, since the mean value for edema over 24, 48, and 72 hours in 2 of 3 animals is > 2.3.

Examples of mixtures fulfilling the criteria for classification:

Mixture Example #1 Skin Corrosion/Irritation		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 4%, Skin Category 1, pH = 1.8 Component 2: 5%, Skin Category 2 Component 3: 5%, not classified Component 4: 86%, No data available Mixture pH = 4.0	Skin Corrosion Category 1	For this mixture, the classification was assigned as a Category 1 because component 1 (Category 1) is in the mixture at ≥ 1% Rationale: – The overall mixture pH of 4.0 does not result in classification in Category 1 since this does not fall within the criteria of pH ≤ 2 or pH ≥ 11.5 – Component 1 with a pH = 1.8 is an ingredient for which additivity might not apply. Expert judgment would be needed to determine whether or not additivity applies. Knowledge of the components is important. Given the limited information in this example, the classifier of this mixture chose to apply non-additivity for a conservative approach. Without information on the mode of action of component 1, the mixture could be corrosive regardless of the overall pH. Therefore, the criteria described in 29 CFR 1910.1200 paragraph A.2.4.3.4 were applied (i.e., "A mixture containing corrosive or irritant ingredients that cannot be classified based on the additivity approach shown in [Table VII.2.3], due to chemical characteristics that make this approach unworkable, should be classified as Skin Category 1 if it contains ≥ 1% of a corrosive ingredient and as Skin Category 2 when it contains ≥ 3% of an irritant ingredient").

Mixture Example #2 Skin Corrosion/Irritation		
Data	**HCS 2012 Classification**	**Rationale**
Tested mixture information Animal 1: Mean Erythema/eschar 3.8, Mean Edema: 2.5 Animal 2: Mean Erythema/eschar 3.5, Mean Edema: 2.9 Animal 3: Mean Erythema/eschar 4.0, Mean Edema: 3.2 Based on the test data the mixture is classified as Skin Irritant Category 2. The tested mixture is aerosolized using a 50/50 mixture of propane/butane as the propellant. *Aerosolized untested mixture information* Component 1: 50%, Tested mixture = Skin Category 2 Component 2: 25%, Liquefied propane Component 3: 25%, Liquefied butane	Skin Irritation Category 2	Applying the aerosols bridging principle, the aerosolized untested mixture can be classified as Skin Irritant Category 2 without additional testing. Rationale: – Classification via application of bridging principles can be considered since there are sufficient data on both the individual ingredients and a similar tested mixture – The aerosols bridging principle can be applied because: (i) The non-aerosolized mixture has been tested, and (ii) The propellant (i.e., 50/50 mixture of liquefied propane/butane) is not corrosive or an irritant, and (iii) The propellant will not affect the irritation properties of the mixture upon spraying.

Mixture Example #3 Skin Corrosion/Irritation		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 91%, no data available Component 2: 5%, Skin Category 2 Component 3: 3%, Skin Category 2 Component 4: 0.9%, Skin Category 1 Component 5: 0.1%, no data available	Skin Irritation Category 2	Use equations from Table VII.2.3 **Category 1 calculation:** a) ∑%Skin Category 1 = 0.9 which is not ≥ 5% **Category 2 calculations:** b) ∑%Skin Category 1= 0.9 which is not ≥ 1% but < 5% c) ∑%Skin Category 2 = 5 + 3 = 8 which is not ≥ 10% d) ∑(10 x %Skin Category 1) + ∑%Skin Category 2 = (10 x 0.9) + (5 + 3) = 17 which is ≥ 10% Rationale – Classification of the mixture based on ingredient data can be considered – In the exercise of expert judgment in applying the "relevant ingredient" concept, the classifier took a conservative approach since component 4 (Skin Category 1) is only slightly below 1% (i.e., 0.9%) and application of the additivity approach includes a weighting factor for Category 1 ingredients.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.2 Skin Corrosion/Irritation.

29 CFR 1910.1200, Hazard Communication. Appendix C, Allocation of Label Elements.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

The Organization for Economic Co-operation and Development (OECD) Guidelines for the Testing of Chemicals.

United States Environmental Protection Agency (EPA) Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Health Effects Test Guidelines.

VII.3 Serious Eye Damage/Eye Irritation

Introduction

Changes at the site of first contact (e.g., skin, eye) can be caused regardless of whether a chemical can become systemically available. These changes are considered local effects. Chemicals causing local effects after a single exposure can be further distinguished as irritant or corrosive chemicals, depending on the reversibility of the effects observed.

Corrosive chemicals are those which can destroy living tissues with which they come into contact. In toxicology, the term "corrosive" normally means causing visible destruction of the skin, eyes, or the lining of the respiratory tract or the gastrointestinal tract on contact. Corrosion is manifested by ulcers, cell death, and scar formation. Generally speaking, corrosive materials have a very low pH (acids) or a very high pH (bases). Strong bases are usually more corrosive than acids. Examples of corrosive materials are sodium hydroxide (lye) and sulfuric acid.

Irritant chemicals are non-corrosive substances which, through immediate contact with the tissue under consideration, may cause inflammation. Dermal irritation is a skin reaction resulting from a single or multiple exposures to a physical or chemical entity at the same site, characterized by the presence of inflammation.

The difference between an irritant and a corrosive is the ability of the body to repair the tissue reaction. With irritants the inflammatory reaction can be reversed, whereas with corrosive damage it is permanent and irreparable.

Appendix A.3 of the HCS addresses the classification of those chemicals which present a corrosion or irritation hazard to the eye.

General Considerations

Classification for serious eye damage/eye irritation should be conducted using a tiered weight–of-evidence approach. In the tiered approach, emphasis should be placed upon existing human data, followed by existing animal data, followed by *in vitro* data and then other sources of information. Classification results directly when the data satisfy the criteria. However, in some cases, classification of a chemical is made on the basis of the weight-of-evidence within a tier. If no decision can be made about classification after following the tiered approach, then a total weight-of-evidence approach to classification should be used. In a total weight-of-evidence approach all available information bearing on the determination of serious eye damage /eye irritation is considered together, including the results of appropriate validated *in vitro* tests, relevant animal data, and human data such as epidemiological and clinical studies and well-documented case reports and observations.

Classification Criteria for Substances

There are two categories assigned for eye effects in the HCS. In addition, the category for eye irritation is subdivided into two subcategories according to specific criteria outlined below.

Substances are allocated to one of the categories within this hazard class, Category 1 (serious eye damage) or Category 2 (eye irritation), as follows:

(a) Category 1 (serious eye damage/irreversible effects on the eye): Substances that have the potential to seriously damage the eyes (see Table VII.3.1);

(b) Category 2 (eye irritation/reversible effects on the eye): Substances that have the potential to induce reversible eye irritation (see Table VII.3.2). Category 2 has two subcategories, Category 2A and Category 2B, which are differentiated by the time it takes for the eye effects to reverse.

Classification criteria for substances using animal test data

Serious eye damage (Category 1)/Irreversible effects on the eye

Serious eye damage is the production of tissue damage in the eye, or serious physical decay of vision, following application of a test substance to the anterior surface of the eye, which is not fully reversible within 21 days of application.

The criteria include animals with grade 4 cornea lesions and other severe reactions (e.g., destruction of cornea) observed at any time during the test, as well as persistent corneal opacity, discoloration of the cornea by a dye substance, adhesion, pannus, and interference with the function of the iris or other effects that impair sight. In this context, persistent lesions are considered those which are not fully reversible within an observation period of normally 21 days.

Hazard classification as Category 1 also includes substances fulfilling the criteria of corneal opacity ≥3 and/or iritis > 1.5 detected in a Draize eye test with rabbits, because severe lesions like these usually do not reverse within a 21-day observation period.

Table VII.3.1. Serious eye damage/Irreversible eye effects category[a,b]

Category	Criteria
Category 1: **Serious eye damage/Irreversible eye effects**	A substance that produces: (a) in at least one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or have not fully reversed within an observation period of normally 21 days; and/or (b) in at least 2 of 3 tested animals, a positive response of: (i) corneal opacity ≥ 3; and/or (ii) iritis > 1.5; calculated as the mean scores following grading at 24, 48 and 72 hours after instillation of the test material.

[a] Grading criteria correspond to those described in OECD Test Guideline 405.
[b] Criteria for evaluation of a 4, 5 or 6-animal study are provided below under the heading "Guidance on evaluation of data from studies with more than three animals."

Eye irritation (Category 2)/Reversible effects on the eye

Eye irritation is the production of changes in the eye following the application of test substance to the anterior surface of the eye, which are fully reversible within 21 days of application.

Substances that have the potential to induce reversible eye irritation should be classified in Category 2. When data are sufficient, substances may be classified in Category 2A or 2B in accordance with the criteria in Table VII.3.2. For substances inducing eye irritant effects reversing within an observation time of normally 21 days, Category 2A applies. For substances inducing eye irritant effects reversing within an observation time of 7 days, Category 2B applies. If there is insufficient data to subdivide into category 2B then the classifier may use the generic term of Category 2. The criteria for the generic Category 2 are equivalent to Category 2A.

For those substances where there is pronounced variability among animal responses, this information may be taken into account in determining the classification.

Table VII.3.2. Reversible eye effects categories[a,b]

	Criteria
	Substances that have the potential to induce reversible eye irritation
Category 2A	Substances that produce in at least 2 of 3 tested animals a positive response of: (a) corneal opacity ≥ 1; and/or (b) iritis ≥ 1; and/or (c) conjunctival redness ≥ 2; and/or (d) conjunctival edema (chemosis) ≥ 2 calculated as the mean scores following grading at 24, 48 and 72 hours after instillation of the test material, and which fully reverses within an observation period of normally 21 days.
Category 2B	Within Category 2A an eye irritant is considered mildly irritating to eyes **(Category 2B)** when the effects listed above are fully reversible within 7 days of observation.

[a] Grading criteria correspond to those described in OECD Test Guideline 405.
[b] Criteria for evaluation of a 4, 5 or 6-animal study are provided below under the heading "Guidance on evaluation of data from studies with more than three animals."

Classification in a tiered approach

A *tiered approach* to the evaluation of initial information must be used, where applicable (Figure VII.3.1), recognizing that not all elements may be relevant.

The tiered approach provides guidance on how to organize existing information on a substance and to make a weight-of-evidence decision about hazard assessment and hazard classification (ideally without conducting new animal tests). Although information might be gained from the evaluation of single parameters within a tier, consideration should be given to the totality of existing information and making an overall weight-of-evidence determination. This is especially true when there is conflict in information available on some parameters.

Existing human and animal data should be the first line of evaluation, as they give information directly relevant to effects on the eye. Possible skin corrosion has to be evaluated prior to consideration of any testing for serious eye damage/eye irritation in order to avoid testing for local effects on eyes with skin corrosive substances.

In vitro alternatives that have been scientifically validated and accepted must be used to make classification decisions.

Likewise, pH extremes such as ≤ 2 and ≥ 11.5 may indicate serious eye damage, especially when associated with significant acid/alkaline reserve (buffering capacity).[10] Generally, such substances are expected to produce significant effects on the eyes. In the absence of any other information, a substance is considered to cause serious eye damage (Category 1) if it has a pH ≤ 2 or ≥ 11.5. However, if consideration of acid/alkaline reserve suggests the substance may not cause serious eye damage despite the low or high pH value, then further evaluation may be necessary. Data from an appropriate scientifically validated *in vitro* test is the preferred method for validation.

In some cases sufficient information may be available from structurally related substances to make classification decisions.

Figure VII.3.1. Tiered evaluation for serious eye damage/eye irritation (see also Tiered evaluation for skin corrosion and irritation)

Step	Parameter	Finding	Conclusion
1a:	Existing human or animal serious eye damage/eye irritation data [a] →	Serious eye damage →	**Category 1**
	↘	Eye irritant →	**Category 2**[b]
	↓ Negative data/Insufficient data/No data ↓		
1b:	Existing human or animal data, skin corrosion →	Skin corrosion →	**Category 1**
	↓ Negative data /Insufficient data/No data ↓		
1c:	Existing human or animal serious eye damage/eye irritation data [a] →	Existing data showing that substance does not cause serious eye damage or eye irritation →	**Not classified**
	↓ No/Insufficient data ↓		
2:	Other, existing skin/eye data in animals [c] →	Yes; other existing data showing that substance may cause serious eye damage or eye irritation →	**Category 1** or **Category 2**[b]
	↓ No/Insufficient data ↓		
3:	Existing *ex vivo/in vitro eye* data [d] →	Positive: serious eye damage →	**Category 1**
	↘	Positive: eye irritant →	**Category 2**[b]
	↓ No/Insufficient data/Negative response ↓		

[10] For further information concerning acid/alkaline reserve, see (1) Young et al. 1988, "Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without test on animals," *Toxicology in Vitro* 2, 19-26 and (2) Young and How, 1994, "Product classification as corrosive or irritant by measuring pH and acid / alkali reserve," *Alternative Methods in Toxicology vol. 10 - In Vitro Skin Toxicology: Irritation, Phototoxicity, Sensitization,* 23-27.

Figure VII.3.1. Tiered evaluation for serious eye damage/eye irritation (see also Tiered evaluation for skin corrosion and irritation)

Step	Parameter	Finding	Conclusion
4:	pH-based assessment (with consideration of acid/alkaline reserve of the chemical) [e] →	pH ≤ 2 or ≥ 11.5 with high acid/alkaline reserve or no data for acid/alkaline reserve →	**Category 1**
	↓ Not pH extreme, no pH data or extreme pH with data showing low/no acid/alkaline reserve ↓		
5:	Validated Structure Activity Relationship (SAR) methods →	Severe damage to eyes →	**Category 1**
		Eye irritant →	**Category 2**[b]
		Skin corrosive →	**Category 1**
	↓ No/Insufficient data ↓		
6:	Consideration of the total weight of evidence [f] →	Serious eye damage →	**Category 1**
	↓	Eye irritant →	**Category 2**[b]
7:	**Not classified**		

[a] Existing human or animal data could be derived from single or repeated exposure(s), for example in occupational, consumer, transport, or emergency response scenarios; from ethically conducted human clinical studies; or from purposely generated data from animal studies conducted according to validated and internationally accepted test methods. Although human data from accident or poison center databases can provide evidence for classification, absence of incidents is not itself evidence for no classification.

[b] Classify in the appropriate category/sub-category, as shown in Tables VII.3.1 and VII.3.2.

[c] Existing animal data should be carefully reviewed to determine if sufficient serious eye damage/eye irritation evidence is available through other, similar information. It is recognized that not all skin irritants are eye irritants. Expert judgment should be exercised prior to making such a determination.

[d] Evidence from studies using validated protocols with isolated human/animal tissues or other non-tissue-based, validated protocols should be assessed. Examples of scientifically validated test methods for identifying eye corrosives and severe irritants (i.e., Serious Eye Damage) include OECD TG 437 (Bovine Corneal Opacity and Permeability (BCOP)) and 438 (Isolated Chicken Eye (ICE)). Presently there are no scientifically validated and internationally accepted in vitro test methods for identifying eye irritation. A positive test result from a scientifically validated in vitro test on skin corrosion would lead to the conclusion to classify as causing serious eye damage.

[e] Measurement of pH alone may be adequate, but assessment of acid or alkali reserve (buffering capacity) would be preferable. Presently, there is no scientifically validated method for assessing this parameter.

[f] All information that is available on a substance should be considered and an overall determination made on the total weight of evidence. This is especially true when there is conflict in information available on some parameters. The weight of evidence including information on skin irritation may lead to classification for eye irritation. Negative results from applicable validated in vitro tests are considered in the total weight of evidence evaluation.

Classification criteria for mixtures

It should be noted that the classification criteria for the health hazards of mixtures usually include a tiered scheme (i.e., stepwise procedure based on a hierarchy principle) in which test data available on the complete mixture are considered as the first tier in the evaluation, followed by the applicable bridging principles, and lastly, cut-off values/concentration limits or additivity.

Tier 1: Classification of mixtures when data are available for the complete mixture

When serious eye damage /eye irritation test data on the mixture itself is available, these data are used to classify the mixture using the criteria for substances and taking into account the tiered weight-of-evidence approach illustrated in Figure VII.3.1.

When considering testing of the mixture, classifiers are encouraged to use a tiered weight-of-evidence approach as included in the criteria for classification of substances for skin corrosion and serious eye damage/eye irritation to help ensure an accurate classification. In the absence of any other information, a mixture is considered to cause serious eye damage (Eye Category 1) if it has a pH ≤ 2 or ≥ 11.5. However, if consideration of alkali/acid reserve suggests the mixture may not cause serious eye damage despite the low or high pH value, then further evaluation may be necessary.

If appropriate test data for the mixture are not available, then the classifier must consider the application of the Bridging Principle criteria in Tier 2, if appropriate, or if application of bridging principles are not appropriate, use the classification resulting from the application of criteria in Tier 3.

Tier 2: Classification of mixtures when data are not available for the complete mixture - bridging principles

Where the mixture itself has not been tested to determine its skin corrosivity or serious eye damage/eye irritation potential, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data are used in accordance with the bridging principles below.

The bridging principles that are applicable to the serious eye damage/eye irritation hazard class include:

- Dilution,
- Batching,
- Concentration of mixtures,
- Interpolation within one toxicity category,
- Substantially similar mixtures,
- Aerosols.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential skin corrosion/irritation hazard.

Dilution

If a tested mixture is diluted with a diluent which has an equivalent or lower classification for serious eye damage/eye irritation classification than the least seriously eye damaging/eye irritant original ingredient and which is not expected to affect the

serious eye damage/eye irritancy of other ingredients, then the new diluted mixture must be classified as equivalent to the original tested mixture. Alternatively, the cut-off values/concentration limits or additivity method could be applied.

Batching

The serious eye damage/eye irritation potential of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the serious eye damage/eye irritation potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures

If a tested mixture classified for serious eye damage (Category 1) is concentrated, the more concentrated untested mixture is classified for serious eye damage (Category 1) without additional testing. If a tested mixture classified for eye irritation (Category 2 or 2A) is concentrated and does not contain serious eye damage ingredients, the more concentrated untested mixture should be classified in the same category (Category 2 or 2A) without additional testing.

Interpolation within one hazard category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same serious eye damage/eye irritation hazard category, and where untested mixture C has the same toxicologically active ingredients as mixtures A and B but has concentrations of toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same serious eye damage/eye irritation category as A and B.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on serious eye damage/eye irritation for A and C are available and substantially equivalent, i.e., they are in the same hazard category and are not expected to affect the serious eye damage/eye irritation potential of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Aerosols

An aerosol form of a mixture must be classified in the same hazard category as the tested non-aerosolized form of the mixture provided that the added propellant does not affect the serious eye damage/eye irritation properties of the mixture upon spraying. Bridging principles apply for the intrinsic hazard classification of aerosols. However, the need to evaluate the potential for "mechanical" eye damage from the physical force of the spray is recognized.

If appropriate data is not available to apply the above bridging principles then the classifier applies the criteria in Tier 3.

Tier 3: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

Cut-off values/concentration limits: Additivity

In general, the approach to classifying a mixture for serious eye damage/eye irritation in Tier 3 is based on the theory of additivity, where each corrosive or irritant ingredient is considered to contribute to the overall corrosive or irritant properties of the mixture. The ingredients are summed in proportion to their concentration and potency (i.e., corrosives carry more weight in the irritation calculations).

Table VII.3.3 provides the cut-off value/concentration limits to be used to determine if the mixture is considered to be corrosive or irritant to the eyes. Six potential additivity calculations are given in the first column. Each calculation has specific concentration cut-offs that will trigger the classification specified in columns 2 and 3 which correspond to Category 1 and Category 2, respectively.

To better illustrate the order in which the equations should be evaluated an arrow has been added to the table. Following the arrow, the first calculation that exceeds the percentage cut-off trigger determines which classification is assigned to the mixture. If none of the sums exceed the cut-off triggers then the mixture is not classified.

Table VII.3.3. Concentration of ingredients of a mixture classified as skin Category 1 and/or eye Category 1 or 2 that would trigger classification of the mixture as hazardous to the eye (Category 1 or 2)[11]

Sum of ingredients classified as	Concentration triggering classification of a mixture as	
	Serious eye damage	Eye irritation
	Category 1	Category 2
Eye Category 1 or Skin Category 1	≥ 3%	≥ 1% but < 3%
Eye Category 2		≥ 10%
(10 × Eye Category 1) + Eye Category 2		≥ 10%
Skin Category 1 + Eye Category 1[a]	≥ 3%	≥ 1% but < 3%
10 × (Skin Category 1 + Eye Category 1)[a] + Eye Category 2		≥ 10%

[a] If an ingredient is classified as both skin Category 1 and eye Category 1 its concentration is considered only once in the calculation.

Note: A mixture is classified as eye Category 2B when all relevant ingredients are classified as eye *Category 2B.*

The Nine Serious Eye Damage/Eye Irritation Mixture Additivity Calculations

There are nine possible calculations that may need to be performed to determine if the mixture should be classified.

Sum of ingredients classified as	Concentration triggering classification of a mixture as	
	Serious eye damage	Eye irritation
	Category 1	Category 2
Eye Category 1	≥ 3% (1)	≥ 1% but < 3% (4)
Skin Category 1	≥ 3% (2)	≥ 1% but < 3% (5)
Eye Category 2		≥ 10% (6)
(10 × Eye Category 1) + Eye Category 2		≥ 10% (7)
Skin Category 1 + Eye Category 1[a]	≥ 3% (3)	≥ 1% but < 3% (8)
10 × (Skin Category 1 + Eye Category 1)[a] + Eye Category 2		≥ 10% (9)

[11] Revision 6 of the GHS contains a similar table that may be easier to understand. See GHS Table 3.3.3.

[a] If an ingredient is classified as both skin Category 1 and eye Category 1 its concentration is considered only once in the calculation

Note: A mixture is classified as eye Category 2B when all relevant ingredients are classified as eye Category 2B.

Serious eye damage Category 1 classification calculations:

(1) Add the percentages of all ingredients classified as Eye Category 1.
If the sum is ≥ 3% the mixture is classified as Category 1 Serious Eye Damage.
Σ % Eye Category 1 ingredients ≥ 3%

(2) Add the percentages of all ingredients classified as Skin Category 1.
If the sum is ≥ 3% the mixture is classified as Category 1 Serious Eye Damage.
Σ % Skin Category 1 ingredients ≥ 3%

(3) First add the percentages of all ingredients classified as Eye Category 1.
Then add the percentages of all ingredients classified as Skin Category 1.
Add these two numbers together. If the sum is ≥ 3%, the mixture is classified as Category 1 Serious Eye Damage.
Σ % Skin Category 1 ingredients + Σ % Eye Category 1 ingredients ≥ 3%

Eye irritation Category 2 classification calculations:

For Category 1 ingredients:

(4) Add the percentages of all ingredients classified as Eye Category 1.
If the sum is ≥ 1% but < 3%, the mixture is classified as Category 2 Eye Irritation.
Σ % Eye Category 1 ingredients ≥ 1% but < 3%

(5) Add the percentages of all ingredients classified as Skin Category 1.
If the sum is ≥ 1% but < 3%, the mixture is classified as Category 2 Eye Irritation.
Σ % Skin Category 1 ingredients ≥ 1% but < 3%

For Category 2 ingredients:

(6) Add the percentages of all ingredients classified as Eye Category 2.
If the sum is ≥ 10% the mixture is classified as Category 2 Eye Irritation.
Σ % Eye Category 2 ingredients ≥ 10%

For Category 1 & 2 ingredients:

(7) First add the percentages of all ingredients classified as Eye Category 1 and multiply this sum by 10.
Then add the percentages of all ingredients classified as Eye Category 2.
Add these two numbers together. If the sum is ≥ 1% but < 3%, the mixture is classified as Category 2 Eye Irritation.
10 (Σ % Eye Category 1 ingredients) + Σ % Eye Category 2 ingredients ≥ 1% but < 3%

For Skin & Eye Category 1 ingredients:

(8) First add the percentages of all ingredients classified as Skin Category 1.
Then add the percentages of all ingredients classified as Eye Category 1.
(If an ingredient is classified as both skin Category 1 and eye Category 1 its concentration is considered only once in the calculation.)
Add these two numbers together. If the sum is ≥ 1% but < 3%, the mixture is classified as Category 2 Eye Irritation.
Σ % Skin Category 1 ingredients + Σ % Eye Category 1 ingredients ≥ 1% but < 3%

For Skin & Eye Category 1 & Eye 2 ingredients:

(9) Add the percentages of all ingredients classified as Skin Category 1.
Add the percentages of all ingredients classified as Eye Category 1.
Add these two numbers. Multiply that sum by 10. This is calculation one.
In calculation two add the percentages of all ingredients classified as Eye Category 2.
In calculation three add the numbers from calculation one and calculation two together.
If the number in calculation 3 is ≥ 10%, the mixture is classified as Category 2 Eye Irritation.

10 (Σ % Skin Category 1 ingredients + Σ % Eye Category 1 ingredients) + Σ % Eye Category 2 ingredients ≥ 10%

Reminder:

A mixture may be classified as eye Category 2B when all relevant ingredients are classified as eye Category 2B. Category 2A is equivalent to Category 2.

Shortcut Serious Eye Damage/Eye Irritation Mixture Additivity Calculations

Shortcut

For those doing the calculations manually, a shortcut that leads to the same classification is to only do the worst-case calculations for the Serious Eye Damage Category 1 classification and the Eye Irritation Category 2 classification. In the shortcut there are only two calculations. The first sum that exceeds the percentage cut-off trigger determines which classification is assigned to the mixture. If neither exceeds the cut-off triggers then the mixture is not classified.

	Concentration triggering classification of a mixture as	
	Serious eye damage	**Eye irritation**
Sum of ingredients classified as	**Category 1**	**Category 2**
Eye Category 1	≥ 3%	≥ 1% but < 3%
Skin Category 1	≥ 3%	≥ 1% but < 3%
Eye Category 2		≥ 10%
(10 × Eye Category 1) + Eye Category 2		≥ 10%
Skin Category 1 + Eye Category 1[a]	≥ 3%	≥ 1% but < 3%
10 × (Skin Category 1 + Eye Category 1)[a] + Eye Category 2		≥ 10%

[a] If an ingredient is classified as both skin Category 1 and eye Category 1 its concentration is considered only once in the calculation

Note: A mixture is classified as eye Category 2B when all relevant ingredients are classified as eye

Category 2B.

Shortcut Serious eye damage Category 1 classification calculation:

(3) First add the percentages of all ingredients classified as Eye Category 1.
Then add the percentages of all ingredients classified as Skin Category 1.
Add these two numbers together. If the sum is ≥ 3%, the mixture is classified as Category 1 Serious Eye Damage.
Σ % Skin Category 1 ingredients + Σ % Eye Category 1 ingredients ≥ 3%

Shortcut Eye irritation Category 2 classification calculation:

(9) Add the percentages of all ingredients classified as Skin Category 1.
Add the percentages of all ingredients classified as Eye Category 1.
Add these two numbers. Multiply that sum by 10. This is calculation one.
In calculation two add the percentages of all ingredients classified as Eye

Category 2.
In calculation three add the numbers from calculation one and calculation two together. If the number in calculation 3 is ≥ 10%, the mixture is classified as Category 2 Eye Irritation.

10 (Σ % Skin Category 1 ingredients + Σ % Eye Category 1 ingredients) + Σ % Eye Category 2 ingredients ≥ 10%

Cut-off values/concentration limits: when the additivity approach does not apply

Particular care must be taken when classifying certain types of chemicals such as acids and bases, inorganic salts, aldehydes, phenols, and surfactants. The additivity approach might not work because many such chemicals are seriously damaging or irritating to the eye at concentrations < 1% and additivity may underestimate the overall corrosive or irritant properties of the mixture.

For mixtures containing strong acids or bases, the pH should be used as the classification criterion since pH will be a better indicator of serious eye damage (subject to consideration of acid/alkali reserve) than the concentration limits in Table VII.3.3. A mixture containing corrosive or serious eye damaging/eye irritating ingredients that cannot be classified based on the additivity approach applied in Table VII.3.3 due to chemical characteristics that make this approach unworkable should be classified using the more conservative cut-off/concentration limit approach summarized below:

- Mixture is Eye Category 1 if it contains ≥ 1% of a corrosive ingredient, and
- Mixture is Eye Category 2 if it contains ≥ 3% of an irritant ingredient.

The cut-off value/concentration limits approach is summarized in HCS Table VII.3.4.

Table VII.3.4. Concentration of ingredients of a mixture when the additivity approach does not apply, that would trigger classification of the mixture as hazardous to the eye

Ingredient	Concentration	Mixture classified as: Eye
Acid with pH ≤ 2	≥ 1%	Category 1
Base with pH ≥ 11.5	≥ 1%	Category 1
Other corrosive (Eye Category 1) ingredient	≥ 1%	Category 1
Other eye irritant (Eye Category 2) ingredient for which additivity does not apply , including acids and bases	≥ 3%	Category 2

Cut-off values/concentration limits: Important Points to Consider

To ensure consistent application of both the additivity and cut-off/concentration limit approaches to classification for Serious Eye Damage/Eye Irritation, the following principles need to be applied where appropriate:

- **Classification Above or Below Cut-Off Values/Concentration Limits**
  On occasion, reliable data may show that the irreversible/reversible eye effects of an ingredient will not be evident when present at a level above the cut-off values/concentration limits mentioned in Tables VII.3.3 and VII.3.4. In these cases the mixture could be classified according to those data (see also HCS 2012 A.0.4.3). Testing of the mixture may be considered. If testing is not performed, the tiered weight-of-evidence approach should be applied.

  If there are data showing that (an) ingredient(s) may be corrosive to the skin or seriously damaging to the eye/eye irritating at a concentration of < 1% (corrosive to the skin or seriously damaging to the eye) or < 3% (eye irritant), the mixture should be classified accordingly.

- **"Relevant Ingredient" Concept**
  For the purpose of applying the cut-off values in Tables VII.3.3 and VII.3.4, only "relevant ingredients" need to be included in the calculation.

  The "relevant ingredients" of a mixture are those which are present in concentrations ≥ 1% (w/w for solids, liquids, dusts, mists and vapors and v/v for gases), unless there is a presumption (e.g., in the case of corrosive ingredients) that an ingredient present at a concentration < 1% can still be relevant for classifying the mixture for serious eye damage/eye irritation. If the classifier suspects that the ingredient could be relevant for classifying the mixture at < 1%, then the classifier must use expert judgment to determine at what concentration below 1% the corrosive Category 1 ingredient(s) should be included in the calculation.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

In classification the data are compared to the serious eye damage/eye irritation classification criteria. If valid data on serious eye damage/eye irritation of a substance or mixture are available, these data should be used for classification. To find the necessary data, a classifier is advised to try the following:

- ask the manufacturer or supplier for the serious eye damage/eye irritation data for the product; or

- check if the serious eye damage/eye irritation data is available in the SDS or any other documentation accompanying the product; or
- find the data available in the open literature, if the chemical identity of the product is known (for a single-component chemical).

Data generated in accordance with internationally recognized scientific principles are acceptable under the HCS.

Examples of scientifically validated test methods
There are a number of methods that use recognized scientific principles for investigation of serious eye damage/eye irritation effects:

- OECD Test Guideline 405: Acute Eye Irritation/Corrosion
- USEPA OTS code: 798.4500;
- USEPA OPP code: 81-4;
- USEPA OPPTS code: 870.2400;
- EEC Directive 92/32/EEC (B.5);
- OECD Test Guideline 437: *In Vitro* Bovine Corneal Opacity and Permeability (BCOP);
- OECD Test Guideline 438: *In Vitro* Isolated Chicken Eye (ICE).

In the *in vivo* test, the substance is applied in a single dose to one of the eyes of an experimental animal (usually a healthy young albino rabbit) while the untreated eye serves as the control. Internationally accepted, validated *in vivo* test methods for identifying eye corrosives and severe irritants (i.e., Serious Eye Damage) include OECD TG 437 - Bovine Corneal Opacity and Permeability (BCOP) and OECD TG 438 - Isolated Chicken Eye (ICE). Presently there are no validated and internationally accepted *in vitro* test methods for identifying eye irritation.

Guidance on evaluation of data from studies with more than three animals
The classification criteria for serious eye damage/eye irritation are given in terms of a 3-animal test. Some older test methods may have used up to 6 animals. However, the serious eye damage/eye irritation criteria do not specify how to classify based on existing data from tests with more than 3 animals.

Criteria for the evaluation of a 4, 5 or 6-animal study are provided in the paragraphs below, depending on the number of animals tested. Scoring is done at 24, 48 and 72 hours after instillation of the test material.

In the case of a study with 6 animals the following principles apply:

(a) The substance or mixture is classified as serious eye damage Category 1 if:

(i) at least in one animal effects on the cornea, iris or conjunctiva are not expected to reverse or have not fully reversed within an observation period of normally 21 days; and/or

(ii) at least 4 out of 6 animals show a mean score per animal of ≥ 3 for corneal opacity and/or > 1.5 for iritis.

(b) The substance or mixture is classified as eye irritation Category 2/2A if at least 4 out of 6 animals show a mean score per animal of:

(i) ≥ 1 for corneal opacity; and/or

(ii) ≥ 1 for iritis; and/or

(iii) ≥ 2 for conjunctival redness; and/or

(iv) ≥ 2 for conjunctival oedema (chemosis)

and which fully reverses within an observation period of normally 21 days.

(c) The substance or mixture is classified as irritating to eyes (Category 2B) if the effects listed in sub-paragraph (b) above are fully reversible within 7 days of observation.

In the case of a study with 5 animals the following principles apply:

(a) The substance or mixture is classified as serious eye damage Category 1 if:

(i) at least in one animal effects on the cornea, iris or conjunctiva are not expected to reverse or have not fully reversed within an observation period of normally 21 days; and/or

(ii) at least 3 out of 5 animals show a mean score per animal of ≥ 3 for corneal opacity and/or > 1.5 for iritis.

(b) The substance or mixture is classified as eye irritation Category 2/2A if at least 3 out of 5 animals show a mean score per animal of:

(i) ≥ 1 for corneal opacity; and/or

(ii) ≥ 1 for iritis; and/or

(iii) ≥ 2 for conjunctival redness; and/or

(iv) ≥ 2 for conjunctival oedema (chemosis)

and which fully reverses within an observation period of normally 21 days.

(c) The substance or mixture is classified as irritating to eyes (Category 2B) if the effects listed in sub-paragraph (b) above are fully reversible within 7 days of observation.

In the case of a study with 4 animals the following principles apply:

(a) The substance or mixture is classified as serious eye damage Category 1 if:

(i) at least in one animal effects on the cornea, iris or conjunctiva are not expected to reverse or have not fully reversed within an observation period of normally 21 days; and/or

(ii) at least 3 out of 4 animals show a mean score per animal of ≥ 3 for corneal opacity and/or > 1.5 for iritis.

(b) Classification as eye irritation Category 2/2A if at least 3 out of 4 animals show a mean score per animal of:

(i) ≥ 1 for corneal opacity; and/or

(ii) ≥ 1 for iritis; and/or

(iii) ≥ 2 for conjunctival redness; and/or

(iv) ≥ 2 for conjunctival oedema (chemosis)

and which fully reverses within an observation period of normally 21 days.

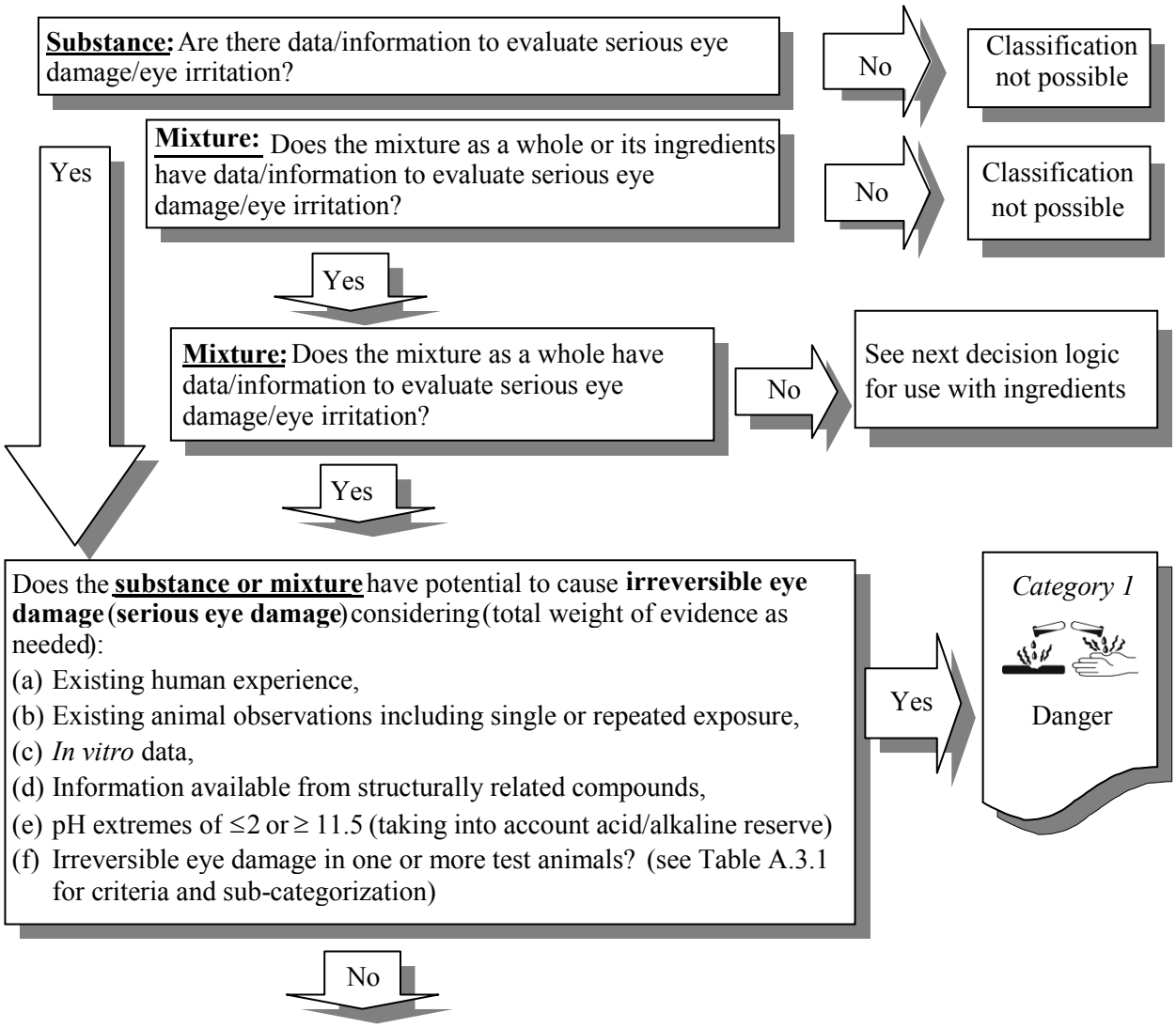
(c) The substance or mixture is classified as irritating to eyes (Category 2B) if the effects listed in sub-paragraph (b) above are fully reversible within 7 days of observation.

Decision logic

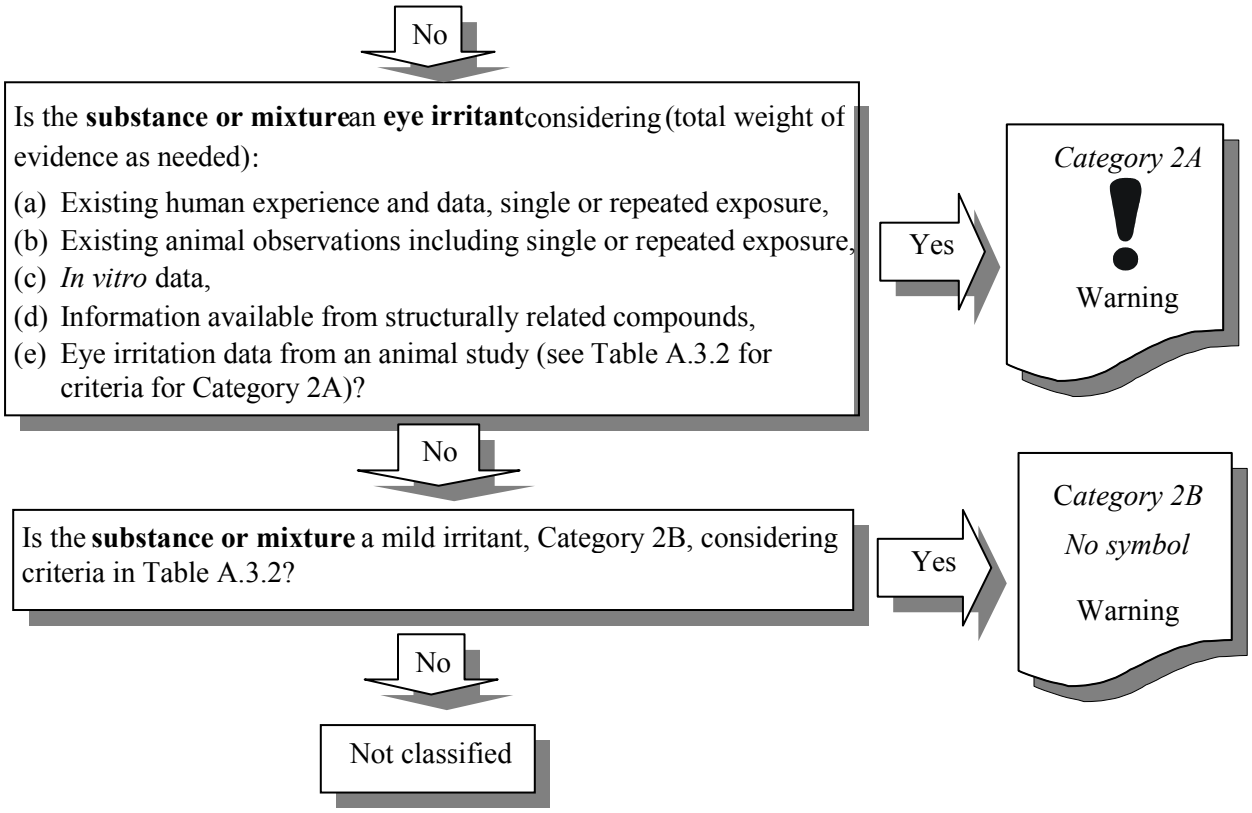
Two decision logics for classifying *Serious Eye Damage/Eye Irritation* are provided. The first decision logic is for substances and for mixtures with data on the mixture as a whole. Use the second decision logic for classifying mixtures on the basis of information/data on similar tested mixtures and/or ingredients. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

These decision logics are essentially flowcharts for classifying substances and mixtures regarding serious eye damage/eye irritation. They present questions in a sequence that walks you through the classification steps and criteria for classifying serious eye damage/eye irritation. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic for serious eye damage/eye irritation

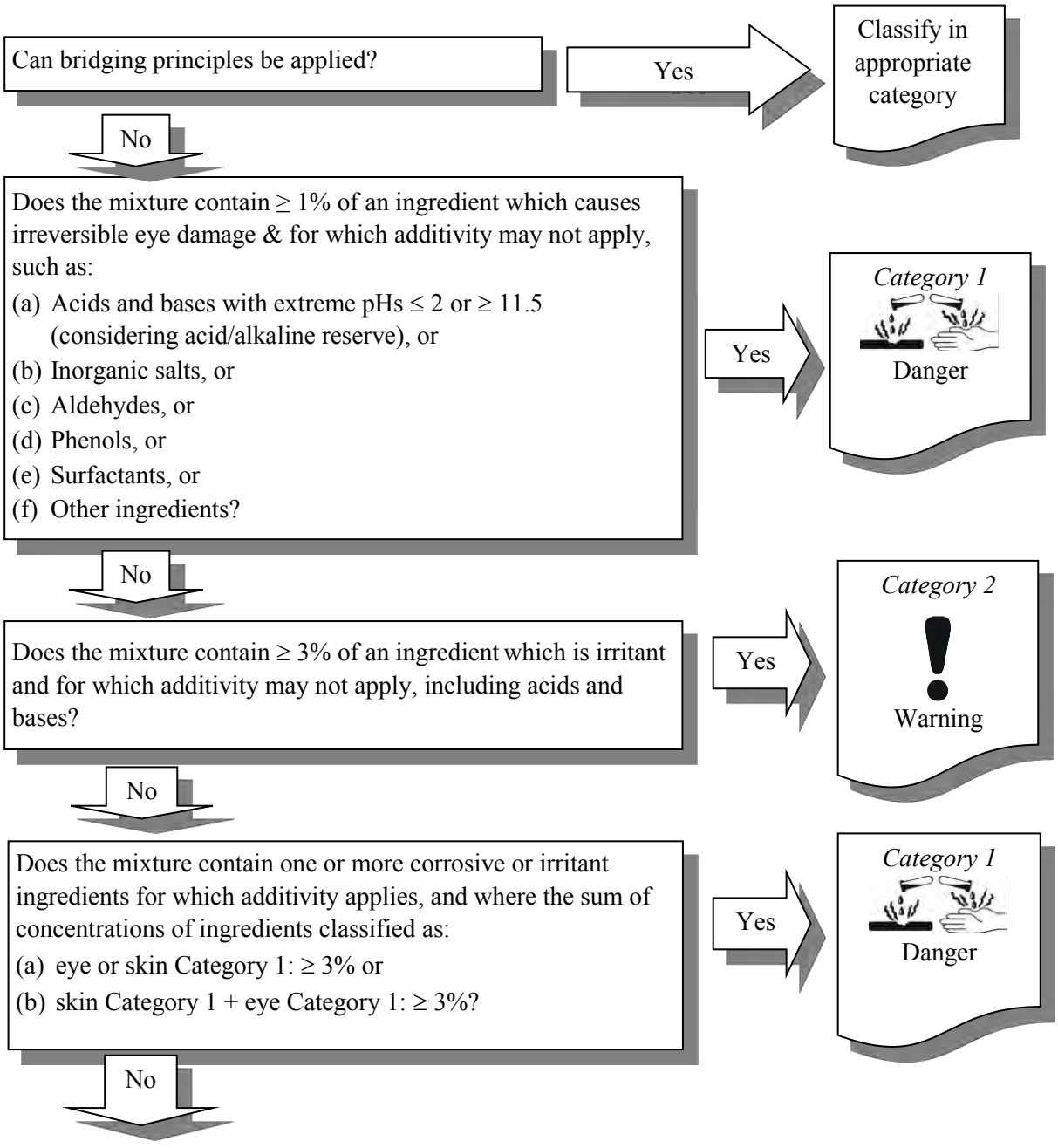


(Cont'd on next page)


No
Is the **substance or mixture** an **eye irritant** considering (total weight of evidence as needed):
(a) Existing human experience and data, single or repeated exposure,
(b) Existing animal observations including single or repeated exposure,
(c) *In vitro* data,
(d) Information available from structurally related compounds,
(e) Eye irritation data from an animal study (see Table A.3.2 for criteria for Category 2A)?
Yes
Category 2A
Warning
No
Is the **substance or mixture** a mild irritant, Category 2B, considering criteria in Table A.3.2?
Yes
Category 2B
No symbol
Warning
No
Not classified

Mixtures decision logic for serious eye damage/eye irritation

Classification of mixtures on the basis of information/data on ingredients



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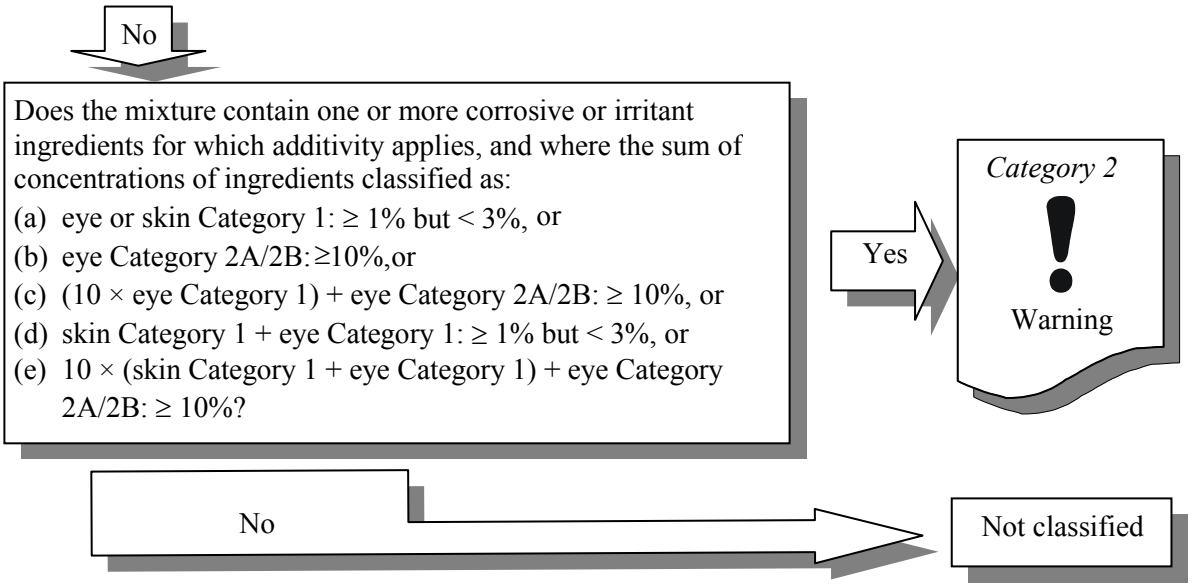

No
Does the mixture contain one or more corrosive or irritant ingredients for which additivity applies, and where the sum of concentrations of ingredients classified as:
(a) eye or skin Category 1: ≥ 1% but < 3%, or
(b) eye Category 2A/2B: ≥10%,or
(c) (10 × eye Category 1) + eye Category 2A/2B: ≥ 10%, or
(d) skin Category 1 + eye Category 1: ≥ 1% but < 3%, or
(e) 10 × (skin Category 1 + eye Category 1) + eye Category 2A/2B: ≥ 10%?
Yes
Category 2
!
Warning
No
Not classified

Serious Eye Damage/Eye Irritation Classification Examples

The following examples are provided to walk you through the serious eye damage/eye irritation calculation and classification processes.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 **Serious Eye Damage**		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity data: neither *in vivo* data nor *in vitro* data available Other relevant information: pH 1.9; no info on buffering capacity	Serious Eye Damage Category 1	Based on a pH < 2, the substance is a Serious Eye Damage Category 1 according to Figure VII.3.1 *Tiered evaluation for serious eye damage/eye irritation, Step 4.*

Substance Example #2 **Eye Irritation**		
Test Data	**HCS 2012 Classification**	**Rationale**
In an OECD Test Guideline 405 study the test substance was applied on the eyes of three rabbits. The scoring results are – Corneal opacity: 2, 2, 1.3 – Iritis: 1, 1, 1 – Conjunctival redness: 2, 1, 1 – Conjunctival edema (chemosis): 3, 1.7, 2.3 – Reversibility: The effects were reversible.	Eye Irritation Category 2	Fulfills criteria – The test results show: Cornea ≥ 1 (in all animals) Iritis ≥ 1 (in all animals) Conjunctival redness ≥ 2 (in 1 animal) Conjunctival edema ≥2 (in 2 of 3 animals) – The Category 2 criteria are fulfilled by the Cornea, Conjunctiva and Iris scores.

Substance Example #3 Serious Eye Damage		
Test Data	**HCS 2012 Classification**	**Rationale**
The material is a new aliphatic secondary amine. No data is available. The test substance has Structure Activity Relationships (SAR) to substances with similar structure known to be corrosive to the skin.	Serious Eye Damage Category 1	Based on expert judgment using SAR information the classifier concluded that Category 1 is justified, since there is much data on aliphatic amines which are skin corrosives Category 1 and thus deemed to cause irreversible eye effects resulting in Serious Eye Damage Category 1 according to Figure VII.3.1 *Tiered evaluation for serious eye damage/eye irritation*, Step 5.

Substance Example #4 Eye Irritation		
Test Data	**HCS 2012 Classification**	**Rationale**
OECD Test Guideline 405: Acute Eye Irritation/Corrosion test results: – Corneal opacity: mean score 0.6 – Iritis: mean score 1.3 – Conjunctival redness: mean score 2.4 (from 2 of 3 animals) – Conjunctival edema (chemosis): mean score 1.4 – Reversibility: The effects were fully reversible after 7 days.	Eye Irritation Category 2B	Fulfills criteria – the mean score for redness over 24, 48, and 72 hours in 2 of 3 animals is 2.4 and therefore > 2.3, – the effects are fully reversible in 7 days, – the criteria for classification in Category 2B are fulfilled.

Examples of a mixture fulfilling the criteria for classification:

Mixture Example #1 Eye Irritation		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 0.5%, Eye Category 1 Component 2: 3.5%, Eye Category 2, surfactant Component 3: 15%, No data available Component 4: 15%, No data available Component 5: 66%, No data available	Eye Irritation Category 2	Mixture is Eye Irritation Category 2 because – Mixture contains 0.5% of an Eye Category 1 which is not ≥ 1% so the mixture is not Category 1; – Mixture contains 3.5% of an Eye Category 2 surfactant which is ≥ 3.0% so the mixture is Category 2. – Classification of the mixture based on ingredient data can be considered. – Component 2 (Surfactant) is a component for which additivity might not apply. Expert judgment would be needed to determine whether or not additivity applies. Knowledge of the components is important. Given the limited information in this example, the classifier of this mixture chose to apply non-additivity for a conservative approach. Therefore, the criteria described in 29 CFR 1910.1200 paragraph A.3.4.3.4 apply (i.e., "A mixture containing corrosive or irritant ingredients that cannot be classified based on the additivity approach shown in [Table VII.3.3], due to chemical characteristics that make this approach unworkable, should be classified as Eye Category 1 if it contains ≥ 1% of a corrosive ingredient and as Eye Category 2/3 when it contains ≥ 3% of an irritant ingredient").

Mixture Example #2 Serious Eye Damage		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 22.06%, Eye Category 1 Component 2: 4%, Eye Category 1 Component 3: 5.5%, Eye Category 2A Component 4: 8%, not classified based on test data Component 5: 0.05%, not classified based on test data Component 5: 0.2%, not classified based on test data Water: 60.19%, %, not classified pH of mixture (neat liquid): 7 – 8 *Mixture BCOP test data:* Mean opacity value = 15 Mean permeability OD490 value = 5 *In Vitro* Irritancy Score (IVIS) = 90	Serious Eye Damage Category 1	IVIS = mean opacity value + (15 x mean permeability OD490 value) A test sample that induces an IVIS ≥ 55.1 is defined as a corrosive or severe irritant to eyes. Applying the *Tiered evaluation for serious eye damage/eye irritation* approach using serious eye damage/eye irritation *in vitro* data from a Bovine Corneal Opacity and Permeability (BCOP) test, the mixture is classified as Serious Eye Damage Category 1 based on test data. – Test results derived using the BCOP test method indicate the mixture is a corrosive or severe eye irritant.

Mixture Example #3 Eye Irritation		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 4%, Eye Irritation Category 2A Component 2: 5%, Eye Irritation Category 2A Component 3: 5%, Eye Irritation Category 2A Component 4: 86%, no data available	Eye Irritation Category 2A	Use equations from Table VII.3.3 **Category 1 calculation:** a) ∑% Eye Category 1 = 0 which is not ≥ 3% b) Σ % Skin Category 1 = 0 which is not ≥ 3% c) Σ % Skin Category 1 + Σ % Eye Category 1 = 0 which is not ≥ 3% **Category 2 calculations:** d) ∑% Eye Category 1 = 0 which is not ≥ 1% but < 3% e) Σ % Skin Category 1 = 0 which is not ≥ 1% but < 3% f) ∑ % Eye Category 2/2A = 4% + 5% + 5% = 14% which is ≥ 10% – Classification of the mixture based on ingredient data can be considered – Apply the calculations in Table VII.3.3 – The mixture is classified as Category 2A since all the classified components were Category 2A.

Example of a substance not fulfilling the criteria for classification:

Substance Example #5 **Eye Irritation**		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity data: Old non-guideline study in rabbits – After 24 hours: questionable redness – Reversibility: full after 8 days	Not classified	According to the classification criteria the slight irritating effect with full reversibility does not justify classification in this hazard class.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.3 Serious Eye Damage/Eye Irritation.

29 CFR 1910.1200, Hazard Communication. Appendix C, Allocation of Label Elements.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

The Organization for Economic Co-operation and Development (OECD) Guidelines for the Testing of Chemicals.

United States Environmental Protection Agency (EPA) Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Health Effects Test Guidelines.

VII.4 Respiratory or Skin Sensitization

Introduction

A sensitizer (allergen) causes little or no reaction in humans or test animals on first exposure. The problem arises on subsequent exposures when a marked immunological response occurs. The response is not necessarily limited to the contact site as it may be a generalized body condition. Skin sensitization is common in industry. Respiratory sensitization and generalized hyperallergy to a few chemicals have also been known to occur. Well-known examples of sensitizers are toluene diisocyanate, nickel compounds, and poison ivy.

A sensitizer is an agent that can cause an allergic response in susceptible individuals. The consequence of this is that following an initial exposure which sensitizes the individual, subsequent exposures via the skin or by inhalation provoke the characteristic adverse health effects of allergic contact dermatitis or asthma (and related respiratory symptoms such as rhinitis), respectively. Although asthma and rhinitis are generally thought to be a result of an allergic reaction, the understanding, in recent years, that other, non-immunological, mechanisms may occur, makes it more appropriate to use a term based on disease rather than mechanism. Thus, the term "respiratory hypersensitivity" is a term that is used to describe asthma and other related respiratory conditions, irrespective of the mechanism by which they are caused.

The term skin sensitization specifies an allergic mechanism of action, while respiratory hypersensitivity does not. For this reason, the two health hazards have been approached differently.

For the purpose of this chapter, sensitization includes two phases:

- induction of specialized immunological memory in an individual by exposure to an allergen; and
- elicitation, i.e., production of a cell-mediated or antibody-mediated allergic response by exposure of a sensitized individual to an allergen.

For respiratory sensitization, the pattern of induction followed by elicitation phases is shared in common with skin sensitization. For skin sensitization, an induction phase is required in which the immune system learns to react; clinical symptoms can then arise when subsequent exposure is sufficient to elicit a visible skin reaction (elicitation phase). Respiratory sensitization may be induced not only by inhalation but also by skin contact.

Tests for sensitization usually follow the same pattern in which there is an induction phase, and then a response, which is measured by a standardized elicitation phase, typically involving a patch test. The local lymph node assay is the exception, directly measuring the induction response. Evidence of skin sensitization in humans normally is assessed by a diagnostic patch test.

Usually, for both skin and respiratory sensitization, lower levels are necessary for elicitation than are required for induction.

The hazard class "respiratory or skin sensitization" is differentiated into:

(a) Respiratory sensitization and

(b) Skin sensitization.

Respiratory Sensitizers

Definition and General Considerations

Respiratory sensitizer means a chemical that will lead to hypersensitivity of the airways following inhalation of the chemical.

Respiratory Sensitizer Classification Criteria for Substances

Effects seen in either humans or animals will normally justify classification using a weight-of-evidence approach for respiratory sensitizers. Substances may be allocated to one of the two sub-categories, 1A or 1B, using a weight-of-evidence approach in accordance with the criteria indicated below and on the basis of reliable and good quality evidence from human cases or epidemiological studies and/or observations from appropriate studies in experimental animals.

Where data are not sufficient for sub-categorization, respiratory sensitizers shall be classified in Category 1.

Table VII.4.1. Hazard category and sub-categories for respiratory sensitizers

Category	Respiratory Sensitizer Criteria
Category 1	A substance is classified as a respiratory sensitizer (a) if there is evidence in humans that the substance can lead to specific respiratory hypersensitivity and/or (b) if there are positive results from an appropriate animal test.[12]
Sub-category 1A	Substances showing a high frequency of occurrence[13] in humans, or a probability of occurrence of a high sensitization rate in humans based on animal or other tests.[12] Severity of reaction may also be considered.
Sub-category 1B	Substances showing a low to moderate frequency of occurrence[13] in humans; or a probability of occurrence of a low to moderate sensitization rate in humans based on animal or other tests.[12] Severity of reaction may also be considered.

[12] At this writing, recognized and validated animal models for the testing of respiratory hypersensitivity are not available. Under certain circumstances, data from animal studies may provide valuable information in a weight-of-evidence assessment

[13] With regard to the criteria for respiratory sensitization, the frequency of occurrence in humans is a matter of expert judgment.

Human evidence

Evidence that a substance can lead to specific respiratory hypersensitivity will normally be based on human experience. In this context, hypersensitivity is normally seen as asthma, but other hypersensitivity reactions such as rhinitis/conjunctivitis and alveolitis are also considered. The condition will have the clinical character of an allergic reaction. However, immunological mechanisms do not have to be demonstrated.

When considering the human evidence, it is necessary that in addition to the evidence from the cases, the following factors should be taken into account:

(a) The size of the population exposed;

(b) The extent of exposure.

The evidence referred to above could be:

(a) Clinical history and data from appropriate lung function tests related to exposure to the substance, confirmed by other supportive evidence which may include:

(i) *In vivo* immunological test (e.g., skin prick test);

(ii) *In vitro* immunological test (e.g., serological analysis);

(iii) Studies that may indicate other specific hypersensitivity reactions where immunological mechanisms of action have not been proven, e.g., repeated low-level irritation, pharmacologically mediated effects

(iv) A chemical structure related to substances known to cause respiratory hypersensitivity;

(b) Data from positive bronchial challenge tests with the substance conducted according to accepted guidelines for the determination of a specific hypersensitivity reaction.

Clinical history should include both medical and occupational history to determine a relationship between exposure to a specific substance and development of respiratory hypersensitivity. Relevant information includes aggravating factors both in the home and workplace, the onset and progress of the disease, family history and medical history of the patient in question. The medical history should also include details of other allergic or airway disorders from childhood and smoking history.

The results of positive bronchial challenge tests are considered to provide sufficient evidence for classification on their own. It is, however, recognized that in practice many of the examinations listed above will already have been carried out.

Animal studies

Data from appropriate animal studies which may be indicative of the potential of a substance to cause sensitization by inhalation in humans may include:

(a) Measurements of Immunoglobulin E (IgE) and other specific immunological parameters, for example in mice

(b) Specific pulmonary responses in guinea pigs.

At this writing, recognized and validated animal models for the testing of respiratory hypersensitivity are not available. Under certain circumstances, data from animal studies may provide valuable information in a weight-of-evidence assessment.

The mechanisms by which substances induce symptoms of asthma are not yet fully known. For preventive measures, these substances are considered respiratory sensitizers. However, if on the basis of the evidence, it can be demonstrated that these substances induce symptoms of asthma by irritation only in people with bronchial hyperactivity, they should not be considered as respiratory sensitizers.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

Classification procedure
In classification, the data are compared to the respiratory sensitizer classification criteria. Data can be found in literature, on SDSs, or be determined by testing, (which is not required by the HCS). For classification of mixtures, follow the three-tier approach discussed below.

To assess the respiratory sensitization hazard of a chemical, identify the relevant data. Effects seen in either humans or animals will normally justify classification using a weight-of-evidence approach for respiratory sensitizers. The weight-of-evidence approach uses expert judgment. All available information bearing on the respiratory sensitizer hazard classification is considered together, including the results of relevant animal data, and human experience, such as epidemiological and clinical studies and well-documented case reports and observations.

The quality and consistency of the data should be considered. Information on chemicals related to the material being classified should be considered, as appropriate. Both positive and negative results shall be considered together in a weight-of-evidence determination. However, positive effects which are consistent with the respiratory sensitizer classification criteria, whether seen in humans or animals, normally justify classification.

Where evidence is available from both humans and animals and there is a conflict between the findings, evaluate the quality and reliability of the evidence from both sources. Reliable, good

quality human data generally takes precedence over other data. Positive results from well-conducted animal studies are not necessarily negated by the lack of positive human experience but require an assessment of the robustness, quality and statistical power of both the human and animal data.

If the data are available, then you must classify the chemical into the appropriate respiratory sensitization sub-category, i.e., category 1A or category 1B. If the data does not allow classification into a sub-category, then you must classify the chemical in respiratory sensitization category 1.

Skin Sensitizers

Definition and General Considerations

Skin sensitizer means a chemical that will lead to an allergic response following skin contact.

Skin Sensitizer Classification Criteria for Substances

Effects seen in either humans or animals will normally justify classification using a weight-of-evidence approach for skin sensitizers. Substances may be allocated to one of the two sub-categories, 1A or 1B, using a weight-of-evidence approach in accordance with the criteria given below, and on the basis of reliable and good quality evidence from human cases or epidemiological studies and/or observations from appropriate studies in experimental animals.

Where data are not sufficient for sub-categorization, skin sensitizers shall be classified in Category 1.

Table VII.4.2. Hazard category and sub-categories for skin sensitizers

Category	Skin Sensitizer Criteria
Category 1	A substance is classified as a skin sensitizer (a) if there is evidence in humans that the substance can lead to sensitization by skin contact in a substantial number of persons, or (b) if there are positive results from an appropriate animal test.
Sub-category 1A	Substances showing a high frequency of occurrence[14] in humans and/or a high potency in animals can be presumed to have the potential to produce significant sensitization in humans. Severity of reaction may also be considered.
Sub-category 1B	Substances showing a low to moderate frequency of occurrence[14] in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce sensitization in humans. Severity of reaction may also be considered.

[14] With regard to the criteria for respiratory sensitization, the frequency of occurrence in humans is a matter of expert judgment.

Human evidence

Human evidence for sub-category 1A may include:

(a) Positive responses at $\leq$ 500 μg/cm^2 (Human Repeat Insult Patch Test (HRIPT), Human Maximization Test (HMT) − induction threshold);

(b) Diagnostic patch test data where there is a relatively high and substantial incidence of reactions in a defined population in relation to relatively low exposure;

(c) Other epidemiological evidence where there is a relatively high and substantial incidence of allergic contact dermatitis in relation to relatively low exposure.

Human evidence for sub-category 1B may include:

(a) Positive responses at > 500 μg/cm^2 (HRIPT, HMT – induction threshold);

(b) Diagnostic patch test data where there is a relatively low but substantial incidence of reactions in a defined population in relation to relatively high exposure;

(c) Other epidemiological evidence where there is a relatively low but substantial incidence of allergic contact dermatitis in relation to relatively high exposure.

Animal studies

Two types of *in vivo* methods to investigate skin sensitization tests have been developed: an adjuvant test in which sensitization is potentiated by the injection of Freunds Complete Adjuvant (FCA), and non-adjuvant tests. There are three animal test methods used to evaluate skin sensitization for substances: the mouse local lymph node assay (LLNA), the guinea pig maximization test (GPMT), and the Buehler occluded patch test. The Organization for Economic Cooperation and Development (OECD) Guidelines describe test methods for skin sensitization: Guideline 406, the Guinea Pig Maximization test and the Buehler guinea pig test and Guideline 429, the Local Lymph Node Assay. Other methods may be used provided that they are scientifically validated. The Mouse Ear Swelling Test (MEST), appears to be a reliable screening test to detect moderate to strong sensitizers, and can be used, in accordance with professional judgment, as a first stage in the assessment of skin sensitization potential.

Animal test results for Skin Sensitization Category 1 include data with values indicated below:

Table VII.4.3. Animal test results for Skin Sensitization Category 1

Assay	Criteria
Adjuvant type test method for skin sensitization	Response in at least 30% of the animals is considered positive.
Non-adjuvant Guinea pig test method	Response in at least 15% of the animals is considered positive.
Local lymph node assay	Stimulation index of three or more is considered a positive response.

Animal test results for Skin Sensitization sub-category 1A can include data with values indicated below:

Table VII.4.4. Animal test results for Skin Sensitization sub-category 1A

Assay	Criteria
Local lymph node assay	EC3 value ≤ 2%
Guinea pig maximization test	≥ 30% responding at ≤ 0.1% intradermal induction dose or ≥ 60% responding at > 0.1% to ≤ 1% intradermal induction dose
Buehler assay	≥ 15% responding at ≤ 0.2% topical induction dose or ≥ 60% responding at > 0.2% to ≤ 20% topical induction dose

Note: EC3 refers to the estimated concentration of the test chemical required to induce a stimulation index of 3 in the local lymph node assay.

Animal test results for Skin Sensitization sub-category 1B can include data with values indicated below:

Table VII.4.5. Animal test results for Skin Sensitization sub-category 1B

Assay	Criteria
Local lymph node assay	EC3 value > 2%
Guinea pig maximization test	≥ 30% to < 60% responding at > 0.1% to ≤ 1% intradermal induction dose or ≥ 30% responding at > 1% intradermal induction dose
Buehler assay	≥ 15% to < 60% responding at > 0.2% to ≤ 20% topical induction dose or ≥ 15% responding at > 20% topical induction dose

Note: EC3 refers to the estimated concentration of the test chemical required to induce a stimulation index of 3 in the local lymph node assay.

Immunological contact urticaria
Substances which cause immunological contact urticaria with or without meeting the criteria for respiratory sensitizers shall be considered for classification as skin sensitizers.

There is no recognized animal model available to identify substances which cause immunological contact urticaria. Therefore, classification will normally be based on human evidence, similar to that for skin sensitization.

Classification procedure
In classification, the data are compared to the skin sensitizer classification criteria. Data can be found in literature, on SDSs, or be determined by testing (which is not required by the HCS). For mixtures, follow the three-tier approach discussed below.

For classification of a substance, evidence shall include one or more of the following conditions using a weight-of-evidence approach:

(a) Positive data from patch testing, normally obtained in more than one dermatology clinic;

(b) Epidemiological studies showing allergic contact dermatitis caused by the substance; Situations in which a high proportion of those exposed exhibit characteristic symptoms are to be looked at with special concern, even if the number of cases is small;
(c) Positive data from appropriate animal studies;

(d) Positive data from experimental studies in humans;

(e) Well-documented episodes of allergic contact dermatitis, normally obtained in more than one dermatology clinic;

(f) Severity of reaction.

Evidence from animal studies is usually much more reliable than evidence from human exposure. However, in cases where evidence is available from both sources, and there is conflict between the results, the quality and reliability of the evidence from both sources must be assessed in order to resolve the question of classification on a case-by-case basis. Normally, human data are not generated in controlled experiments with volunteers for the purpose of hazard classification but rather as part of risk assessment to confirm lack of effects seen in animal tests. Consequently, positive human data on skin sensitization are usually derived from case-control or other, less defined studies. Evaluation of human data must, therefore, be carried out with caution as the frequency of cases reflect, in addition to the inherent properties of the substances, factors such as the exposure situation, bioavailability, individual predisposition and preventive measures

taken. Negative human data should not normally be used to negate positive results from animal studies. For both animal and human data, consideration should be given to the impact of the vehicle used.

If none of the above-mentioned conditions ((a)-(f) above) are met, the substance need not be classified as a skin sensitizer. However, a combination of two or more indicators of skin sensitization, as listed below, may alter the decision. This shall be considered on a case-by-case basis.

(a) Isolated episodes of allergic contact dermatitis;

(b) Epidemiological studies of limited power, e.g., where chance, bias or confounders have not been ruled out fully with reasonable confidence;

(c) Data from animal tests, performed according to existing guidelines, which do not meet the criteria for a positive result described in 29 CFR 1910.1200 Paragraph A.4.2.2.3, but which are sufficiently close to the limit to be considered significant;

(d) Positive data from non-standard methods;

(e) Positive results from close structural analogues.

If the data is available, then you must classify into the appropriate skin sensitization sub-category, i.e., category 1A or category 1B. If the data does not allow classification into a sub-category, then you must classify in skin sensitization category 1.

Sensitizer Classification Criteria for Mixtures

The approach to classifying mixtures for both skin and respiratory sensitizers incorporates a tiered approach (i.e., stepwise procedure based on a hierarchy).

Tier 1: Classification of mixtures when data are available for the complete mixture

When reliable and good evidence from human experience or appropriate animal studies is available for the mixture then it should be used in a weight-of-evidence approach using the same criteria as those specified for substances. Care should be exercised in evaluating such data to ensure the dose used does not render the results inconclusive. If test data for the mixture is not available, then the classifier should consider the application of the criteria in Tier 2 or 3, as appropriate.

Tier 2: Classification of mixtures when data are not available for the complete mixture – bridging principles

Where the mixture itself has not been tested to determine its sensitizing properties, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazard of the mixture, these data can be used in accordance with the following bridging principles.

All six bridging principles are applicable to the skin and respiratory sensitization classes:

- Dilution,
- Batching,
- Concentration of mixtures,
- Interpolation within one toxicity category,
- Substantially similar mixtures, and
- Aerosols.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential skin or respiratory sensitization hazard.

Dilution

If a tested mixture is diluted with a diluent which is not a sensitizer and which is not expected to affect the sensitization of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

Batching

The sensitizing properties of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the sensitization potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures

If a tested mixture is classified in Category 1 or sub-category 1A, and the concentration of the ingredients of the tested mixture that are in Category 1 and sub-category 1A is increased, the resulting untested mixture should be classified in Category 1 or sub-category 1A without additional testing.

Interpolation within one category/sub-category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same sensitizer category/sub-category, and where untested mixture C has the same sensitization toxicologically active ingredients as mixtures A and B but has concentrations of sensitization toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same sensitizer category/sub-category as A and B.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Ingredient B is a sensitizer and ingredients A and C are not sensitizers;

(e) A and C are not expected to affect the sensitizing properties of B.

If mixture (i) or (ii) is already classified by testing for sensitization, then the other mixture can be assigned the same hazard category.

Aerosols

An aerosol form of the mixture may be classified in the same hazard category as the tested non-aerosolized form of the mixture provided that the added propellant does not affect the sensitizing properties of the mixture upon spraying.

If appropriate data is not available to apply the above bridging principles then the classifier should consider the application of the cut-off value/concentration limit approach described in Tier 3.

Tier 3: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

If there are not sufficient data to apply the bridging principles, then the third tier for sensitizers is to classify the mixture using the cut-off/concentration limit approach.

The mixture shall be classified as a *respiratory* sensitizer when at least one ingredient has been classified as a respiratory sensitizer and is present at or above the appropriate respiratory sensitizer cut-off value/concentration limit for a solid/liquid or gas. See table below.

Table VII.4.6. Cut-off values/concentration limits of ingredients of a mixture classified as respiratory sensitizers that would trigger classification of the mixture

	Cut-off values/concentration limits triggering classification of a mixture as:	
	Respiratory sensitizer Category 1	
Ingredient classified as:	*Solid/Liquid*	*Gas*
Respiratory sensitizer Category 1	≥ 0.1%	≥ 0.1%
Respiratory sensitizer Sub-category 1A	≥ 0.1%	≥ 0.1%
Respiratory sensitizer Sub-category 1B	≥ 1.0%	≥ 0.2%

The mixture shall be classified as a *skin* sensitizer when at least one ingredient has been classified as a skin sensitizer and is present at or above the appropriate skin sensitizer cut-off value/concentration limit. See table below.

Table VII.4.7. Cut-off values/concentration limits of ingredients of a mixture classified as skin sensitizers that would trigger classification of the mixture

	Cut-off values/concentration limits triggering classification of a mixture as:
	Skin sensitizer Category 1
Ingredient classified as:	*All physical states*
Skin sensitizer Category 1	≥ 0.1%
Skin sensitizer Sub-category 1A	≥ 0.1%
Skin sensitizer Sub-category 1B	≥ 1.0%

The respiratory and skin sensitization assessments are carried out separately.

Some chemicals that are classified as sensitizers may elicit a response, when present in a mixture in quantities below the cut-offs established in the above tables in individuals who are already sensitized to the chemical. 29 CFR 1910.1200 paragraph A.0.4.3.2 states that if the classifier has information that the hazard of an ingredient will be evident (i.e., it presents a health risk) below the above cut-off values/concentration limits, then the mixture should be classified according to those lower cut-off values.

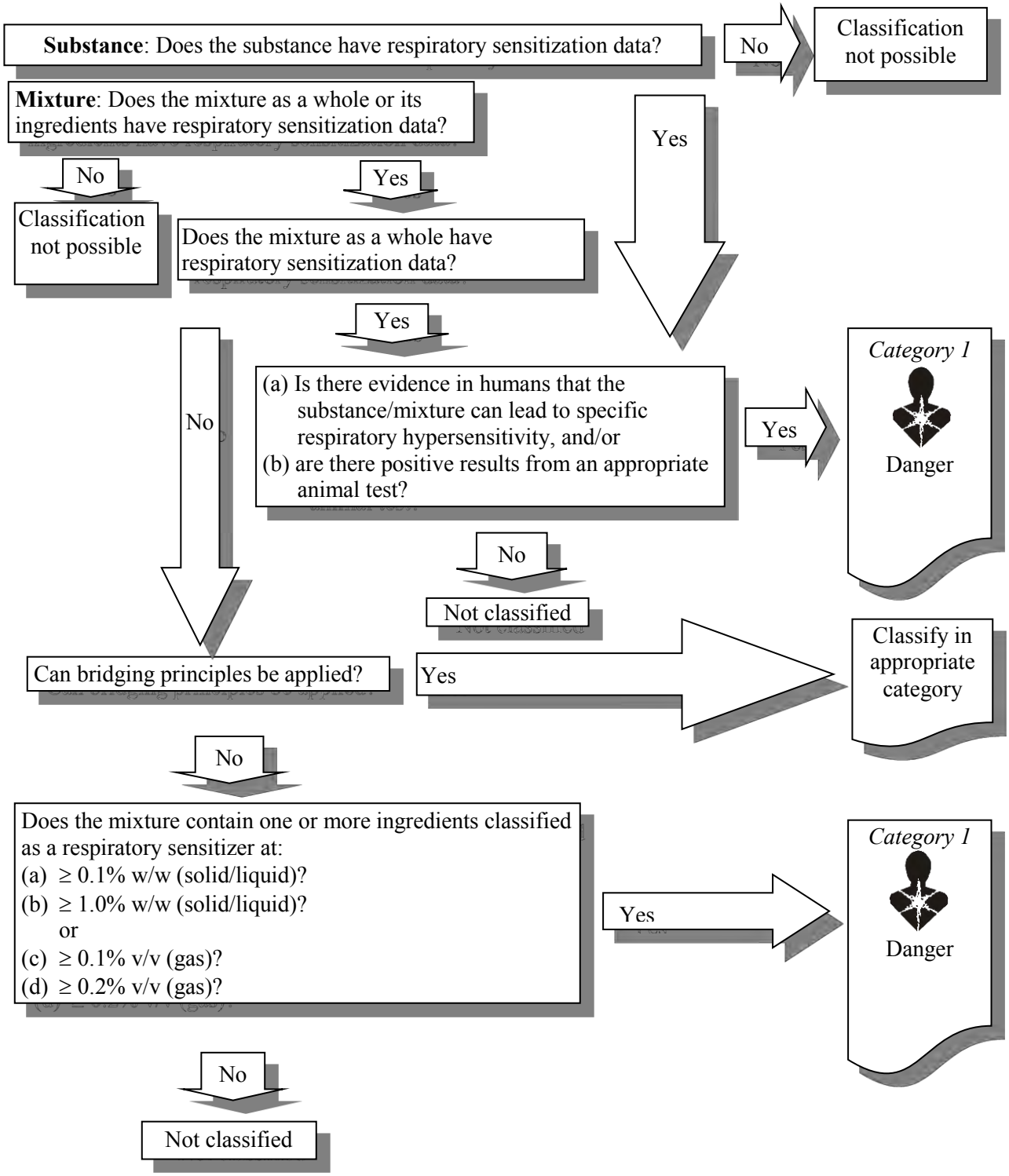
- If the classifier has reliable data that show the respiratory or skin sensitization potential of an ingredient will not be evident above the cut-off values/concentration limits then the mixture may be classified according to those higher substance specific cut-off values.

Decision logic

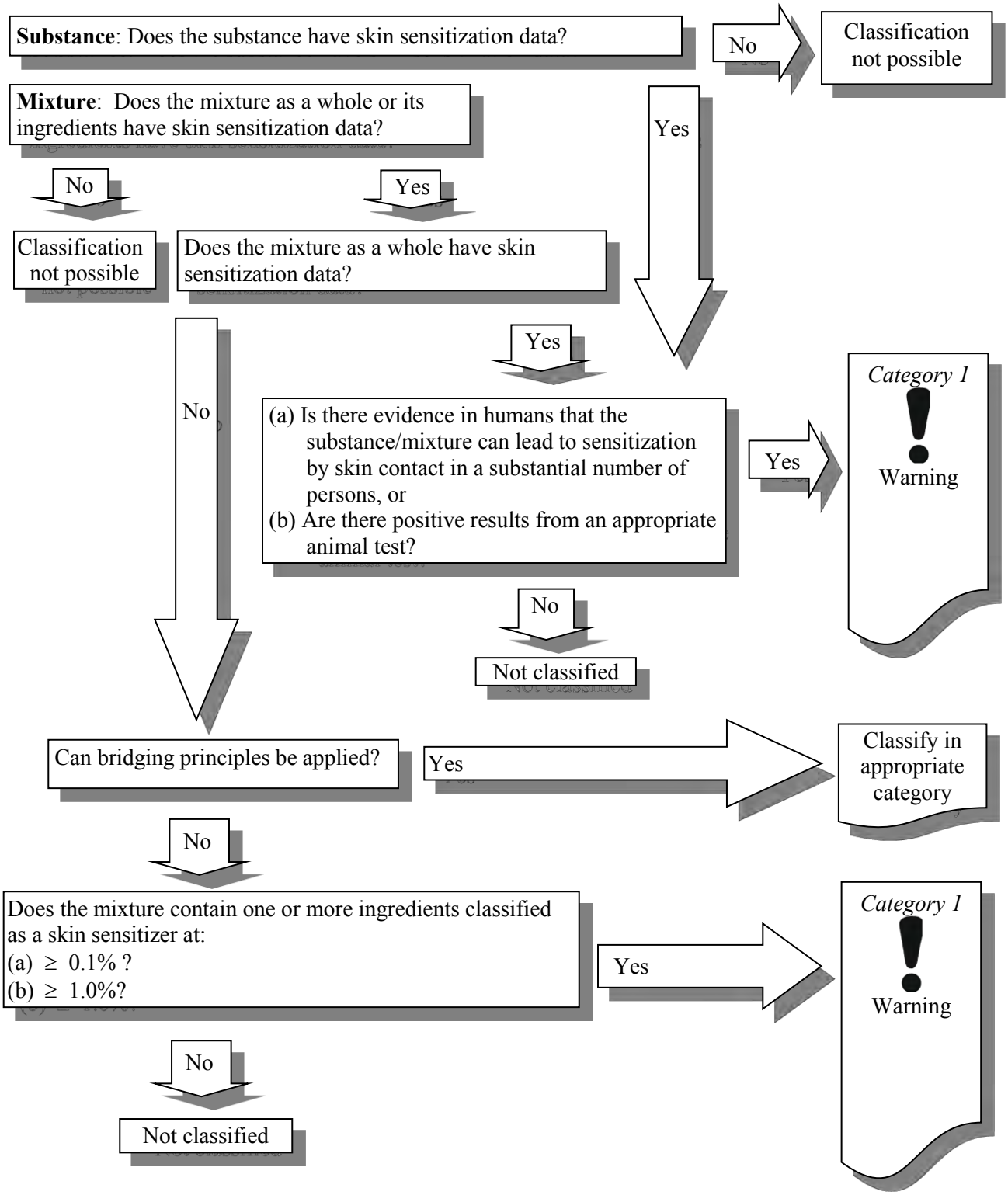
Decision logics for classifying *respiratory and skin sensitizers* are provided. The decision logics are for both substances and mixtures and are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logics.

The decision logics are essentially flowcharts for classifying substances and mixtures regarding sensitization. It presents questions in a sequence that walks you through the classification steps and criteria for classifying respiratory and skin sensitizers. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic for respiratory sensitization



Decision logic for skin sensitization



Respiratory and Skin Sensitization Classification Examples

The following examples are provided to walk you through respiratory and/or skin sensitization classification.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 **Respiratory and Skin Sensitization**		
Test Data	**HCS 2012 Classification**	**Rationale**
The material is a new isocyanate. No data are available for the new material. The test substance has Structure Activity Relationships (SAR) to substances with similar structure known to be respiratory and skin sensitizers in humans (e.g., methyl isocyanate).	Respiratory Sensitizer Category 1 Skin Sensitizer Category 1 (cannot differentiate sub-categories since this is not based on data for the actual substance)	Fulfills criteria. Based on expert judgment using SAR information the classifier concluded that classification as a Category 1 Respiratory Sensitizer and Category 1 Skin Sensitizer is justified, since there is ample available data on isocyanates that are respiratory and skin sensitizers in humans.

Substance Example #2 **Respiratory Sensitization**		
Test Data	**HCS 2012 Classification**	**Rationale**
The material is an enzyme with many well-documented human case studies for respiratory sensitization occurring in workers exposed during the manufacturing process.	Respiratory Sensitizer Category 1	Fulfills criteria. Because of the clear evidence from valid human studies, classification for respiratory sensitization is warranted.

Substance Example #3 Skin Sensitization		
Test Data	**HCS 2012 Classification**	**Rationale**
In an OECD Test Guideline 406 Skin Sensitization study, 4 animals out of 10 had a positive response. In a Freund's Complete Adjuvant test in guinea pigs, 4 animals out of 8 showed a positive reaction.	Skin Sensitizer Category 1	Fulfills Category 1 criteria. The criteria for Skin Sensitizer Category 1 classification are fulfilled, since in two independent adjuvant tests the response was ≥ 30% positive.

Substance Example #4 Skin Sensitization		
Test Data	**HCS 2012 Classification**	**Rationale**
Toxicity data: A high frequency of well documented human case reports on contact sensitization at very low concentrations (≤ 500 µg/cm^2) and in addition positive animal study results showing a high potency	Skin Sensitizer, Category 1A	Fulfills Category 1A criteria. The classification criteria are fulfilled based both on human and animal evidence.

Substance Example #5 Skin Sensitization		
Test Data	**HCS 2012 Classification**	**Rationale**
Substance X gave a positive result in the Local Lymph Node Assay (LLNA) with an EC3-value of 10.4%.	Skin Sensitizer Category 1B	Fulfills Category 1B criteria. This EC3-value is above the Category 1A criteria cut-off of 2% and meets the Category 1B criteria.

Substance Example #6 Skin Sensitization		
Test Data	**HCS 2012 Classification**	**Rationale**
Substance Y tested positive in the LLNA with an EC3-value of 0.5%. In the Guinea Pig Maximization Test (GPMT) a dermal induction concentration of 0.375% produced a positive response in 70% of the animals.	Skin Sensitizer Category 1A	Fulfills Category 1A criteria on the basis of the EC3-value and the response in the GPMT.

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 Skin Sensitization		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 2: 20%, Skin Sensitization Category 1B	Skin Sensitization Category 1B	Fulfills cutoff value criteria. Component 2 is 20% which is ≥1% Skin Sensitization Category 1B criteria are fulfilled.

Examples of mixtures and substances not fulfilling the criteria for classification:

Mixture Example #2 Skin Sensitization		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 3: 0.8%, Skin Sensitization Category 1B	Not classified for skin sensitization	While a component meets the criteria for Skin Sensitization Category 1B, the component is present in the mixture at less than the cutoff value for Skin Sensitization Category 1B. The mixture criteria for Skin Sensitization Category 1B are not fulfilled.

Substance Example #7 Skin Sensitization		
Test Data	**HCS 2012 Classification**	**Rationale**
In the LLNA a maximum stimulation index of 2.2 was reported.	Not classified for skin sensitization	The criteria for Skin Sensitization Category 1 is not met since the maximum stimulation index is less than 3.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.4, Respiratory or Skin Sensitization

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

VII.5 Germ Cell Mutagenicity

Introduction

Genotoxicity is a toxic end-point which may be associated with somatic mutation and germ cell mutation. A chemical's ability to induce germ cell mutations, which may continue to affect future generations, is an important consideration in the protection of human health.

Genetic effects result from damage to DNA and altered genetic expression. This process is known as mutagenesis. The genetic change is referred to as a mutation and the agent causing the change as a mutagen.

There are several types of genetic change: Gene mutation is a change in DNA sequence within a gene. Chromosome aberrations are changes in the chromosome structure. Aneuploidy/polyploidy is an increase or decrease in the number of chromosomes.

Mutagenicity refers to the ability of some chemicals to modify the genetic material in the nucleus of cells in ways that allow the changes to be transmitted during cell division. Germ cell mutations occur in germinal cells – (sperm and ova) – where there is no effect on the exposed person; rather the effect is passed on to future generations. Somatic mutations occur in other cell types (all body cells except sperm and ova), and may result in cell death (e.g., teratogenesis) or the transmission of a genetic defect to other cells in the same tissue. Current genotoxicity tests are aimed largely at detecting somatic cell mutations and are used as predictive indicators of carcinogenic potential. Relatively few genotoxic agents have been demonstrated to affect germ cells *in vivo*.

Definition and General Considerations

A *mutation* is defined as a permanent change in the amount or structure of the genetic material in a cell. The term *mutation* applies both to heritable genetic changes that may be manifested at the phenotypic level and to the underlying DNA modifications when known (including, for example, specific base pair changes and chromosomal translocations). The terms *mutagenic* and *mutagen* will be used for agents giving rise to an increased occurrence of mutations in populations of cells and/or organisms.

The more general terms *genotoxic* and *genotoxicity* apply to agents or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Genotoxicity test results are usually taken as indicators for mutagenic effects.

This hazard class is primarily concerned with chemicals that may cause mutations in the germ cells of humans that can be transmitted to the progeny. However, mutagenicity/genotoxicity tests *in vitro* and in mammalian somatic cells *in vivo* are also considered in classifying substances and mixtures within this hazard class.

Classification Criteria for Substances

There are two hazard categories for germ cell mutagens to accommodate the weight-of-evidence available. Category 1 is subdivided into two subcategories according to specific criteria outlined below.

Table VII.5.1. Hazard categories for germ cell mutagens

Category	Criteria
CATEGORY 1	**Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans**
Category 1A	**Substances known to induce heritable mutations in germ cells of humans** Positive evidence from human epidemiological studies.
Category 1B	**Substances which should be regarded as if they induce heritable mutations in the germ cells of humans** (a) Positive result(s) from *in vivo* heritable germ cell mutagenicity tests in mammals; or (b) Positive result(s) from *in vivo* somatic cell mutagenicity tests in mammals, in combination with some evidence that the substance has potential to cause mutations to germ cells. This supporting evidence may, for example, be derived from mutagenicity/genotoxicity tests in germ cells *in vivo*, or by demonstrating the ability of the substance or its metabolite(s) to interact with the genetic material of germ cells; or (c) Positive results from tests showing mutagenic effects in the germ cells of humans, without demonstration of transmission to progeny; for example, an increase in the frequency of aneuploidy in sperm cells of exposed people.
CATEGORY 2	**Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans** Positive evidence obtained from experiments in mammals and/or in some cases from *in vitro* experiments, obtained from: (a) Somatic cell mutagenicity tests *in vivo*, in mammals; or (b) Other *in vivo* somatic cell genotoxicity tests which are supported by positive results from *in vitro* mutagenicity assays**.** *Note: Substances which are positive in in vitro mammalian mutagenicity assays, and which also show a chemical structure activity relationship to known germ cell mutagens, should be considered for classification as Category 2 mutagens.*

Specific considerations for classification of substances as germ cell mutagens

The HCS is hazard-based, classifying chemicals on the basis of their intrinsic ability to induce mutations in germ cells. The HCS criteria are not meant for the quantitative risk assessment of chemical substances.

For classification, test results are considered from experiments determining mutagenic and/or genotoxic effects in germ and/or somatic cells of animals. Mutagenic and/or genotoxic effects determined in *in vitro* tests shall also be considered. Examples of various tests for mutagenic effects are given later in this chapter.

Classification for heritable effects in human germ cells is made on the basis of scientifically validated tests. Evaluation of the test results shall be done using expert judgment and all the available evidence shall be weighed for classification.

The classification of substances shall be based on the total weight-of-evidence available, using expert judgment. In those instances where a single well-conducted test is used for classification, it shall provide clear and unambiguously positive results. The relevance of the route of exposure used in the study of the substance compared to the route of human exposure should also be taken into account.

Classification criteria for mixtures

It should be noted that the HCS classification criteria for health hazards often include a tiered scheme in which test data available on the complete mixture are considered as the first tier in the evaluation, followed by the applicable bridging principles, and lastly, cut-off values/concentration limits or additivity. However, this approach is not used for Germ Cell Mutagenicity. The criteria for Germ Cell Mutagenicity consider the cut-off values/concentration limits as the primary tier and allow the classification to be modified only on a case-by-case evaluation based on available test data for the mixture as a whole.

Tier 1: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

The mixture will be classified as a mutagen when at least one ingredient has been classified as a Category 1A, Category 1B or Category 2 mutagen and is present at or above the appropriate cut-off value/concentration limit specified below for Category 1 and Category 2, respectively.

An assessment is carried out separately for each Category 1A, Category1B or Category 2 ingredient in the mixture. In the case where the mixture has Category 1A, Category 1B and Category 2 ingredients above the cut-off/concentration limit the mixture is classified in the most severe category.

Table VII.5.2. Cut-off values/concentration limits of ingredients of a mixture classified as germ cell mutagens that would trigger classification of the mixture

Ingredient classified as:	Cut-off/concentration limits triggering classification of a mixture as:		
	Category 1 mutagen		Category 2 mutagen
	Category 1A	Category 1B	
Category 1A mutagen	≥ 0.1%	--	--
Category 1B mutagen	--	≥ 0.1%	--
Category 2 mutagen	--	--	≥ 1.0%

Note: The cut-off values/concentration limits in the table above apply to solids and liquids (w/w units) as well as gases (v/v units).

Tier 2: Classification of mixtures when data are available for the complete mixture

On a case-by-case basis the Germ Cell Mutagenicity classification, which normally considers results obtained with the individual ingredients, may be modified using available test data for the mixture as a whole.

The concern with using test data for the mixture as a whole is that as the concentration of a germ cell mutagen is reduced in a mixture, the dilution effect may result in a misleading test result (i.e., false negative) if the study was not appropriately designed to factor in the concentration of the germ cell mutagen in the mixture. In these cases, mixtures that could cause Germ Cell Mutation would not be classified and labeled. Accordingly, the HCS states that the test results for the mixture as a whole must be conclusive taking into account dose, and other factors such as duration, observations and analysis (e.g., statistical analysis, test sensitivity) of germ cell mutagenicity test systems. If appropriate test data for the mixture is not available then the classifier can consider the application of the Bridging Principle criteria in Tier 3, if appropriate, or as stated above use the classification resulting from the application of criteria in Tier 1.

Tier 3: Classification of mixtures when data are not available for the complete mixture - bridging principles

Where the mixture itself has not been tested to determine its germ cell mutagenicity hazard, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the below bridging principles. If data on another mixture are used in the application of the bridging principles, the data on that mixture must be conclusive as discussed above in Tier 2.

Only the following bridging principles are applicable to the Germ Cell Mutagenicity hazard class:

- Dilution,
- Batching,
- Substantially similar mixtures.

Dilution

If a tested mixture is diluted with a diluent which is not expected to affect the germ cell mutagenicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

Batching

The germ cell mutagenic potential of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product, when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation in composition such that the germ cell mutagenic potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e. they are in the same hazard category and are not expected to affect the germ cell mutagenicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

Examples of scientifically validated test methods

There are a number of scientifically recognized methods for investigation of mutagenic effects.

Examples of *in vivo* heritable germ cell mutagenicity tests are:

(a) Rodent dominant lethal mutation test (OECD 478)
(b) Mouse heritable translocation assay (OECD 485)
(c) Mouse specific locus test

Examples of *in vivo* somatic cell mutagenicity tests are:

(a) Mammalian bone marrow chromosome aberration test (OECD 475)
(b) Mouse spot test (OECD 484)
(c) Mammalian erythrocyte micronucleus test (OECD 474)

Examples of mutagenicity/genotoxicity tests in germ cells are:

(a) Mutagenicity tests:
    (i) Mammalian spermatogonial chromosome aberration test (OECD 483)
    (ii) Spermatid micronucleus assay
(b) Genotoxicity tests:
    (i) Sister chromatid exchange analysis in spermatogonia
    (ii) Unscheduled DNA synthesis test (UDS) in testicular cells

Examples of genotoxicity tests in somatic cells are:

(a) Liver Unscheduled DNA Synthesis (UDS) *in vivo* (OECD 486)
(b) Mammalian bone marrow Sister Chromatid Exchanges (SCE)

Examples of *in vitro* mutagenicity tests are:

(a) *In vitro* mammalian chromosome aberration test (OECD 473)
(b) *In vitro* mammalian cell gene mutation test (OECD 476)
(c) Bacterial reverse mutation tests (OECD 471)

As new, scientifically validated tests arise, these may also be used in the total weight-of-evidence to be considered.

Classification procedure

In classification, the data are compared to the germ cell mutagenicity classification criteria. Data can be found in literature, on SDSs, or be determined by testing (which is not required by the HCS). For mixtures, follow the above modified three-tier approach.

Classification is made on the basis of the appropriate criteria and an assessment of the total *weight-of-evidence.* The validity and usefulness of each of the data sets to the overall assessment of mutagenicity should be individually assessed, taking account of protocol design (including route of administration) and current expert views on the value of the test systems. See considerations below.

If the data is available, then you must classify into the appropriate germ cell mutagenicity sub-category, i.e., Category 1A or Category 1B. If the data does not allow classification into a sub-category, then you must classify in germ cell mutagenicity category 1.

Currently, there is no example of a substance classified in germ cell mutagen category 1A. To date, epidemiological studies have not provided evidence to classify a substance as a Category 1A mutagen. Hereditary diseases in humans for the most part have an unknown origin and show a varying distribution in different populations. Due to the random distribution of mutations in the genome it is not expected that one particular substance would induce one specific genetic disorder. It is unlikely that epidemiological studies will provide evidence for classifying a substance as a Category 1A mutagen.

Considerations

Considerations When Evaluating Negative Test Results	
Doses or concentrations	Were the doses or concentrations of test substance used high enough?
Sensitivity of test system	Was the test system used sensitive to the nature of the genotoxic changes that might have been expected?
Volatility of the test substance	Were the concentrations maintained in tests conducted *in vitro*?
Metabolism	Was the metabolic activation suitable in the test systems *in vitro*?
Exposure to target organ	Was the substance reaching the target organ, for studies *in vivo*? (taking also toxicokinetic data into consideration)
Reactivity of the substance	Was the test substance reactive? (e.g., rate of hydrolysis, electrophilicity, presence or absence of structural alerts and other available indications)
Response in the control	What was the response of the positive and negative controls?

Considerations When Evaluating Positive/Contradictory Test Results	
Conflicting results	Conflicting results obtained in non-mammalian systems and in mammalian cell tests may be addressed by considering possible differences in substance uptake, metabolism or in the organization of genetic material. The results of mammalian tests may be considered of higher significance.
Positive in the *in vitro* SCE assay	Positive results in the *in vitro* SCE assay should be viewed with caution, as this assay is associated with a relatively high incidence of false positive results. Thus, a positive result in this assay would not be considered to be evidence of a significant clastogenic potential *in vitro* if negative results were available in an *in vitro* chromosome aberration assay.
Positive in the DNA binding assay	Interpretation of results from DNA binding assays should be viewed with caution as these assays are only considered to be indicators of DNA damage. Consequently, the observance of *in vivo* DNA adducts alone in the absence of positive findings from *in vitro* assays is generally not considered sufficient evidence of a significant genotoxic potential *in vivo*.
Contradiction between *in vitro* and *in vivo*	If contradictory findings are obtained *in vitro* and *in vivo*, in general, the results of *in vivo* tests indicate a higher degree of reliability. However, for evaluation of negative results *in vivo*, it should be considered whether there is adequate evidence of target tissue exposure.
Sensitivity and specificity of test systems	The sensitivity and specificity of different test systems varies for different classes of substances. If available testing data for other related substances permits assessment of the performance of difference assays for the class of substance under evaluation, the result from the test system known to produce more accurate responses would be given higher priority.
Positive in high toxic concentration	The consequences of "positive" findings only at highly toxic/cytotoxic concentrations, and the presence or absence of a dose-response relationship should be considered. The default assumption for genotoxic chemicals, in the absence of mechanistic evidence to the contrary, is that they have a linear dose response relationship. However, both direct and indirect mechanisms of genotoxicity can be non-linear or threshold, and sometimes this default assumption may be inappropriate. When interpreting positive results, considerations of the dose-response relationship and of possible mechanisms of action are important components of a hazard assessment.

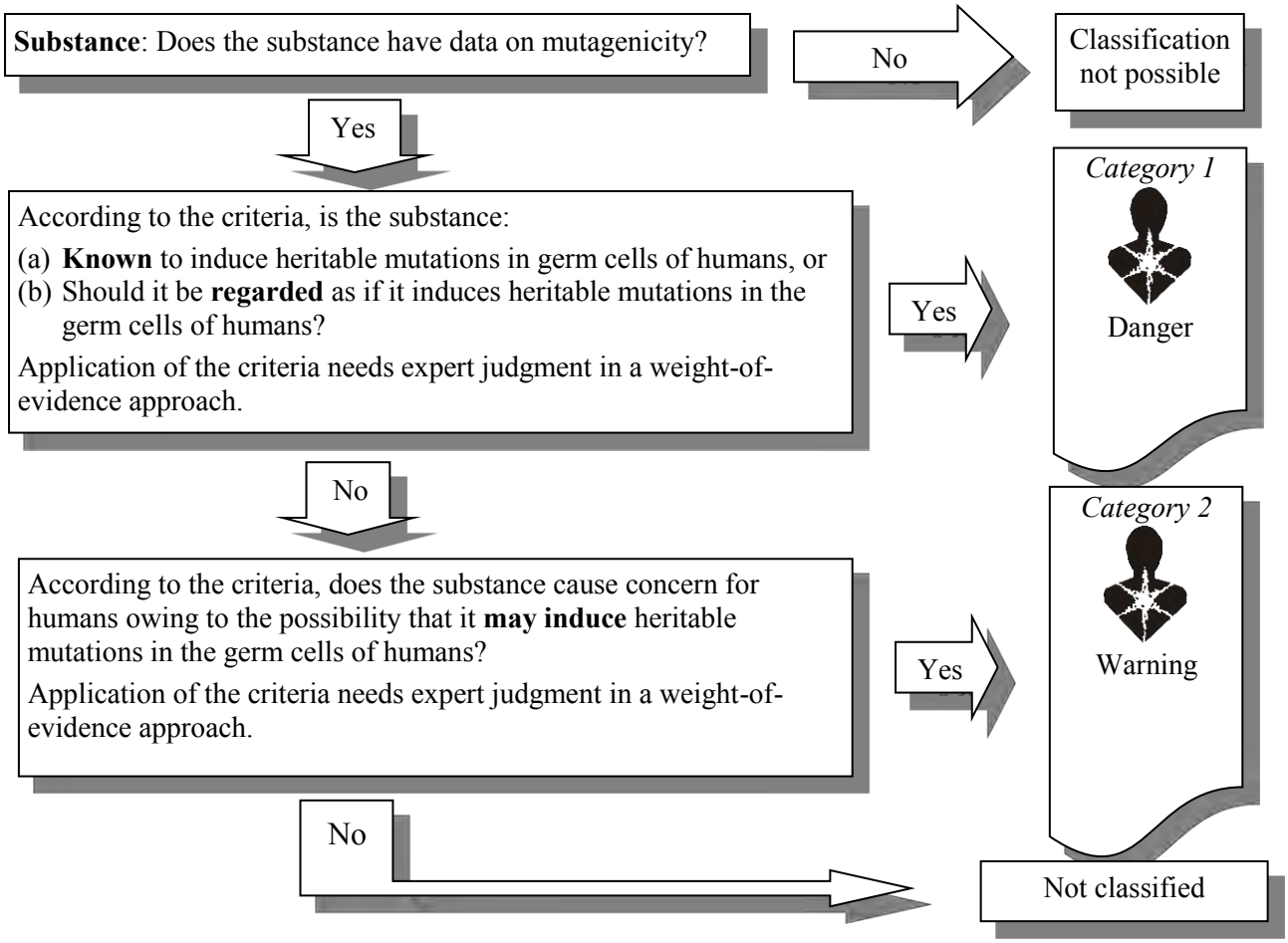
Considerations When Evaluating Positive/Contradictory Test Results	
Expert judgment	Conflicting results may also be available from the same test, performed by different laboratories or on different occasions. In this case, expert judgment should be used to reach an overall evaluation of the data. In particular, the quality of each of the studies and of the data provided should be evaluated, with special consideration of the study design, reproducibility of data, dose-effect relationships, and biological relevance of the findings. The purity of the test substance may also be a factor to take into account. In the case where an OECD guideline is available for a test method, the quality of a study using the method is regarded as being higher if it was conducted in compliance with the requirements stated in the guideline. Furthermore, studies compliant with Good Laboratory Practices (GLP) may be regarded as being of a higher quality.

Decision Logic

Two decision logics for classifying *germ cell mutagenicity* are provided. The first decision logic is for substances. Use the second decision logic for classifying mixtures. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logics.

These decision logics are essentially flowcharts for classifying substances and mixtures regarding germ cell mutagenicity. They present questions in a sequence that walks you through the classification steps and criteria for classifying germ cell mutagenicity. Once you answer the questions provided, you will arrive at the appropriate classification.

Substance decision logic for germ cell mutagenicity



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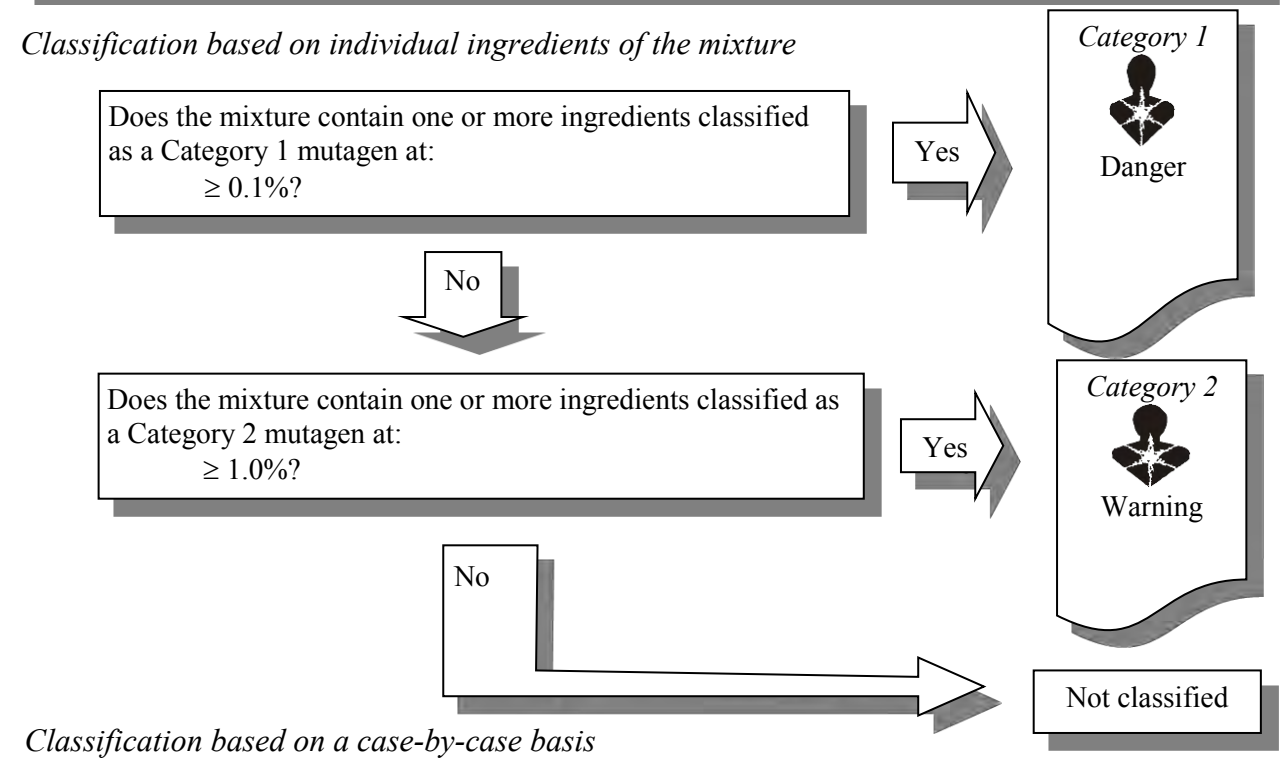
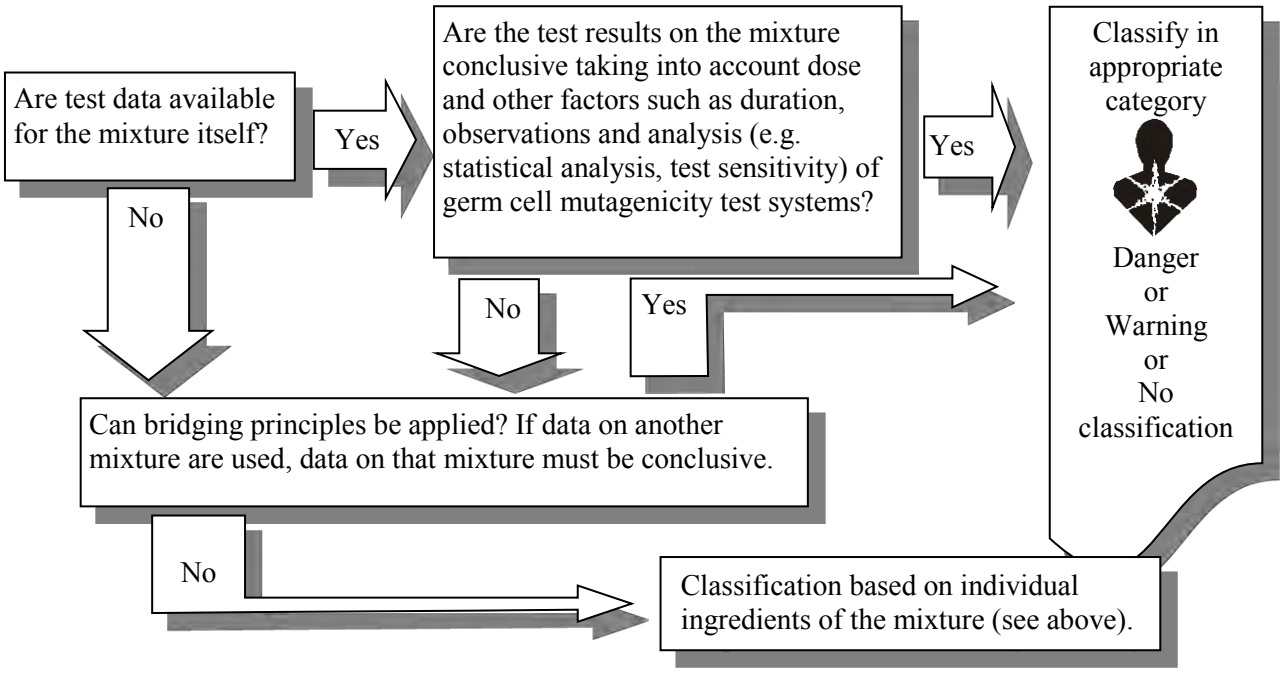
Mixtures decision logic for germ cell mutagenicity

Mixture:
Classification of mixtures will be based on the available test data for the **individual ingredients** of the mixture, using cut-off values/concentration limits for those ingredients. The classification may be **modified on a case-by-case basis** based on the available test data for the mixture itself or based on bridging principles. See modified classification on a case-by-case basis below.

Classification based on individual ingredients of the mixture



Classification based on a case-by-case basis



Germ cell mutagenicity Classification Examples

The following examples are provided to walk you through germ cell mutagenicity classification.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 **Germ Cell Mutagenicity**		
Test Data	**HCS 2012 Classification**	**Rationale**
Positive result in the Rodent Dominant Lethal Mutation Test (OECD Test Guideline 478)	Germ Cell Mutagenicity Category 1B	The test result fulfills the Germ Cell Mutagenicity Category 1B classification criteria of a positive result from an *in vivo* heritable germ cell mutagenicity test in mammals.

Substance Example #2 **Germ Cell Mutagenicity**		
Test Data	**HCS 2012 Classification**	**Rationale**
Positive result in the Mammalian Bone Marrow Chromosome Aberration Test (OECD Test Guideline 475)	Germ Cell Mutagenicity Category 2	The test result fulfills the Germ Cell Mutagenicity Category 2 classification criteria of positive evidence obtained from a somatic cell mutagenicity test *in vivo* in mammals

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 **Germ Cell Mutagenicity**		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1:0.09%, GCM Category 1B Component 2: 3%, GCM Category 2 Component 3: 2%, GCM Category 1B	Germ Cell Mutagenicity Category 1B	The GCM cut-off values/concentration limits are used for classification. – Component 1 is not ≥ 0.1% so the mixture does not meet the Category 1B criteria. – Component 2 is ≥ 1.0% so the mixture meets the Category 2 criteria. – Component 3 is ≥ 0.1% so the mixture meets the Category 1B criteria. When the criteria are satisfied by more than one ingredient for more than one category the most severe category is used to classify the mixture. Therefore, this mixture is classified as Germ Cell Mutagen Category 1B.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.5 Germ Cell Mutagenicity

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

VII.6 Carcinogenicity

Introduction

The terminology used to describe cancer may be confusing. Cancer is a type of tumor. A tumor (also known as a neoplasm) is simply an uncontrolled growth of cells. Tumors may be benign or malignant. Benign tumors grow only at the site of origin, and do not invade adjacent tissues or go to distant sites in the body (known as "metastasis"). Except for those that develop deep in vital organs (such as the brain), benign tumors can be successfully treated (usually by surgical removal) and the potential for causing death is low. Malignant tumors are cancers and can grow outside their original site in an organ, invade surrounding tissue, or metastasize to distant organs where they can start new growths of the cancerous tissue. Cancers vary greatly in type and behavior in the body. Some cancers grow slowly and rarely metastasize. Others are highly invasive and metastasize rapidly. Cancers are usually named for the specific cell type or organ of origination. For example, squamous cell carcinoma of the lung is a cancer that arose from a squamous cell in the lung. A hepatocellular carcinoma is a cancer arising from a liver cell (hepatocyte). Sometimes the name given to a cancer also reflects its nature. For example, chronic lymphocytic leukemia is a cancer involving lymphocytes (a type of blood cell) in which the leukemia is chronic or long-lasting in nature. OSHA, NTP, and IARC list the specific chemicals they consider to be carcinogens. These lists will be discussed later in this chapter.

Definition and General Considerations

Carcinogen means a substance or a mixture of substances which induces cancer or increases its incidence. Substances and mixtures which have induced benign and malignant tumors in well-performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans.

Classification of a substance or mixture as posing a carcinogenic hazard is based on its inherent properties and does not provide information on the level of the human cancer risk which the use of the substance or mixture may represent.

Classification Criteria for Substances

For the purpose of classification for carcinogenicity, substances are allocated to one of two categories based on strength of evidence and additional weight-of-evidence considerations. In certain instances, route-specific classification may be warranted.

Table VII.6.1 Hazard categories for carcinogens

Category	Criteria
CATEGORY 1	**Known or presumed human carcinogens** The classification of a substance as a Category 1 carcinogen is done on the basis of epidemiological and/or animal data. This classification is further distinguished on the basis of whether the evidence for classification is largely from human data (Category 1A) or from animal data (Category 1B).
Category 1A	**Known to have carcinogenic potential for humans.** Classification in this category is largely based on human evidence.
Category 1B	**Presumed to have carcinogenic potential for humans**. Classification in this category is largely based on animal evidence.
	The classification of a substance in Category 1A and 1B is based on strength of evidence together with weight-of-evidence considerations. Such evidence may be derived from: - human studies that establish a causal relationship between human exposure to a substance and the development of cancer (known human carcinogen); or - animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen). In addition, on a case-by-case basis, scientific judgment may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.
CATEGORY 2	**Suspected human carcinogens** The classification of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1A or B. This classification is based on strength of evidence together with weight-of-evidence considerations. Such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.
Other considerations	Where the weight of evidence for the carcinogenicity of a substance does not meet the above criteria, any positive study conducted in accordance with established scientific principles, and which reports statistically significant findings regarding the carcinogenic potential of the substance, must be noted on the safety data sheet.

Where OSHA has included cancer as a health hazard to be considered by classifiers for a chemical covered by 29 CFR part 1910, Subpart Z, Toxic and Hazardous Substances, chemical manufacturers, importers, and employers shall classify the chemical as a carcinogen. See the table below for the substance-specific OSHA standards listing cancer as a health effect.

Table VII.6.2 Standards listing cancer as a health effect

Standard Number	Substance
1910.1001	Asbestos
1910.1003	4-Nitrobiphenyl
1910.1004	alpha-Naphthylamine
1910.1006	Methyl chloromethyl ether
1910.1007	3,'-Dichlorobenzidine (and its salts)
1910.1008	bis-Chloromethyl ether
1910.1009	beta-Naphthylamine
1910.1010	Benzidine
1910.1011	4-Aminodiphenyl
1910.1012	Ethyleneimine
1910.1013	beta-Propiolactone
1910.1014	2-Acetylaminofluorene
1910.1015	4-Dimethylaminoazobenzene
1910.1016	N-Nitrosodimethylamine
1910.1017	Vinyl chloride
1910.1018	Inorganic arsenic
1910.1026	Chromium VI
1910.1027	Cadmium
1910.1028	Benzene
1910.1029	Coke oven emissions
1910.1044	1,2-dibromo-3-chloropropane
1910.1045	Acrylonitrile
1910.1047	Ethylene oxide
1910.1048	Formaldehyde
1910.1050	Methylenedianiline
1910.1051	1,3-Butadiene
1910.1052	Methylene chloride

Specific considerations for classification of substances as carcinogens

Classification as a carcinogen is made on the basis of evidence from reliable and acceptable methods, and is intended to be used for substances which have an intrinsic property to produce such toxic effects. The evaluations are to be based on all existing data, peer-reviewed published studies and additional data accepted by regulatory agencies.

Carcinogen classification is a one-step, criterion-based process that involves two interrelated determinations: evaluations of strength of evidence and consideration of all other relevant information to place substances with human cancer potential into hazard categories.

Strength of evidence involves the enumeration of tumors in human and animal studies and determination of their level of statistical significance. Sufficient human evidence demonstrates causality between human exposure and the development of cancer, whereas sufficient evidence in animals shows a causal relationship between the agent and an increased incidence of tumors. Limited evidence in humans is demonstrated by a positive association between exposure and cancer, but a causal relationship cannot be stated. Limited evidence in animals is provided when data suggest a carcinogenic effect, but are less than sufficient to demonstrate causation. (Guidance on consideration of important factors in the classification of carcinogenicity and a more detailed description of the terms "limited" and "sufficient" have been developed by the International Agency for Research on Cancer (IARC) and are provided in non-mandatory Appendix F to the HCS. See below detailed discussion.)

Weight-of-evidence: Beyond the determination of the strength of evidence for carcinogenicity, a number of other factors should be considered that influence the overall likelihood that an agent may pose a carcinogenic hazard in humans. These factors will be discussed later in this chapter.

Sources for establishing that a substance is a carcinogen or potential carcinogen

The following sources may be treated as establishing that a substance is a carcinogen or potential carcinogen for hazard communication purposes in lieu of applying the criteria described in Table VII.6.1:

- National Toxicology Program (NTP), "Report on Carcinogens" (latest edition)
- International Agency for Research on Cancer (IARC) "Monographs on the Evaluation of Carcinogenic Risks to Humans" (latest editions).

When performing classifications, the HCS provides classifiers with the option of relying on the classification listings of IARC and NTP to make classification decisions regarding carcinogenicity, rather than applying the criteria themselves. This will make classification easier, as well as lead to greater consistency in carcinogen classification. In addition, the HCS has provided guidance on hazard classification for carcinogenicity in non-mandatory Appendix F to 29 CFR 1910.1200. Part A of Appendix F includes background guidance provided by the GHS based on the Preamble of the IARC "Monographs on the Evaluation of Carcinogenic Risks to Humans" (2006). Part B provides IARC classification information. Part C provides background guidance from the National NTP "Report on Carcinogens" (RoC), and Part D is a table that compares HCS carcinogen hazard categories to carcinogen classifications under IARC and NTP, allowing classifiers to be able to use information from IARC and NTP RoC carcinogen classifications to complete their classifications under the HCS. The table relating carcinogen classification information from IARC and NTP to the HCS is provided below.

Table VII.6.3 Approximate Equivalences Among Carcinogen Classification Schemes

Approximate Equivalences Among Carcinogen Classification Schemes		
IARC	**HCS**	**NTP RoC**
Group 1	Category 1A	Known
Group 2A	Category 1B	Reasonably Anticipated (See Note 1)
Group 2B	Category 2	Reasonably Anticipated (See Note 1)

Note 1:

1. Limited evidence of carcinogenicity from studies in humans (corresponding to IARC 2A/HCS 1B);
2. Sufficient evidence of carcinogenicity from studies in experimental animals (again, essentially corresponding to IARC 2A/HCS 1B);
3. Less than sufficient evidence of carcinogenicity in humans or laboratory animals; however:
   a. The agent, substance, or mixture belongs to a well-defined, structurally-related class of substances whose members are listed in a previous RoC as either ‘‘Known’’ or ‘‘Reasonably Anticipated’’ to be a human carcinogen, or
   b. There is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

OSHA considers the determinations of IARC and NTP as sufficient evidence in establishing the classification of a carcinogen. If the classifier uses the determinations of IARC or NTP then they do not have to conduct their own weight-of-evidence evaluation with regards to carcinogenicity. However, if the classifier does perform their own hazard evaluation and their determination differs from that of IARC and/or NTP, they would need to justify with evidence why their classification result differs from that of IARC and/or NTP.

In addition, the National Institute for Occupational Safety and Health (NIOSH) has revised its policy for classifying carcinogens. The updated policy evaluates the carcinogen hazard assessments made by NTP, IARC, and the Environmental Protection Agency (EPA) and aligns their cancer designations into the appropriate HCS carcinogen categories. The classification scheme developed by NIOSH is an acceptable alternative to using Table VII.6.3.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

Examples of scientifically validated test methods

There are a number of scientifically validated methods for investigation of carcinogenic effects:

- OECD Test Guideline 451: Carcinogenicity Studies
- OECD Test Guideline 453: Combined Chronic Toxicity/Carcinogenicity Studies

Other test methodologies that meet the requirements for testing carcinogenicity potential include:

Carcinogenicity Studies:

- USEPA OTS code: 798.3300;
- USEPA OPP code: 83-2;
- USEPA OPPTS code: 870.4200;

Combined Chronic Toxicity and Carcinogenicity Studies:

- USEPA OTS code: 798.3320;
- USEPA OPP code: 83-5;
- USEPA OPPTS code: 870.4300;

The objective of a long-term carcinogenicity study is to observe test animals for a major portion of their life span for the development of neoplastic lesions during or after exposure to various doses of a test substance by an appropriate route of administration.

Carcinogenicity Studies (also known as Oncogenicity Studies) are performed to determine the carcinogenic potential and dose-response relationships of the test chemical. They produce data on the production of tumors as well as pre-neoplastic lesions and other indications of chronic toxicity that may provide evidence of treatment-related effects and insights into the mechanism of carcinogenesis. Given that development of tumors is age-related and that large groups are required to detect increases in treated animals, carcinogenicity studies are normally conducted in small rodents (usually mice and rats) over most of their life span.

Combined Chronic Toxicity/Carcinogenicity Studies encompass both neoplastic effects and general toxicity, including neurological, physiological, biochemical, hematological and pathological effects. Typically, rats are used for combined chronic toxicity/carcinogenicity assessment except in respect of the dermal route, for which mice are preferred. The study design incorporates groups of treated and control animals scheduled for interim sacrifice after 12 months of study for investigation of pathological abnormalities that are uncomplicated by age-related changes. OECD Test Guideline 453 and US EPA Health Effects Test Guidelines 870.4300 specify the same duration of exposure as in carcinogenicity studies.

Classification procedure

In classification, the data are compared to the carcinogenicity classification criteria. Data can be found in literature, on SDSs, or be determined by testing (which is not required by the HCS). For mixtures follow the modified three-tier approach discussed below.

If the data is available, then you must classify into the appropriate carcinogenicity sub-category, i.e., category 1A or category 1B. If the data does not allow classification into a sub-category, then you must classify in carcinogenicity category 1.

This guidance discusses some additional considerations in classification and an approach to analysis, rather than hard-and-fast rules. It is consistent with 29 CFR 1910.1200 Appendix A.6, and should help in evaluating information to determine carcinogenicity.

The terms "sufficient" and "limited" evidence are used in the HCS as they have been defined by IARC and are outlined below.

Carcinogenicity in humans The evidence relevant to carcinogenicity from studies in humans is classified into one of the following 2 categories:	
Sufficient evidence of carcinogenicity in humans:	A causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence.
Limited evidence of carcinogenicity in humans:	A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

Carcinogenicity in experimental animals The evidence relevant to carcinogenicity in experimental animals is classified into one of the following 2 categories:	
Sufficient evidence of carcinogenicity in experimental animals:	A causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in two or more species of animals or two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. An increased incidence of tumors in both sexes of a single species in a well-conducted study, ideally conducted under Good Laboratory Practices, can also provide sufficient evidence. Exceptionally, a single study in one species and sex might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumor or age at onset, or when there are strong findings of tumors at multiple sites.
Limited evidence of carcinogenicity in experimental animals:	The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g., the evidence of carcinogenicity is restricted to a single experiment; there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the studies; the agent increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential; or the evidence of carcinogenicity is restricted to studies that demonstrate only promoting activity in a narrow range of tissues or organs.

Guidance on how to consider important factors in classification of carcinogenicity

Carcinogenicity classification is based on strength of evidence and additional weight-of-evidence considerations. The weight-of-evidence analysis called for in the HCS is an integrative approach that considers important factors in determining carcinogenic potential along with the strength of evidence analysis.

The full list of factors that influence this determination is very lengthy, but some of the important ones are considered here. Factors can be viewed as either increasing or decreasing the level of concern for human carcinogenicity. The relative emphasis accorded to each factor depends upon the amount and coherence of evidence bearing on each. Generally there is a requirement for more complete information to decrease than to increase the level of concern.

Additional considerations (weight-of-evidence) should be used in evaluating the tumor findings and the other factors in a case-by-case manner. Some important factors which may be taken into consideration, when assessing the overall level of concern are summarized below.

Factors that increase concerns	
Tumor type and background incidence	A carcinogen that increases the incidence of a neoplastic disease that is rare in the test species or strain is of greater concern than a carcinogen that increases the incidence of a neoplasm having a high spontaneous incidence. Unusual tumor types or tumors occurring with reduced latency may add to the weight-of-evidence for the carcinogenic potential of a substance, even if the tumors are not statistically significant.
Reduced tumor latency	Unusual tumor types or tumors occurring with reduced latency may add to the weight-of-evidence for the carcinogenic potential of a substance, even if the tumors are not statistically significant.
Progression of lesions to malignancy	At first, it may appear logical that a carcinogen that increases only benign tumors in experimental animals is of lesser significance to human health than a test chemical that causes malignancies. However, it should never be assumed that an agent that causes benign tumors in animals will not cause malignancy in humans. In any case, benign tumors are potentially serious, even lethal, depending on their size, growth rate and site of origin.
Multiple responses	The formation of tumors at several sites is viewed with greater concern than tumor formation at a single site.
Whether responses are in single or both sexes	It is worth observing that a carcinogenic response in experimental animals is more significant for human health if it occurs in more than one species and/or in both sexes. If tumors are seen only in one sex of an animal species, the mode of action should be carefully evaluated to see if the response is consistent with the postulated mode of action. Effects seen only in one sex in a test species may be less convincing than effects seen in both sexes, unless there is a clear patho-physiological difference consistent with the mode of action to explain the single sex response.
Whether responses are in a single species or several species	Positive responses in several species add to the weight-of-evidence that a chemical is a carcinogen.
Responses in multiple animal experiments	A carcinogenic response confined to one species assumes greater human significance if it is seen in two or more studies conducted at different times, in different laboratories or under different protocols.

Factors that increase concerns	
	Taking into account all of the factors discussed here, chemicals with positive outcomes in two or more species would be provisionally considered to be classified in Category 1B until human relevance of animal results are assessed in their entirety. It should be noted, however, that positive results for one species in at least two independent studies, or a single positive study showing unusually strong evidence of malignancy may also lead to Category 1B.
Structural similarity to a chemical(s) for which there is good evidence of carcinogenicity Mode of action and its relevance to humans, such as mutagenicity, cytotoxicity with growth stimulation, mitogenesis, immunosuppression	A chemical that has not been tested for carcinogenicity may in certain instances be classified for carcinogenicity based on tumor data from a structural analogue together with substantial support from consideration of other important factors such as formation of common significant metabolites (e.g., for benzidine congener based dyes) Animal carcinogens that are genotoxic, or structurally similar to known human carcinogens, also assume greater significance. It is recognized that genetic events are central in the overall process of cancer development. Therefore evidence of mutagenic activity *in vivo* may indicate that a chemical has a potential for carcinogenic effects.

Factors that reduce concerns	
Comparison of absorption, distribution, metabolism and excretion between test animals and humans	If a metabolism and toxicokinetic behavior of a chemical in humans is fundamentally different from its behavior in the species in which it is carcinogenic, or if the animal study employs an inappropriate route of administration, or demonstrates carcinogenic activity only at doses that causes excessive toxicity.
Routes of exposure	Certain tumor types in animals may be associated with toxicokinetics or toxicodynamics that are unique to the animal species tested and may not be predictive of carcinogenicity in humans (e.g., the lack of human relevance of kidney tumors in male rats associated with compounds causing α2υ-globulin nephropathy). Even when a particular tumor type may be discounted, expert judgment must be used in assessing the total tumor profile in any animal experiment.

Factors that reduce concerns	
The possibility of a confounding effect of excessive toxicity at test doses	Tumors occurring only at excessive doses associated with severe toxicity generally have doubtful potential for carcinogenicity in humans.
Localized effects	In addition, tumors occurring only at sites of contact and/or only at excessive doses need to be carefully evaluated for human relevance for carcinogenic hazard (e.g., forestomach tumors, following administration by gavage of an irritating or corrosive, non-mutagenic chemical, may be of questionable relevance). However, such determinations must be evaluated carefully in justifying the carcinogenic potential for humans; any occurrence of other tumors at distant sites must also be considered.
Mode of action not relevant to humans	One must look closely at any mode of action in animal experiments taking into consideration comparative toxicokinetics/toxicodynamics between the animal test species and humans to determine the relevance of the results to humans. This may lead to the possibility of discounting very specific effects of certain types of chemicals. Life-stage-dependent effects on cellular differentiation may also lead to qualitative differences between animals and humans. Only if a mode of action of tumor development is conclusively determined not to be operative in humans may the carcinogenic evidence for that tumor be discounted. However, a weight-of-evidence evaluation for a substance calls for any other tumorigenic activity to be evaluated, as well.

In addition to the factors listed above, another important consideration with regard to carcinogen classification is the significance of a single positive study. In evaluating the weight-of-evidence, the carcinogen classification criteria indicate that one positive study conducted according to good scientific principles and with statistically and biologically significant positive results may justify classification. OSHA expects classification of a chemical if one positive study is available. However, if following the evaluation of available scientific data, the classifier deems non-classification to be the appropriate result, the one positive carcinogen study must still be communicated on the SDS.

Classification criteria for mixtures

It should be noted that the classification criteria for health hazards often include a tiered scheme in which test data available on the complete mixture are considered as the first tier in the evaluation, followed by the applicable bridging principles, and lastly, cut-off

values/concentration limits or additivity. However, this approach is not used for Carcinogenicity. The criteria for Carcinogenicity consider the cut-off values/concentration limits as the primary tier and allow the classification to be modified only on a case-by-case evaluation based on available test data for the mixture as a whole.

Tier 1: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

The approach to classifying a mixture for carcinogenicity in Tier 1 is to use a cut-off/concentration limit. An assessment is carried out separately for each Category 1A, Category 1B or Category 2 ingredient in the mixture. In the case where the mixture has Category 1A, Category 1B and Category 2 ingredients above the cut-off/concentration limit the mixture is classified in the most severe category.

The mixture will be classified as a carcinogen when at least one ingredient has been classified as a Category 1A, Category 1B or Category 2 Carcinogen and is present at or above the appropriate cut-off value/concentration limit specified below for Category 1 and Category 2, respectively.

Table VII.6.4. Cut-off values/concentration limits of ingredients of a mixture classified as a carcinogen that would trigger classification of the mixture

	Cut-off/concentration limits triggering classification of a mixture as:		
	Category 1 carcinogen		
Ingredient classified as:	**Category 1A**	**Category 1B**	**Category 2 carcinogen**
Category 1A carcinogen	≥ 0.1 %	--	--
Category 1B carcinogen	--	≥ 0.1 %	--
Category 2 carcinogen	--	--	≥ 0.1% (Note)

Note: If a Category 2 carcinogen ingredient is present in the mixture at a concentration between 0.1% and 1%, information is required on the SDS for the mixture. However, a label warning is optional. If a Category 2 carcinogen ingredient is present in the mixture at a concentration of ≥ 1%, both an SDS and a label are required and the information must be included on each.

Tier 2: Classification of mixtures when data are available for the complete mixture

On a case-by-case basis the classification which normally considers results obtained with the individual ingredients may be modified using available test data for the mixture as a whole.

The concern with using test data for the mixture as a whole is that as the concentration of a carcinogenic ingredient is reduced in a mixture the dilution effect may result in misleading test results (i.e., false negative) if the study was not appropriately designed to factor in the concentration of the carcinogenic ingredient in the mixture. In these cases, mixtures that would

cause cancer would not be classified and labeled. Accordingly, the GHS provides guidance that the test results for the mixture as a whole must be conclusive taking into account dose, and other factors such as duration, observations and analysis (e.g., statistical analysis, test sensitivity) of carcinogenicity test systems. If appropriate test data for the mixture is not available then the classifier can consider the application of the Bridging Principle criteria in Tier 3, if appropriate, or as stated above use the classification resulting from the application of criteria in Tier 1.

Tier 3: Classification of mixtures when data are not available for the complete mixture - bridging principles

Where the mixture itself has not been tested to determine its carcinogenic hazard, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the below bridging principles. If data on another mixture are used in the application of the bridging principles, the data on that mixture must be conclusive as discussed above in Tier 2.

Only the following bridging principles are applicable to the Carcinogenicity hazard class:

- Dilution,
- Batching,
- Substantially similar mixtures.

Dilution

If a tested mixture is diluted with a diluent that is not expected to affect the carcinogenicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

Batching

The carcinogenic potential of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product, when produced by or under the control of the same manufacturer unless there is reason to believe there is significant variation in composition such that the carcinogenic potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e., they are in the same hazard category and are not expected to affect the carcinogenicity of B.

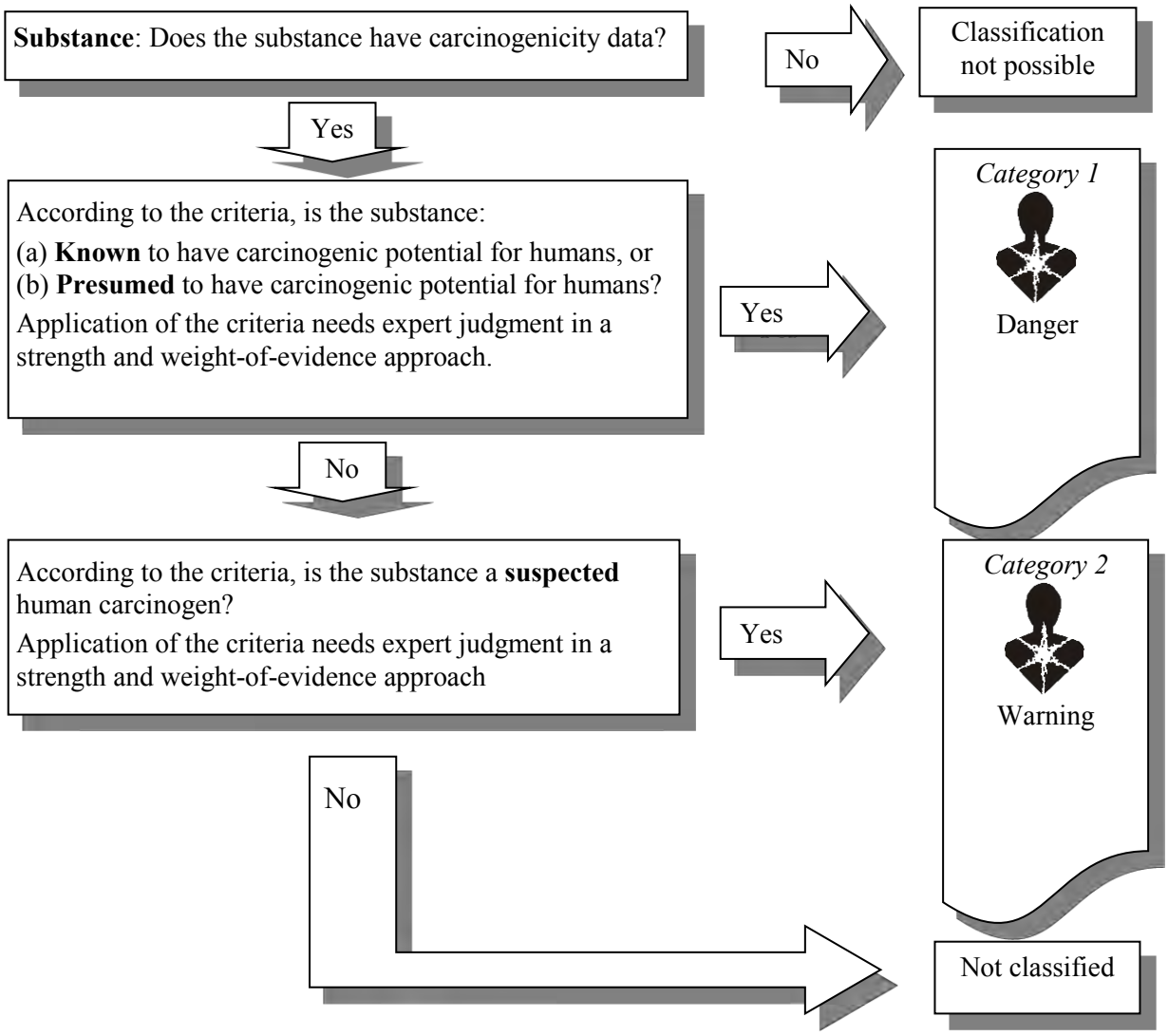
If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Decision Logic

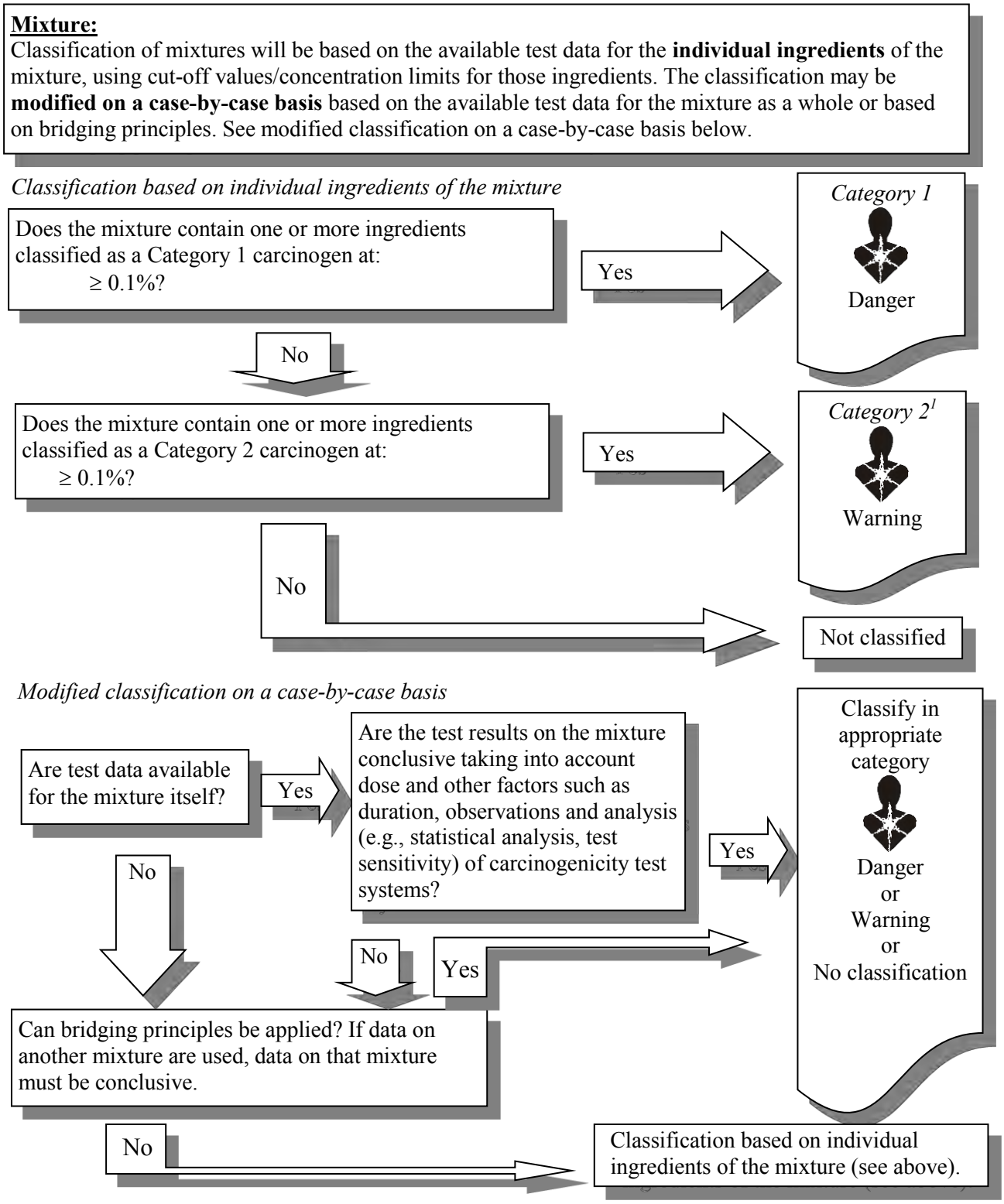
Two decision logics for classifying *carcinogenicity* are provided. The first decision logic is for substances. Use the second decision logic for classifying mixtures. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

These decision logics are essentially flowcharts for classifying substances and mixtures regarding carcinogenicity. They present questions in a sequence that walks you through the classification steps and criteria for classifying carcinogenicity. Once you answer the questions provided, you will arrive at the appropriate classification.

Substance decision logic for carcinogenicity



Mixtures decision logic for carcinogenicity



[1] Between 0.1% and 1% information is required on the SDS and a label warning is optional. At ≥ 1% both an SDS and a label are required.

Carcinogenicity Classification Examples

The following examples are provided to walk you through carcinogenicity classification.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1: S32 Carcinogenicity		
Test Data	**HCS 2012 Classification**	**Rationale**
Occupational exposure has been strongly associated with bladder cancer in numerous case reports from many countries. The association has also been observed in several epidemiological studies. In one extreme instance, all five of a group of workers continuously employed in S32 manufacture for 15 years or more developed bladder cancer. S32 was tested in mice, rats and hamsters by oral administration, in mice and rats by subcutaneous administration and in rats by inhalation and intraperitoneally. Following its oral administration to mice of different strains, both sexes, newborn and adult, and following its subcutaneous administration, it significantly increased the incidence of liver-cell tumors (benign and malignant). In female rats, it markedly increased the incidence of mammary tumors; and in male and female hamsters, it increased the incidence of liver tumors following its oral administration. S32 induced bladder carcinomas in dogs. The subcutaneous administration of S32 to rats produced a high incidence of Zymbal-gland tumors; colonic tumors were also reported. The results of the inhalation study in rats could not be interpreted. The intraperitoneal administration of S32 to rats resulted in a marked increase in the incidence of mammary and Zymbal-gland tumors. It was also tested in dogs by oral administration, producing bladder carcinomas. Studies in fish, rabbits and frogs could not be evaluated. No data were available on the genetic and related effects of S32 in humans.	Carcinogenicity Category 1A	Fulfills criteria – There is sufficient evidence that S32 is carcinogenic to mice, rats, hamsters and dogs and there is sufficient evidence that S32 is carcinogenic to humans – Sufficient human evidence demonstrates causality between human exposure and the development of cancer, and sufficient evidence in animals shows a causal relationship between S32 and an increased incidence of tumors fulfills HCS criteria

Substance Example #2: S33 Carcinogenicity		
Test Data	**HCS 2012 Classification**	**Rationale**
Five S33 samples all produced skin tumors, including carcinomas, when applied to the skin of mice. One of the S33 samples also produced lung tumors in mice after skin application. In two limited studies, a basic fraction of S33 was not carcinogenic for the skin of mice. S33 was mutagenic in S. typhimurium and was positive in the mouse lymphoma L5178Y system, in the presence of an exogenous metabolic system. The urine from rats administered S33 was mutagenic in S. typhimurium in the presence of an exogenous metabolic system. A mortality analysis of many occupations indicated an increased risk of mortality from scrotal cancer for S33-exposed workers. Malignant epitheliomas, about a third of which were of the scrotum, have been reported in several case reports of workers exposed to S33. A cohort study of workers in Norway and Sweden who had been exposed to S33 reported a statistically significant excess incidence of non-melanoma skin cancer. A study of workers in Norway did not report any statistically significant increase in the incidence of cancer, although the risk for non-melanoma cancer was slightly increased. A nested case–control study of lung cancer among a cohort of workers in France reported an increased risk for exposure to S33. A cohort study of workers in the USA who had used S33 indicated the possibility of an increase in mortality from lung cancer; a nested case–control study found no evidence of an exposure–response relationship between exposure to S33 and cancer. A study that applied a job–exposure matrix to job titles in the Swedish census and linked this to cancer incidence found an increase in the incidence of urinary bladder cancer that was related to S33.	Carcinogen Category 1B	Fulfills criteria – There is *sufficient evidence* for the carcinogenicity in experimental animals of S33. There is *limited evidence* that S33 is carcinogenic in humans. The data indicate that S33 is probably carcinogenic to humans. – The category 1B criteria are fulfilled by evidence from animal experiments for which there is sufficient evidence to demonstrate animal carcinogenicity (presumed human carcinogen) and limited evidence in humans.

Substance Example #3 Carcinogenicity		
Test Data	**HCS 2012 Classification**	**Rationale**
NTP listed as *Reasonably Anticipated to be Human Carcinogen* IARC listed as Group 2B*: Possibly Carcinogenic to Humans* ACGIH listed as Category A3: *Confirmed Animal Carcinogen with Unknown Relevance to Humans* Listed in EU CLP Table 3.1 as Category 2/Table 3.2 Category 3	Carcinogen Category 2	Fulfills criteria – Due to the fact that the substance is listed by NTP as *Reasonably Anticipated to be Human Carcinogen* and by IARC as *Group 2B* – Per 29 CFR 1910.1200 A.6.4, NTP and IARC may be treated as establishing that a substance is a carcinogen or potential carcinogen for hazard communication purposes in lieu of applying the criteria – Per 29 CFR 1910.1200 Annex F Part D, IARC Group 2B is Carcinogen Category 2

Substance Example #4 Carcinogenicity		
Test Data	**HCS 2012 Classification**	**Rationale**
Listed by NTP as *Reasonably Anticipated to be Human Carcinogen*) Listed by IARC as Group 2A: *Probably Carcinogenic to Humans* Listed as 2A: *Probably Carcinogenic to Humans* by the Japan Society for Occupational Health	Carcinogen Category 1B	Fulfills criteria – Due to the fact that the substance is listed by NTP as *Reasonably Anticipated to be Human Carcinogen* and by IARC as *Group 2A* – Per 29 CFR 1910.1200 A.6.4, NTP and IARC may be treated as establishing that a substance is a carcinogen or potential carcinogen for hazard communication purposes in lieu of applying the criteria – Per 29 CFR 1910.1200 Annex F Part D, IARC Group 2A is Carcinogen Category 1B

Example of a substance not fulfilling the criteria for classification:

Substance Example #5 Carcinogenicity		
Test Data	**HCS 2012 Classification**	**Rationale**
Listed by IARC as Group 3: *Not Classifiable as to Carcinogenicity to Humans* Listed by ACGIH as Category A4: *Not Classifiable as a Human Carcinogen* Listed by EPA as Category D: *Not Classifiable as to Human Carcinogenicity*	Not classified for Carcinogenicity	Does not fulfill criteria – The substance is listed by IARC as *Group 3* – Per 29 CFR 1910.1200 A.6.4, NTP and IARC may be treated as establishing that a substance is a carcinogen or potential carcinogen for hazard communication purposes in lieu of applying the criteria – Per 29 CFR 1910.1200 Annex F Part D, IARC Group 3 is not an equivalent cancer HCS 2012 classification

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 Carcinogenicity		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 0.05%, Carcinogen Category 1B Component 2: 0.5%, Carcinogen Category 2	Carcinogen Category 2	Fulfills the criteria – Component 1 is not ≥ 0.1% so the mixture does not meet the Carcinogen Category 1B criteria. – Component 2 is ≥ 0.1% so the mixture meets the Carcinogen Category 2 criteria. This mixture is classified as Carcinogen Category 2 and a label warning is optional.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.6 Carcinogenicity

29 CFR 1910.1200, Hazard Communication, Appendix F Guidance for Hazard Classifications Re: Carcinogenicity (Non-Mandatory)

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements

National Toxicology Program (NTP), "Report on Carcinogens" (latest edition)

International Agency for Research on Cancer (IARC) "Monographs on the Evaluation of Carcinogenic Risks to Humans" (latest editions).

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

VII.7 Reproductive Toxicity

Introduction

The term “reproductive toxicity” is used to describe the adverse effects induced by a chemical on any aspect of mammalian reproduction. It covers all phases of the reproductive cycle, including impairment of male or female reproductive organs and/or function or capacity and the induction of non-heritable adverse effects in the progeny such as death, growth retardation, structural and functional effects.

Definition and General Considerations

Reproductive toxicity includes *adverse effects on sexual function and fertility* in adult males and females, as well as *adverse effects on development of the offspring*. Some reproductive toxic effects cannot be clearly assigned to either impairment of sexual function and fertility or to developmental toxicity. Nonetheless, chemicals with these effects shall be classified as reproductive toxicants.

For classification purposes, the known induction of genetically based inheritable effects in the offspring is addressed in the *Germ cell mutagenicity* hazard class (see Chapter VII.5).

Adverse effects on sexual function and fertility means any effect of a chemical that interferes with reproductive ability or sexual capacity. This includes, but is not limited to, alterations to the female and male reproductive system; adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, parturition, or pregnancy outcomes; premature reproductive senescence; or modifications in other functions that are dependent on the integrity of the reproductive systems.

Adverse effects on development of the offspring means any effect of a chemical that interferes with normal development of the conceptus either before or after birth, which is induced during pregnancy or results from parental exposure. These effects can be manifested at any point in the life span of the organism. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth and functional deficiency. A term often used to describe effects manifested as malformations of the newborn is teratogenicity.

Adverse effects on or via lactation are also included in reproductive toxicity, but for classification purposes, such effects are treated in a separate hazard category.

Classification Criteria for Substances

For the purpose of classification for reproductive toxicity, substances shall be classified in one of two categories. Category 1, known or presumed human reproductive toxicant, is subdivided into two subcategories according to specific criteria outlined below. Category 2 includes criteria for suspected human reproductive toxicants. Effects on sexual function and fertility, and on development, shall also be considered. In addition, effects on or via lactation shall be classified in a separate hazard category.

Table VII.7.1. Hazard categories for reproductive toxicants

Category	Criteria
CATEGORY 1	**Known or presumed human reproductive toxicant** A substance shall be classified in Category 1 for reproductive toxicity when it is known to have produced an adverse effect on sexual function and fertility or on development in humans or when there is evidence from animal studies, possibly supplemented with other information, to provide a strong presumption that the substance has the capacity to interfere with reproduction in humans. The classification of a substance is further distinguished on the basis of whether the evidence for classification is primarily from human data (Category 1A) or from animal data (Category 1B).
Category 1A	**Known human reproductive toxicant** The classification of a substance in this category is largely based on evidence from humans.
Category 1B	**Presumed human reproductive toxicant** The classification of a substance in this category is largely based on evidence from experimental animals. Data from animal studies shall provide sufficient evidence of an adverse effect on sexual function and fertility or on development in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of other toxic effects. However, when there is mechanistic information that raises doubt about the relevance of the effect for humans, classification in Category 2 may be more appropriate.
CATEGORY 2	**Suspected human reproductive toxicant** A substance shall be classified in Category 2 for reproductive toxicity when there is some evidence from humans or experimental animals, possibly supplemented with other information, of an adverse effect on sexual function and fertility, or on development, in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of the other toxic effects, and where the evidence is not sufficiently convincing to place the substance in Category 1. For instance, deficiencies in the study may make the quality of evidence less convincing, and in view of this, Category 2 would be the more appropriate classification.

Table VII.7.2. Hazard category for effects on or via lactation

Category	Criteria
Effects On or Via Lactation	Effects on or via lactation shall be classified in a separate single category. Chemicals that are absorbed by women and have been shown to interfere with lactation or that may be present (including metabolites) in breast milk in amounts sufficient to cause concern for the health of a breastfed child, shall be classified to indicate this property.[15] Classification for effects via lactation shall be assigned on the basis of:[16] (a) absorption, metabolism, distribution and excretion studies that indicate the likelihood the substance would be present in potentially toxic levels in breast milk; and/or (b) results of one or two generation studies in animals which provide clear evidence of adverse effect in the offspring due to transfer in the milk or adverse effect on the quality of the milk; and/or (c) human evidence indicating a hazard to babies during the lactation period.

Basis of classification for Reproductive Toxicity

Classification for reproductive toxicity is on the basis of the criteria, an assessment of the total weight-of-evidence, and the use of expert judgment. Classification as a reproductive toxicant is intended to be used for chemicals that have an intrinsic, specific property to produce an adverse effect on reproduction; chemicals should not be so classified if such an effect is produced solely as a non-specific secondary consequence of other toxic effects.

In the evaluation of toxic effects on the developing offspring, it is important to consider the possible influence of maternal toxicity.

CATEGORY 1
Classification in Category 1A is largely based on evidence from humans. Evidence used for classification shall be from well-conducted epidemiological studies, if available, which include the use of appropriate controls, balanced assessment, and consideration of bias or confounding factors. Less rigorous data from studies in humans may be sufficient for a Category 1A classification if supplemented with adequate data from studies in experimental animals, but classification in Category 1B may also be considered.

[15] In Figure A.7.1(b) of Appendix A of 29 CFR 1910.1200 this sentence ends with the phrase "hazardous to breastfed babies." The inclusion of that language renders the sentence grammatically incorrect, and incorrect as a matter of substance, because classification can also be based on effects on lactation, rather than only effects via lactation. OSHA intends to correct the sentence in the standard.
[16] The words "for effects via lactation" do not appear in Figure A.7.1.(b) of Appendix A of 29 CFR 1910.1200, but the words are inserted here to make clear that the stated criteria only apply to that effect, and do not apply to exclude classification for effects on lactation. OSHA intends to correct the sentence in the standard.

Weight-of-evidence

Classification as a reproductive toxicant is made on the basis of an assessment of the total weight-of-evidence using expert judgment. This means that all available information that bears on the determination of reproductive toxicity is considered together. Included is information such as epidemiological studies and case reports in humans and specific reproduction studies along with sub-chronic, chronic and special study results in animals that provide relevant information regarding toxicity to reproductive and related endocrine organs. Evaluation of substances chemically related to the material under study may also be included, particularly when information on the material is scarce. The weight given to the available evidence will be influenced by factors such as

- the quality of the studies;
- consistency of results;
- nature and severity of effects;
- level of statistical significance for intergroup differences;
- number of endpoints affected;
- relevance of route of administration to humans; and
- freedom from bias.

Both positive and negative results are considered together in a weight-of-evidence determination. However, a single, positive study performed according to good scientific principles and with statistically or biologically significant positive results should be enough to justify classification unless the classifier shows that there is no relevance to humans or exposure as discussed below.

Considerations When Evaluating Weight-of-Evidence

Factors	**Weight-of-Evidence Evaluation**
Experimental data quality/ adequacy:	A number of internationally accepted test methods are available; these include methods for developmental toxicity testing, methods for peri-natal and post-natal toxicity testing and methods for one- or two-generation toxicity testing. Results obtained from screening tests can also be used to justify classification, although it is recognized that the quality of this evidence is less reliable than that obtained through full studies. Adverse effects or changes, seen in short- or long-term repeated dose toxicity studies, which are judged likely to impair reproductive function and which occur in the absence of significant generalized toxicity, may be used as a basis for classification, e.g., histopathological changes in the gonads.

Factors	Weight-of-Evidence Evaluation
	Evidence from *in vitro* assays, or non-mammalian tests, and from analogous substances using structure-activity relationship (SAR), can contribute to the procedure for classification. In all cases of this nature, expert judgment must be used to assess the adequacy of the data. Inadequate data should not be used as a primary support for classification. A single, positive study performed according to good scientific principles and with statistically or biologically significant positive results should justify classification.
Toxicokinetics/ mode of action:	If it can be conclusively demonstrated that the clearly identified mechanism or mode of action has no relevance for humans or when the toxicokinetic differences are so marked that it is certain that the hazardous property will not be expressed in humans, then a substance that produces an adverse effect on reproduction in experimental animals should not be classified.
Routes of administration:	It is preferable that animal studies are conducted using appropriate routes of administration which relate to the potential route of human exposure. However, in practice, reproductive toxicity studies are commonly conducted using the oral route, and such studies will normally be suitable for evaluating the hazardous properties of the substance with respect to reproductive toxicity. Studies involving routes of administration such as intravenous or intraperitoneal injection, which may result in exposure of the reproductive organs to unrealistically high levels of the test substance, or which elicit local damage to the reproductive organs, (e.g., by irritation) must be interpreted with extreme caution, such studies on their own would not normally be the basis for classification.
Limit dose:	There is general agreement about the concept of a limit dose, above which the production of an adverse effect may be considered to be outside the criteria which lead to classification. Some test guidelines specify a limit dose; other test guidelines qualify the limit dose with a statement that higher doses may be necessary if anticipated human exposure is sufficiently high that an adequate margin of exposure would not be achieved. Also, due to species differences in toxicokinetics, establishing a specific limit dose may not be adequate for situations where humans are more sensitive than the animal model.

Factors	Weight-of-Evidence Evaluation
	In principle, adverse effects on reproduction seen only at very high dose levels in animal studies (for example, doses that induce prostration, severe inappetence, excessive mortality) would not normally lead to classification, unless other information is available, e.g., toxicokinetics information indicating that humans may be more susceptible than animals, to suggest that classification is appropriate. Specification of the actual "limit dose" will depend upon the test method that has been used to provide the test results (e.g., in the OECD Test Guideline for repeated dose toxicity studies by the oral route, an upper dose of 1000 mg/kg) unless expected human response indicates the need for a higher dose level to be used as a limit dose.
Effects of minimal or low toxicological significance:	In some reproductive toxicity studies in experimental animals the only effects recorded may be considered of low or minimal toxicological significance and classification may not necessarily be the outcome. These include, for example, small changes in semen parameters or in the incidence of spontaneous defects in the fetus, small changes in the proportions of common fetal variants such as are observed in skeletal examinations, or in fetal weights, or small differences in postnatal developmental assessments.
Maternal toxicity:	If developmental toxicity occurs together with other toxic effects in the dam (mother), the potential influence of the generalized adverse effects should be assessed to the extent possible. The preferred approach is to consider adverse effects in the embryo/fetus first, and then evaluate maternal toxicity, along with any other factors, which are likely to have influenced these effects. Generally, the presence of maternal toxicity should not be used to negate findings of embryo/fetal effects, unless it can be clearly demonstrated that the effects are secondary non-specific effects (e.g., maternal stress, disruption of homeostasis). Developmental effects, which occur even in the presence of maternal toxicity, are considered to be evidence of developmental toxicity, unless it can be unequivocally demonstrated on a case-by-case basis that the developmental effects are secondary to maternal toxicity. Moreover, classification should be considered where there is significant toxic effect in the offspring, e.g., irreversible effects such as structural malformations, embryo/fetal lethality, or significant post-natal functional deficiencies.

Factors	Weight-of-Evidence Evaluation
	Classification should not automatically be discounted for chemicals that produce developmental toxicity only in association with maternal toxicity, even if a specific maternally-mediated mechanism has been demonstrated. In such a case, classification in Category 2 may be considered more appropriate than Category 1. However, when a chemical is so toxic that maternal death or severe inanition results, or when the dams (mothers) are prostrate and incapable of nursing the pups, it may be reasonable to assume that developmental toxicity is produced solely as a secondary consequence of maternal toxicity and discount the developmental effects. Classification may not necessarily be the outcome in the case of minor developmental changes (e.g., small reduction in fetal/pup body weight, or retardation of ossification when seen in association with maternal toxicity).

Maternal toxicity

Maternal toxicity deserves careful consideration. Development of the offspring throughout gestation and during the early postnatal stages can be influenced by toxic effects in the mother either through non-specific mechanisms related to stress and the disruption of maternal homeostasis, or by specific maternally-mediated mechanisms. So, in the interpretation of the developmental outcome that is used to decide classification for developmental effects, it is important to consider the possible influence of maternal toxicity. This is a complex issue because of uncertainties surrounding the relationship between maternal toxicity and developmental outcome. Expert judgment and a weight-of-evidence approach, using all available studies, shall be used to determine the degree of influence to be attributed to maternal toxicity when interpreting the criteria for classification for developmental effects. As weight-of-evidence to help reach a conclusion about classification, the adverse effects in the embryo/fetus shall be first considered; and then maternal toxicity, along with any other factors which are likely to have influenced these effects.

Based on pragmatic observation, it is believed that maternal toxicity may, depending on severity, influence development via non-specific secondary mechanisms, producing effects such as depressed fetal weight, retarded ossification, and possibly resorptions and certain malformations in some strains of certain species. However, the limited number of studies which have investigated the relationship between developmental effects and general maternal toxicity have failed to demonstrate a consistent, reproducible relationship across species.

Some of the endpoints used to assess maternal toxicity are provided below. Data on these endpoints, if available, shall be evaluated in light of their statistical or biological significance and dose-response relationship.

(a) *Maternal mortality*: An increased incidence of mortality among the treated dams over the controls shall be considered evidence of maternal toxicity if the increase occurs in a dose-related manner and can be attributed to the systemic toxicity of the test material. Maternal mortality greater than 10% is considered excessive and the data for that dose level shall not normally be considered to need further evaluation.

(b) *Mating index* (Number of animals with seminal plugs or sperm/Number of matings × 100)

(c) *Fertility index* (Number of animals with implants/Number of matings × 100)

(d) *Gestation length* (If allowed to deliver)

(e) *Body weight and body weight change*: Consideration of the maternal body weight change and/or adjusted (corrected) maternal body weight shall be included in the evaluation of maternal toxicity whenever such data are available. The calculation of an adjusted (corrected) mean maternal body weight change, which is the difference between the initial and terminal body weight minus the gravid uterine weight (or alternatively, the sum of the weights of the fetuses), may indicate whether the effect is maternal or intrauterine. In rabbits, the body weight gain may not be a useful indicator of maternal toxicity because of normal fluctuations in body weight during pregnancy.

(f) *Food and water consumption* (if relevant): The observation of a significant decrease in the average food or water consumption in treated dams (mothers) compared to the control group may be useful in evaluating maternal toxicity, particularly when the test material is administered in the diet or drinking water. Changes in food or water consumption must be evaluated in conjunction with maternal body weights when determining if the effects noted are reflective of maternal toxicity or, more simply, unpalatability of the test material in feed or water.

(g) *Clinical evaluations* (including clinical signs, markers, and hematology and clinical chemistry studies): The observation of increased incidence of significant clinical signs of toxicity in treated dams (mothers) relative to the control group is useful in evaluating maternal toxicity. If this is to be used as the basis for the assessment of maternal toxicity, the types, incidence, degree and duration of clinical signs shall be reported in the study. Clinical signs of maternal intoxication include, but are not limited to: coma, prostration, hyperactivity, loss of righting reflex, ataxia, or labored breathing.

(h) *Post-mortem data*: Increased incidence and/or severity of post-mortem findings may be indicative of maternal toxicity. This can include gross or microscopic pathological findings or organ weight data, including absolute organ weight, organ-to-body weight ratio, or organ-to-brain weight ratio. When supported by findings of adverse histopathological effects in the affected organ(s), the observation of a significant change

in the average weight of suspected target organ(s) of treated dams (mothers), compared to those in the control group, may be considered evidence of maternal toxicity.

Classification criteria for mixtures

It should be noted that the classification criteria for health hazards often include a tiered scheme in which test data available on the complete mixture are considered as the first tier in the evaluation, followed by the applicable bridging principles, and lastly, cut-off values/concentration limits or additivity. However, this approach is not used for Reproductive Toxicity. The criteria for Reproductive Toxicity consider the cut-off values/concentration limits as the primary tier and allow the classification to be modified only on a case-by-case evaluation based on available test data for the mixture as a whole.

Tier 1: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

The approach to classifying a mixture for reproductive toxicity in Tier 1 is to use a cut-off/concentration limit. An assessment is carried out separately for each Category 1A, Category 1B or Category 2 ingredient in the mixture. In the case where the mixture has Category 1A, Category 1B and Category 2 ingredients above the cut-off/concentration limit, the mixture is classified in the most severe category.

The mixture will be classified as a reproductive toxicant when at least one ingredient has been classified as a Category 1A, Category 1B or Category 2 reproductive toxicant and is present at or above the appropriate cut-off value/concentration limit specified below for Category 1 and Category 2, respectively.

Additionally, a separate evaluation will be made to determine if the mixture will be classified for effects on or via lactation. If at least one ingredient in the mixture is classified in the category for effects on or via lactation and is present at or above the appropriate cut-off/concentration limit, then the mixture will be classified for effects on or via lactation.

Table VII.7.3. Cut-off values/concentration limits of ingredients of a mixture classified as reproductive toxicants or for effects on or via lactation that would trigger classification of the mixture

Ingredient classified as:	Cut-off/concentration limits triggering classification of a mixture as:			
	Category 1 reproductive toxicant		Category 2 reproductive toxicant	Additional category for effects on or via lactation
	Category 1A	Category 1B		
Category 1A reproductive toxicant	≥ 0.1%	--	--	--
Category 1B reproductive toxicant	--	≥ 0.1%	--	--
Category 2 reproductive toxicant	--	--	≥ 0.1%	--
Additional category for effects on or via lactation	--	--	--	≥ 0.1%

Tier 2: Classification of mixtures when data are available for the complete mixture

On a case-by-case basis the Reproductive Toxicity classification, which normally considers results obtained with the individual ingredients, may be modified using available test data for the mixture as a whole.

The concern with using test data for the mixture as a whole is that as the concentration of a reproductive toxicant is reduced in a mixture the dilution effect may result in a misleading test results (i.e., false negative) if the study was not appropriately designed to factor in the concentration of the reproductive toxicant in the mixture. In these cases, mixtures that would cause Reproductive Toxicity would not be classified and labeled. Accordingly, the HCS provides guidance that the test results for the mixture as a whole must be conclusive, taking into account dose, and other factors such as duration, observations and analysis (e.g., statistical analysis, test sensitivity) of reproduction test systems.

If appropriate test data for the mixtures is not available, then the classifier can consider the application of the Bridging Principle criteria in Tier 3, if appropriate, or use the classification resulting from the application of the criteria in Tier 1.

Tier 3: Classification of mixtures when data are not available for the complete mixture - bridging principles

Where the mixture itself has not been tested to determine its reproductive toxicity, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, then these data can be used in accordance with the bridging principles below. If data on another mixture are used in the application of the bridging principles, the data on that mixture must be conclusive as discussed in Tier 2 above.

Only the following bridging principles are applicable to the Reproductive Toxicity hazard class:

- Dilution,
- Batching,
- Substantially similar mixtures.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential reproductive toxicity hazard.

Dilution

If a tested mixture is diluted with a diluent which is not expected to affect the reproductive toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

Batching

The reproductive toxicity potential of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product, when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation in composition such that the reproductive toxicity potential of the untested batch has changed. If the latter occurs, a new classification is necessary.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent (i.e., they are in the same hazard category and are not expected to affect the reproductive toxicity of B).

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical. Data generated in accordance with internationally recognized scientific principles are acceptable under the HCS.

Examples of scientifically validated test methods

There are a number of internationally recognized methods for investigation of reproductive toxicity effects:

- Prenatal Developmental Toxicity Study (OECD Test Guideline 414)
- One-Generation Reproduction Toxicity Study (OECD Test Guideline 415)
- Two-Generation Reproduction Toxicity Study (OECD Test Guideline 416)
- Reproduction/Developmental Toxicity Screening Test (OECD Test Guideline 421)
- Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD Test Guideline 422)

Other test methodologies that meet the requirements for testing of reproductive toxicity include:

- Preliminary developmental toxicity screen (EPA 798.4420/870.3500)
- Inhalation developmental toxicity study (EPA 798.4350/870.3600)
- Prenatal developmental toxicity study (EPA 798.4900/ 870.3700)
- Prenatal developmental toxicity study (EEC Directive 92/32/EEC B.31)
- Reproduction and fertility effects (EPA 798.4700/870.3800)
- One-generation reproduction toxicity test study (EEC Directive 92/32/EEC B.34)
- Two-generation reproduction toxicity study (EEC Directive 92/32/EEC B.35)

Classification procedure

In classification, the data are compared to the reproductive toxicity classification criteria. If valid data on the reproductive toxicity of a substance or mixture are available, then these data should be used for classification. To find the necessary data, a classifier is advised to try the following:

- ask the manufacturer or supplier for the reproductive toxicity data for the product; or
- check to see if the reproductive toxicity data is available in the SDS or any other documentation accompanying the product; or
- find the data available in the open literature if the chemical identity of the product is known (for a single-component chemical).

For mixtures follow the three-tier approach discussed above.

Considerations

Classification is made on the basis of the appropriate HCS criteria and an assessment of the total *weight-of-evidence*. The validity and usefulness of each test data set to the overall assessment of reproductive toxicity should be individually assessed, taking account of protocol design (including route of administration) and current expert views on the value of the test systems.

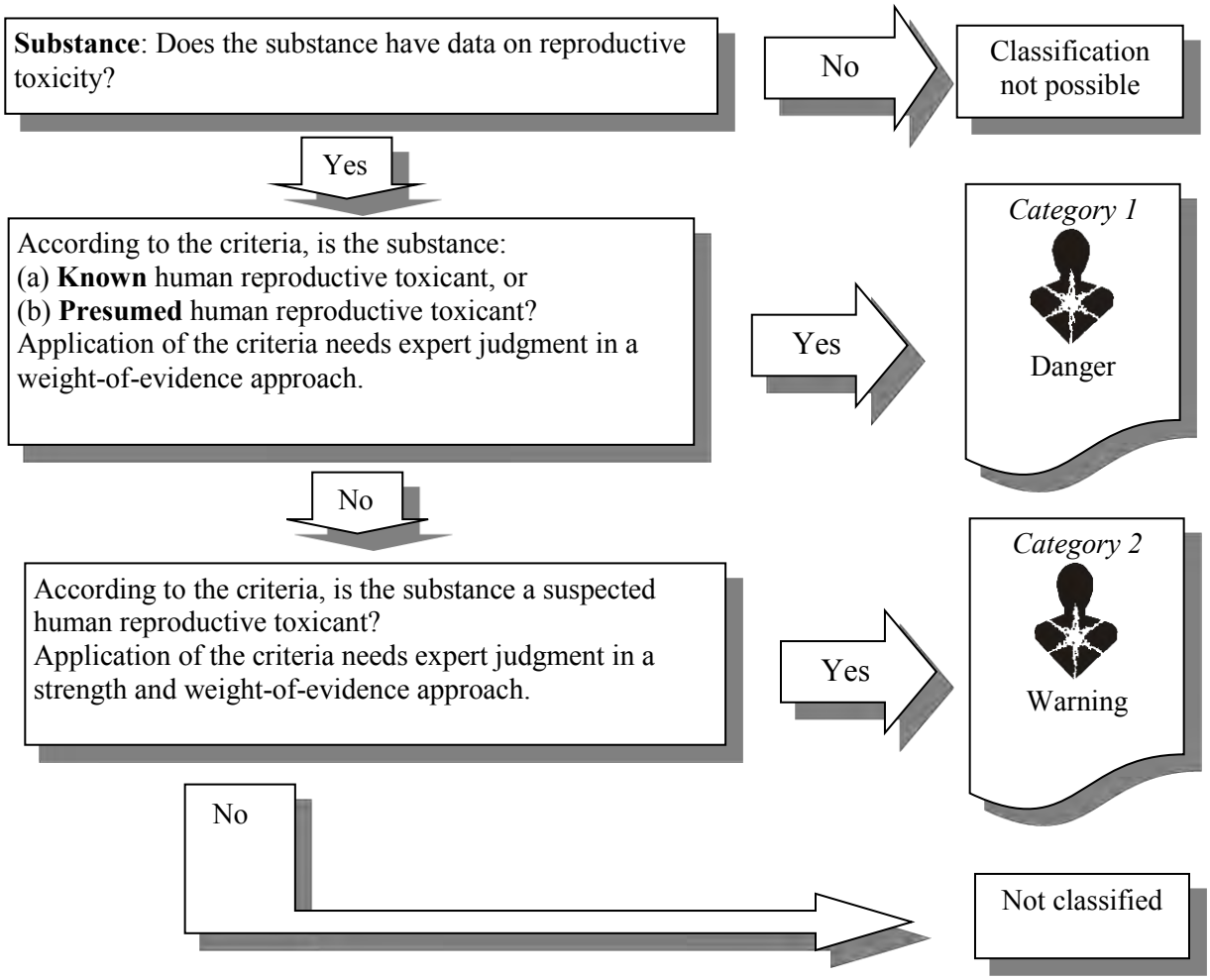
If the data are available, then you must classify into the appropriate reproductive toxicity sub-category (i.e., category 1A or category 1B). If the data does not allow classification into a sub-category, then you must classify in reproductive toxicity category 1.

Decision logic

Three decision logics for classifying *reproductive toxicity* are provided. The first decision logic is for reproductive toxic substances. Use the second decision logic for classifying reproductive toxic mixtures. There is an additional decision logic for classifying effects on or via lactation for both substances and mixtures. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

These decision logics are essentially flowcharts for classifying substances and mixtures regarding reproductive toxicity. They present questions in a sequence that walks you through the classification steps and criteria for classifying reproductive toxicity. Once you answer the questions provided, you will arrive at the appropriate classification.

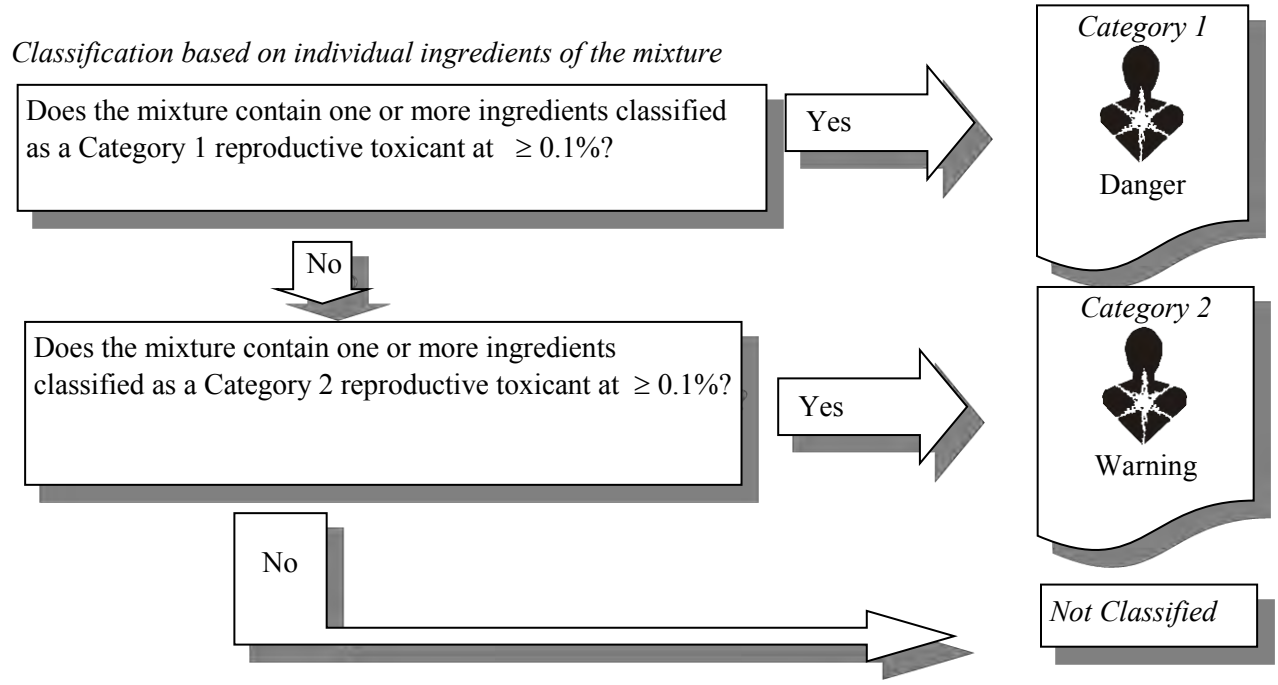
Substance decision logic for reproductive toxicity



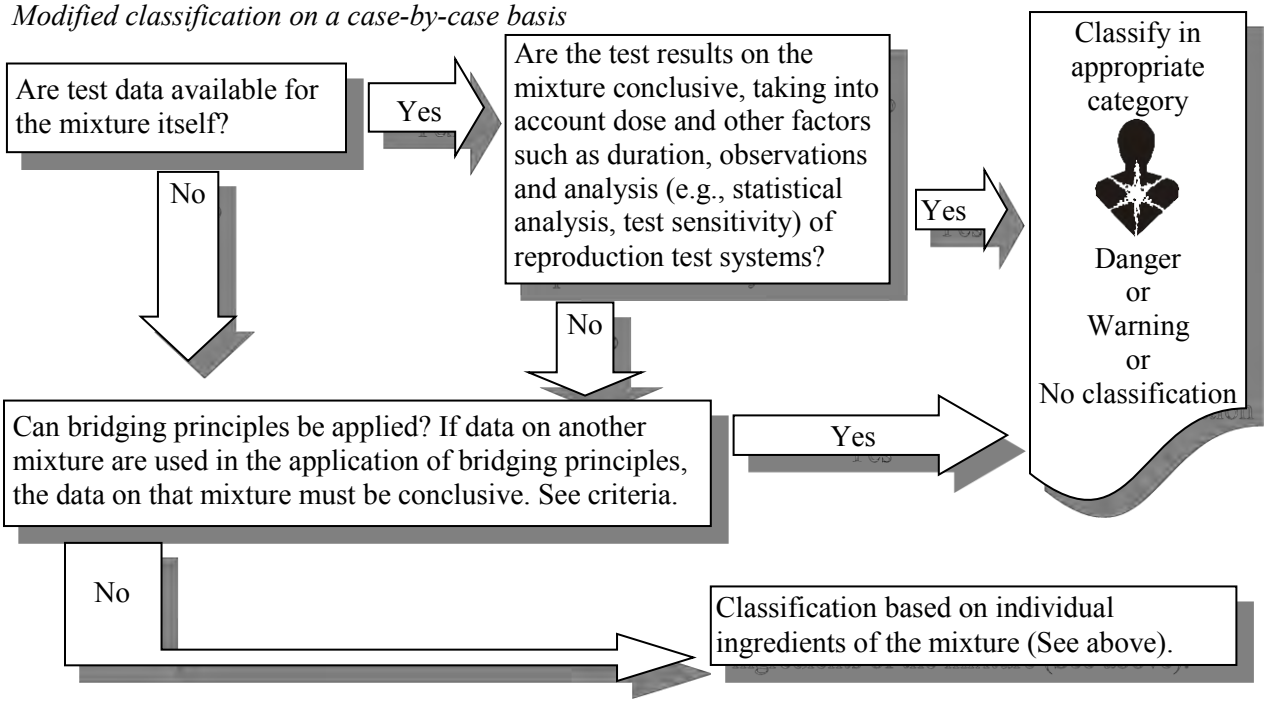
Mixtures decision logic for reproductive toxicity

Mixture: Classification of mixtures will be based on the available test data for the **individual ingredients** of the mixture, using cut-off values/concentration limits for those ingredients. The classification may be **modified on a case-by-case basis** based on the available test data for the mixture as a whole or based on bridging principles. See modified classification on a case-by-case basis below. For further details see criteria.

Classification based on individual ingredients of the mixture

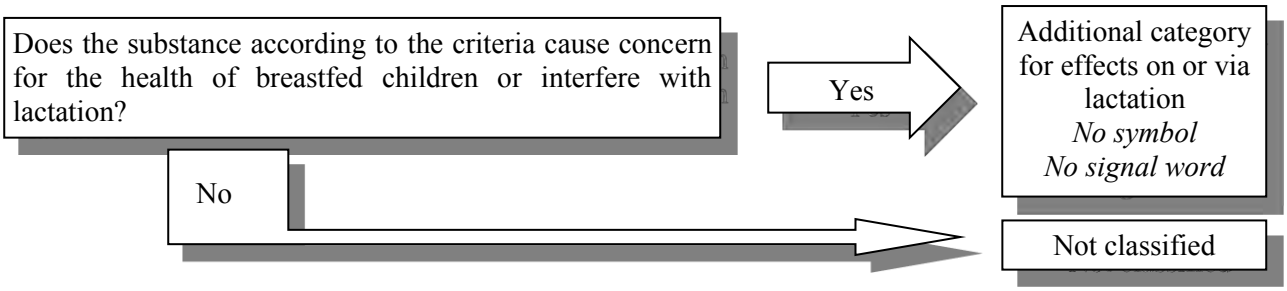


Modified classification on a case-by-case basis



Decision logic for effects on or via lactation

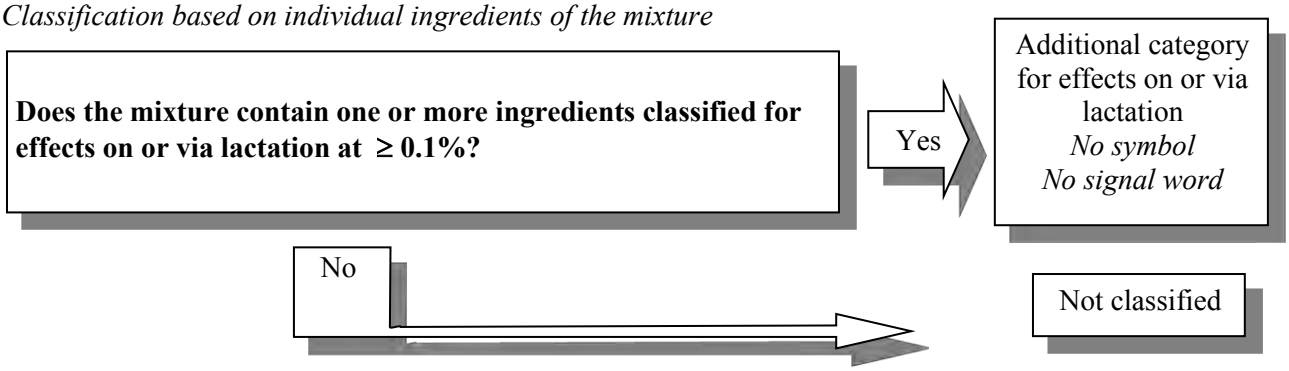
Decision logic for substances



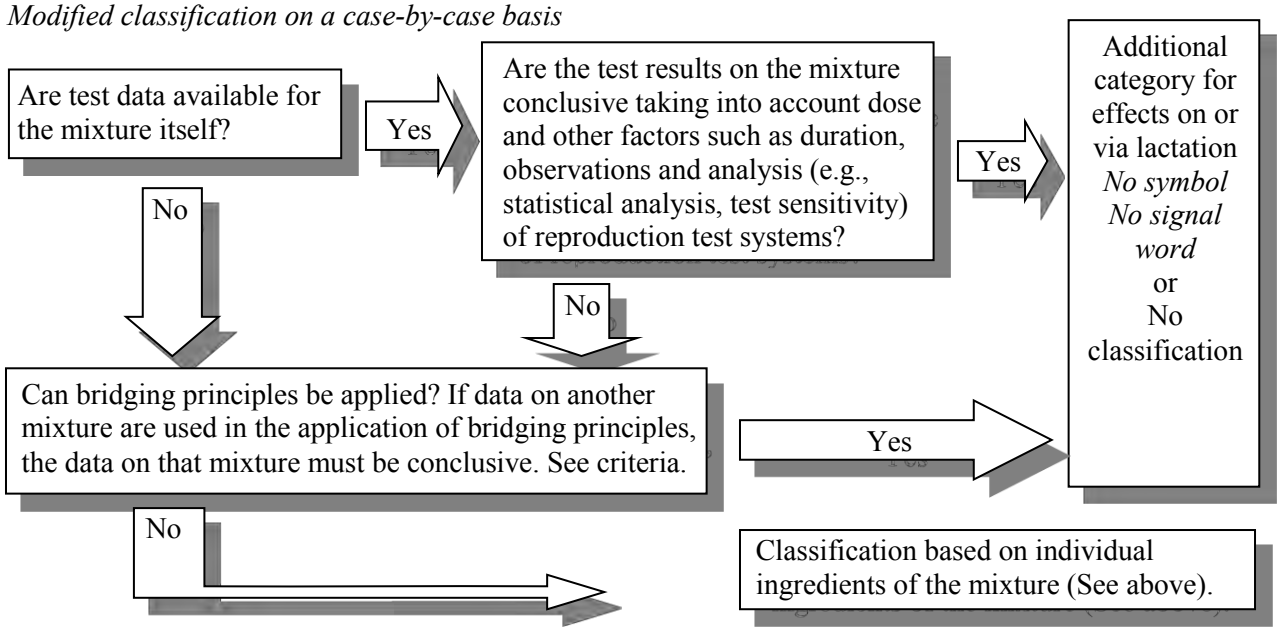
Decision logic for mixtures

Mixture: Classification of mixtures will be based on the available test data for the **individual ingredients** of the mixture, using cut-off values/concentration limits for those ingredients. The classification may be **modified on a case-by-case basis** based on the available test data for the mixture as a whole or based on bridging principles. See modified classification on a case-by-case basis below. For further details see criteria.

Classification based on individual ingredients of the mixture



Modified classification on a case-by-case basis



Reproductive Toxicity Classification Examples

The following examples are provided to walk you through reproductive toxicity classification.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 Reproductive Toxicity		
Test Data	**HCS 2012 Classification**	**Rationale**
Evidence of decreased number of fetuses per brood, decline in the ability of males to impregnate females, increased incidence of preimplantation embryo death, etc. at dosing levels causing no general toxicity.	Reproductive Toxicity Category 1B	Fulfills criteria – Data from animal studies providing clear evidence of an adverse effect on sexual function and fertility or on development in the absence of other toxic effects.

Substance Example #2 Reproductive Toxicity		
Test Data	**HCS 2012 Classification**	**Rationale**
Human epidemiological studies in IRIS Toxicological review (2005) and ATSDR (2000), describe increased incidence of natural abortion after exposure, abnormal development and malformation of newborns caused by prenatal abuse and decreased plasma concentrations of luteinizing hormone and testosterone after exposure. Increased risk of late spontaneous abortions associated with exposure at levels around 88 ppm (range 50-150 ppm). Evidence of increased incidences of fetal death and delayed ossification, a decrease and unossification of sternebrae, a shift in rib profile, excess ribs, retarded skeletal development, delayed reflex response, learning disability and early vaginal opening and testes descent at dosing levels not toxic to dams from rat and mouse teratogenicity tests.	Reproductive Toxicity Category 1A	Fulfills criteria – Evidence of adverse effects on development in humans and in animal studies.

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 Reproductive Toxicity		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 0.05%, Category 1B Component 2: 2%, Category 2 Component 3: 0.2%, Effect on or via lactation Component 4: 97.75%	Reproductive Toxicity Category 2 and Additional category for effects on or via lactation	The Reproductive Toxicity cut-off values/concentration limits are used for classification. Fulfills criteria – Component 1 is not ≥ 0.1% so the mixture does not meet the Category 1B criteria. – Component 2 is ≥ 0.1% so the mixture meets the Category 2 criteria. – Component 3 is ≥ 0.1% so the mixture meets the effect on or via lactation criteria.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.7 Reproductive Toxicity

29 CFR 1910.1200, Hazard Communication, Appendix C Allocation of Label Elements

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

The Organization for Economic Co-operation and Development (OECD) Guidelines for the Testing of Chemicals.

United States Environmental Protection Agency (EPA), Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Health Effects Test Guidelines.

VII.8 Specific Target Organ Toxicity – Single Exposure

Introduction

Chemical exposures can potentially result in adverse effects on one or more of the body's organ systems such as the renal or nervous systems. The HCS provides criteria for the evaluation of data related to a specific target organ or type of effect.

The specific target organ toxicity (STOT) classification addresses chemicals that affect various target organ systems of the body after either a single or repeated exposure. These criteria address those target organ systems that are not covered by the HCS criteria for acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity and aspiration toxicity. Specific target organ toxicity criteria apply to significant health effects that can impair function, both reversible and irreversible, which can be immediate and/or delayed. Specific target organ toxicity can occur by any route that is relevant for human exposures (i.e., principally oral, dermal or inhalation).

The HCS addresses two different types of STOT hazards: toxicity that occurs after a single exposure to a chemical, and toxicity that occurs after repeated exposures to a chemical. To conform to the HCS, this guidance addresses the two STOT hazard classes separately: STOT – single exposure in Chapter VII.8 and STOT – repeated exposure in Chapter VII.9.

Substances and mixtures shall be classified for either or both single and repeated dose toxicity independently.

Definition and General Considerations

Specific target organ toxicity - single exposure (STOT-SE) means specific, non-lethal target organ toxicity arising from a single exposure to a chemical. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in Chapters VII.1 to VII.7 and VII.10 are included. Specific target organ toxicity following repeated exposure is classified in accordance with Specific Target Organ Toxicity – Repeated Exposure and is not included here but is discussed in the next chapter, VII.9.

The adverse health effects produced by a single exposure include consistent and identifiable toxic effects in humans; or, in experimental animals, toxicologically significant changes which have affected the function or morphology of a tissue/organ, or have produced serious changes to the biochemistry or hematology of the organism, and these changes are relevant for human health. Human data is the primary source of evidence for this hazard class.

Assessment shall take into consideration not only significant changes in a single organ or biological system but also generalized changes of a less severe nature involving several organs.

Specific target organ toxicity can occur by any route that is relevant for humans (i.e., principally oral, dermal or inhalation).

The classification criteria for specific organ systemic toxicity – single exposure are organized as criteria for substances Categories 1 and 2, criteria for substances Category 3 and criteria for mixtures.

Classification Criteria for Substances

Substances of Category 1 and Category 2

Substances shall be classified for immediate or delayed effects separately, by the use of expert judgment on the basis of the weight of all evidence available, including the use of recommended guidance values. Substances shall then be classified in Category 1 or 2, depending upon the nature and severity of the effect(s) observed.

Figure VII.8.1. Hazard categories for specific target organ toxicity following single exposure

Category	Criteria
Category 1	**Substances that have produced significant toxicity in humans, or that, on the basis of evidence from studies in experimental animals can be presumed to have the potential to produce significant toxicity in humans following single exposure** Substances are classified in Category 1 for STOT-SE on the basis of: (a) reliable and good quality evidence from human cases or epidemiological studies; or (b) observations from appropriate studies in experimental animals in which significant and/or severe toxic effects of relevance to human health were produced at generally low exposure concentrations. Guidance dose/concentration values are provided below to be used as part of weight-of-evidence evaluation.
Category 2	**Substances that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to be harmful to human health following single exposure** Substances are classified in Category 2 for STOT-SE on the basis of observations from appropriate studies in experimental animals in which significant toxic effects, of relevance to human health, were produced at generally moderate exposure concentrations. Guidance dose/concentration values are provided below in order to help in classification. In exceptional cases, human evidence can also be used to place a substance in Category 2.

Category	Criteria
Category 3	**Transient target organ effects** There are target organ effects for which a substance does not meet the criteria to be classified in Categories 1 or 2 indicated above. These are effects which adversely alter human function for a short duration after exposure and from which humans may recover in a reasonable period without leaving significant alteration of structure or function. This category includes only narcotic effects and respiratory tract irritation. Substances are classified specifically for these.

Note: The primary target organ/system shall be identified where possible, and where this is not possible, the substance shall be identified as a general toxicant. The data shall be evaluated and, where possible, shall not include secondary effects (e.g., a hepatotoxicant can produce secondary effects in the nervous or gastro-intestinal systems).

Specific considerations for classification of substances as specific target organ toxicity – single exposure

Classification is determined by expert judgment, on the basis of the weight of all evidence available.

Weight-of-evidence of all available data, including human incidents, epidemiology, and studies conducted in experimental animals is used to substantiate specific target organ toxic effects that merit classification.

The relevant route(s) of exposure by which the classified substance produces damage shall be identified.

The information required to evaluate specific target organ toxicity comes either from single exposure in humans (e.g., exposure at home, in the workplace or environmentally), or from studies conducted in experimental animals. The standard animal studies in rats or mice that provide this information are acute toxicity studies which can include clinical observations and detailed macroscopic and microscopic examination to enable the toxic effects on target tissues/organs to be identified. Results of acute toxicity studies conducted in other species may also provide relevant information.

In most cases chemicals with human evidence of target organ toxicity will be classified in Category 1. Only in exceptional cases, based on expert judgment, it may be appropriate to place certain substances with human evidence of target organ toxicity in Category 2: (a) when the weight of human evidence is not sufficiently convincing to warrant Category 1 classification, and/or (b) based on the nature and severity of effects. However, the following considerations should be kept in mind when applying this concept. Dose/concentration levels in humans shall not be considered in the classification. Additionally, any available evidence from animal studies

shall be consistent with the Category 2 classification. In other words, if there are also animal data available on the substance that warrant Category 1 classification, the chemical shall be classified as Category 1.

Effects considered to support classification for Categories 1 and 2

Classification is supported by evidence associating single exposure to the substance with a consistent and identifiable toxic effect.

Evidence from human experience/incidents is usually restricted to reports of adverse health consequences, often with uncertainty about exposure conditions, and may not provide the scientific detail that can be obtained from well-conducted studies in experimental animals.

Therefore, evidence from appropriate studies in experimental animals can furnish much more detail, in the form of clinical observations and macroscopic and microscopic pathological examination; this can often reveal hazards that may not be life-threatening but could indicate functional impairment. Consequently, all available evidence, including evidence relevant to human health, must be taken into consideration in the classification process. Relevant toxic effects in humans and/or animals include, but are not limited to:

(a) Morbidity resulting from single exposure;

(b) Significant functional changes, more than transient in nature, in the respiratory system, central or peripheral nervous systems, other organs or other organ systems, including signs of central nervous system depression and effects on special senses (e.g., sight, hearing and sense of smell);

(c) Any consistent and significant adverse change in clinical biochemistry, hematology, or urinalysis parameters;

(d) Significant organ damage that may be noted at necropsy and/or subsequently seen or confirmed at microscopic examination;

(e) Multi-focal or diffuse necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity;

(f) Morphological changes that are potentially reversible but provide clear evidence of marked organ dysfunction; and

(g) Evidence of appreciable cell death (including cell degeneration and reduced cell number) in vital organs incapable of regeneration.

Effects considered not to support classification for Categories 1 and 2

Effects may be seen in humans and/or animals that do not justify classification. Such effects include, but are not limited to:

(a) Clinical observations or small changes in body weight gain, food consumption or water intake that may have some toxicological importance but that do not, by themselves, indicate "significant" toxicity;

(b) Small changes in clinical biochemistry, hematology or urinalysis parameters and/or transient effects, when such changes or effects are of doubtful or of minimal toxicological importance;

(c) Changes in organ weights with no evidence of organ dysfunction;

(d) Adaptive responses that are not considered toxicologically relevant; and

(e) Substance-induced species-specific mechanisms of toxicity, i.e., demonstrated with reasonable certainty to be not relevant for human health.

Guidance values to assist with classification based on the results obtained from studies conducted in experimental animals for Categories 1 and 2

In order to help reach a decision about whether a substance shall be classified or not, and to what degree it shall be classified (Category 1 vs. Category 2), dose/concentration "guidance values" are provided for consideration of the dose/concentration which has been shown to produce significant health effects. The principal argument for proposing such guidance values is that all chemicals are potentially toxic and there has to be a reasonable dose/concentration above which a degree of toxic effect is acknowledged.

Thus, in animal studies, when significant toxic effects are observed that indicate classification, consideration of the dose/concentration at which these effects were seen, in relation to the suggested guidance values, provides useful information to help assess the need for classification (since the toxic effects are a consequence of the hazardous property(ies) and also the dose/concentration).

The guidance value ranges for single-dose exposure which has produced a significant non-lethal toxic effect apply to acute toxicity testing, as shown in the table below.

Table VII.8.1. Guidance value ranges for single-dose exposures

Route of exposure	Units	Guidance values (dose/concentration)		
		Category 1	Category 2	Category 3
Oral (rat)	mg/kg body weight	≤ 300	> 300 and ≤ 2000	Guidance values do not apply
Dermal (rat or rabbit)	mg/kg body weight	≤ 1000	> 1000 and ≤ 2000	
Inhalation (rat) gas	ppm	≤ 2500	> 2500 and ≤ 5000	
Inhalation (rat) vapor	mg/1	≤ 10	> 10 and ≤ 20	
Inhalation (rat) dust/mist/fume	mg/l/4h	≤ 1.0	> 1.0 and ≤ 5.0	

The guidance values and ranges mentioned in the above table are intended only for guidance purposes, i.e., to be used as part of the weight-of-evidence approach, and to assist with decisions about classification. They are not intended as strict demarcation values. Guidance values are not provided for Category 3 since this classification is primarily based on human data; animal data may be included in the weight-of-evidence evaluation.

It is possible that even where a specific profile of toxicity occurs at a dose/concentration below the guidance value, e.g., < 2000 mg/kg body weight by the oral route, the nature of the effect may result in the decision not to classify. Conversely, a specific profile of toxicity may be seen in animal studies occurring at above a guidance value, e.g., ≥ 2000 mg/kg body weight by the oral route, and in addition there is supplementary information from other sources, e.g., other single dose studies, or human case experience, which supports a conclusion that, in view of the weight-of-evidence, classification is the prudent action to take.

Other considerations when classifying using animal data

When a substance is characterized only by use of animal data, the classification process must include reference to dose/concentration guidance values as one of the elements that contribute to the weight-of-evidence approach.

Evidence in humans

When well-substantiated human data are available showing a specific target organ toxic effect that can be reliably attributed to a single exposure to a substance, the substance shall be classified. Positive human data, regardless of probable dose, predominates over animal data. Thus, if a substance is unclassified because specific target organ toxicity observed was considered not relevant or significant to humans, if subsequent human incident data become available showing a specific target organ toxic effect, the substance shall be classified.

Non-test data

A substance that has not been tested for specific target organ toxicity shall, where appropriate, be classified on the basis of data from a scientifically validated structure activity relationship and expert judgment-based extrapolation from a structural analogue that has previously been classified together with substantial support from consideration of other important factors such as formation of common significant metabolites.

Substances of Category 3

Criteria for respiratory tract irritation

The criteria for classifying substances as Category 3 for respiratory tract irritation are:

(a) Respiratory irritant effects (characterized by localized redness, edema, pruritus and/or pain) that impair function with symptoms such as cough, pain, choking, and breathing difficulties are included. It is recognized that this evaluation is based primarily on human data;

(b) Subjective human observations supported by objective measurements of clear respiratory tract irritation (RTI) (e.g., electrophysiological responses, biomarkers of inflammation in nasal or bronchoalveolar lavage fluids);

(c) The symptoms observed in humans shall also be typical of those that would be produced in the exposed population rather than being an isolated idiosyncratic reaction or response triggered only in individuals with hypersensitive airways. Ambiguous reports simply of “irritation” should be excluded as this term is commonly used to describe a wide range of sensations including those such as smell, unpleasant taste, a tickling sensation, and dryness, which are outside the scope of classification for respiratory tract irritation;

(d) There are currently no scientifically validated animal tests that deal specifically with RTI; however, useful information may be obtained from the single and repeated inhalation toxicity tests. For example, animal studies may provide useful information in terms of clinical signs of toxicity (dyspnea, rhinitis, etc.) and histopathology (e.g., hyperemia, edema, minimal inflammation, thickened mucous layer) which are reversible and may reflect the characteristic clinical symptoms described above. Such animal studies can be used as part of the weight-of-evidence evaluation; and

(e) This special classification will occur only when more severe organ effects including the respiratory system are not observed, as those effects would require a higher classification.

Criteria for narcotic effects

The criteria for classifying substances in Category 3 for narcotic effects are:

> (a) Central nervous system depression including narcotic effects in humans such as drowsiness, narcosis, reduced alertness, loss of reflexes, lack of coordination, and vertigo are included. These effects can also be manifested as severe headache or nausea, and can lead to reduced judgment, dizziness, irritability, fatigue, impaired memory function, deficits in perception and coordination, reaction time, or sleepiness; and
>
> (b) Narcotic effects observed in animal studies may include lethargy, lack of coordination righting reflex, narcosis, and ataxia. If these effects are not transient in nature, then they shall be considered for classification as Category 1 or 2.

Classification criteria for mixtures

Mixtures are classified using the same criteria that are used to classify substances; or alternatively, as described below. As with substances, mixtures may be classified for specific target organ toxicity following single exposure, repeated exposure, or both.

The approach to classifying mixtures for specific target organ toxicity – single exposure incorporates the tiered approach (i.e., stepwise procedure based on a hierarchy).

Tier 1: Classification of mixtures when data are available for the complete mixture

When reliable and good evidence from human experience or appropriate animal studies is available for the mixture, then the mixture can be classified by use of a weight-of-evidence approach using the same criteria as specified for substances. Specifically for mixtures, care should be exercised in evaluating data so that the dose, duration of exposure, observation or analysis, does not render the results inconclusive. If test data for the mixture is not available then the classifier should consider application of the criteria in Tier 2 or Tier 3 below, as appropriate.

Tier 2: Classification of mixtures when data are not available for the complete mixture - bridging principles

Where the mixture itself has not been tested to determine its specific target organ toxicity, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the below bridging principles.

All six bridging principles are applicable to the specific target organ toxicity-single exposure hazard class:

- Dilution,
- Batching,

- Concentration of mixtures,
- Interpolation within one toxicity category,
- Substantially similar mixtures,
- Aerosols.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential specific target organ toxicity-single exposure hazard.

Dilution

If a tested mixture is diluted with a diluent which has the same or a lower toxicity classification as the least toxic original ingredient and which is not expected to affect the specific target organ toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

Batching

The specific target organ toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the specific target organ toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures

If in a tested mixture of STOT-SE Category 1, the concentration of a specific target organ toxic ingredient is increased, the resulting concentrated mixture should be classified in STOT-SE Category 1 without additional testing.

Interpolation within one toxicity category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same STOT-SE category, and where untested mixture C has the same specific target organ toxicologically active ingredients as mixtures A and B but has concentrations of specific target organ toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same STOT-SE category as A and B.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;

(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e., they are in the same hazard category and are not expected to affect the specific target organ toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Aerosols

An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolized form of the mixture for oral and dermal specific target organ toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolized mixtures for specific target organ toxicity by the inhalation route should be considered separately.

If appropriate data is not available to apply the above bridging principles then the classifier should consider application of the criteria in Tier 3.

Tier 3: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

The approach to classifying a mixture for specific target organ toxicity in Tier 3 is to use a cut-off/concentration limit.

Where there is no reliable evidence or test data for the specific mixture itself, and the bridging principles cannot be used to enable classification, then classification of the mixture is based on the classification of the ingredient substances. In this case, the mixture shall be classified as a specific target organ toxicant (specific organ specified), following a single exposure when at least one ingredient has been classified as a Category 1 or Category 2 specific target organ toxicant and is present at or above the appropriate cut-off value/concentration limit specified in the below table for Categories 1 and 2, respectively.

Table VII.8.2. Cut-off values/concentration limits of ingredients of a mixture classified as a specific target organ toxicant that would trigger classification of the mixture as Category 1 or 2

Ingredient Classified as:	Cut-off/concentration limits triggering classification of a mixture as:	
	Category 1	**Category 2**
Category 1 Target organ toxicant	≥ 1.0%	
Category 2 Target organ toxicant	-	≥ 1.0%

Care shall be exercised when toxicants affecting more than one organ system are combined that the potentiation or synergistic interactions are considered, because certain substances can cause target organ toxicity at < 1% concentration when other ingredients in the mixture are known to potentiate its toxic effect.

Additionally, a mixture can also be classified in STOT – Single Exposure Category 3 for respiratory tract irritation and/or narcotic effects using a cut off/concentration limit of 20%, as appropriate.

Table VII.8.3. Cut-off values/concentration limits of ingredients of a mixture classified as a specific target organ toxicant that would trigger classification of the mixture as Category 3

Sum of Ingredients Classified as:	Cut-off/concentration limits triggering classification of a mixture as STOT SE:	
	Category 3 Respiratory Tract Irritant	**Category 3 Narcotic Effects**
STOT SE Category 3 - Respiratory Tract Irritant	20%	-
STOT SE Category 3 - Narcotic Effects	-	20%

Care shall be exercised when extrapolating the toxicity of a mixture that contains Category 3 ingredient(s). A cut-off value/concentration limit of 20%, considered as an additive of all Category 3 ingredients for each hazard endpoint, is appropriate; however, this cut-off value/concentration limit may be higher or lower depending on the Category 3 ingredient(s) involved and the fact that some effects such as respiratory tract irritation may not occur below a certain concentration while other effects such as narcotic effects may occur below this 20% value. Expert judgment shall be

exercised. Respiratory tract irritation and narcotic effects are to be evaluated separately. When conducting classifications for these hazards, the contribution of each ingredient should be considered additive, unless there is evidence that the effects are not additive.

Since the mixture criteria for STOT-SE Category 3 ingredients are generally additive, the concept of relevant ingredients can be considered. The “relevant ingredients” of a mixture are those which are present in concentration ≥ 1% (w/w for solids, liquids, dusts, mists and vapors and v/v for gases), unless there is a reason to suspect that an ingredient present at a concentration < 1% can still be relevant for classifying the mixture for respiratory tract irritation or narcotic effects.

Note that the additivity approach does NOT apply when classifying mixtures for STOT-SE categories 1 and 2.

Mixtures containing from 1% to less than 10% of Category 1 STOT-SE ingredients may be classified as Category 2 STOT-SE under the limited following circumstances. The criteria allow for the classification of mixtures under the criteria as used for substances. Where the classification of the ingredients is based on animal data only, the use of the guidance values in Table VII.8.1 is appropriate as a part of the total weight-of-evidence approach. It may be appropriate, in light of the guidance values, to classify a mixture containing from 1% to less than 10% of Category 1 STOT-SE substances as a Category 2 STOT-SE hazard, where warranted by the weight of evidence. Such a classification must be consistent with all of the criteria in 29 CFR 1910.1200 A.8.2.1 ("Substances of Category 1 and Category 2"), including consideration of the severity of the effect observed. However, OSHA would not accept a determination not to classify a mixture based on this approach.

Classification Procedure and Guidance

Test data

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

Old-style acute toxicity tests on animals use death as the main observational endpoint, usually in order to determine LD_{50} or LC_{50} values. These tests will generally not provide useful information for STOT-SE categories 1 and 2. Findings of narcosis and respiratory tract irritation are sometimes reported in clinical observations in standard acute toxicity tests.

Some of the current acute toxicity tests, such as the fixed dose and up-down procedures (e.g., OECD Test Guideline 420 Acute oral toxicity – Fixed dose procedure and OECD Test Guideline 425 Acute oral toxicity – Up-and-down procedure), have observations on signs of non-lethal toxicity and may provide useful information for STOT-SE.

Classification procedure

Specific target organ toxicity after a single exposure addresses effects on the body other than death (which is addressed by acute toxicity criteria). These effects may be reversible or irreversible, and immediate or delayed. The criteria specifically note that, if available, human data will be the primary source of evidence for this hazard class.

Relevant information with respect to toxicity after a single exposure may be available from case reports, epidemiological studies, medical surveillance and poison centers.

Classification for STOT-SE Category 1 and 2 is based on findings of "significant" or "severe" toxic effects. Significant effects mean changes which clearly indicate functional disturbance or morphological changes which are toxicologically relevant. Severe effects are generally more profound or serious than significant effects and are of a considerably adverse nature with substantial impact on health. Both factors have to be evaluated by weight-of-evidence and expert judgment.

Considerations

The STOT criteria are applied independently for STOT – single exposure and STOT – repeated exposure (RE). Substances and mixtures can be classified into both hazard classes and either Category 1 or Category 2 for each hazard class, as well as the additional STOT - SE Category 3 where respiratory tract irritation and/or narcotic effects are evaluated separately.

If the chemical is classified into more than one STOT hazard class and/or category, then all relevant classifications should be communicated on the Safety Data Sheet in Section 2 and all appropriate hazard statements should be communicated along with the specific affected organs on the label.

Classification for STOT-SE and acute toxicity are independent of each other and both may be assigned to a chemical if the respective criteria are met. However, it is not necessary to classify in both classes for the same toxic effect. See Substance Example #5 at the end of this chapter. Classification for STOT-SE is warranted where there is clear evidence of specific organ toxicity especially in absence of lethality which then may be classified under a separate hazard class such as acute toxicity.(e.g., methanol and tricresylphosphate).

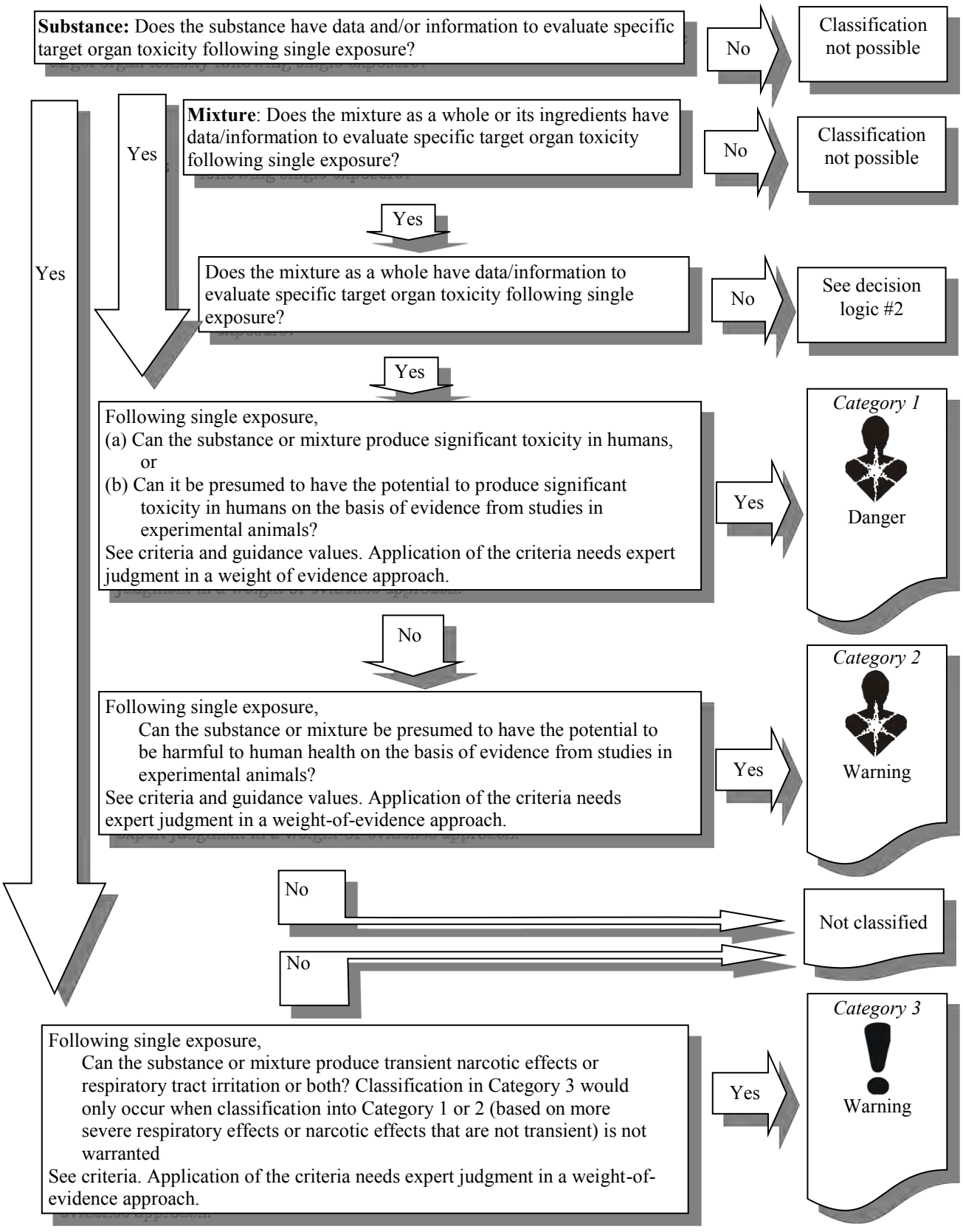
The specific target organ(s) should be identified for both substances and mixtures whenever known. All known specific target organs should be identified for mixtures classified by any of the three tiers. If the mixture is classified on the basis of ingredients, then the target organs effects from the ingredients should be identified. This information should be provided on SDSs and labels.

Decision Logic

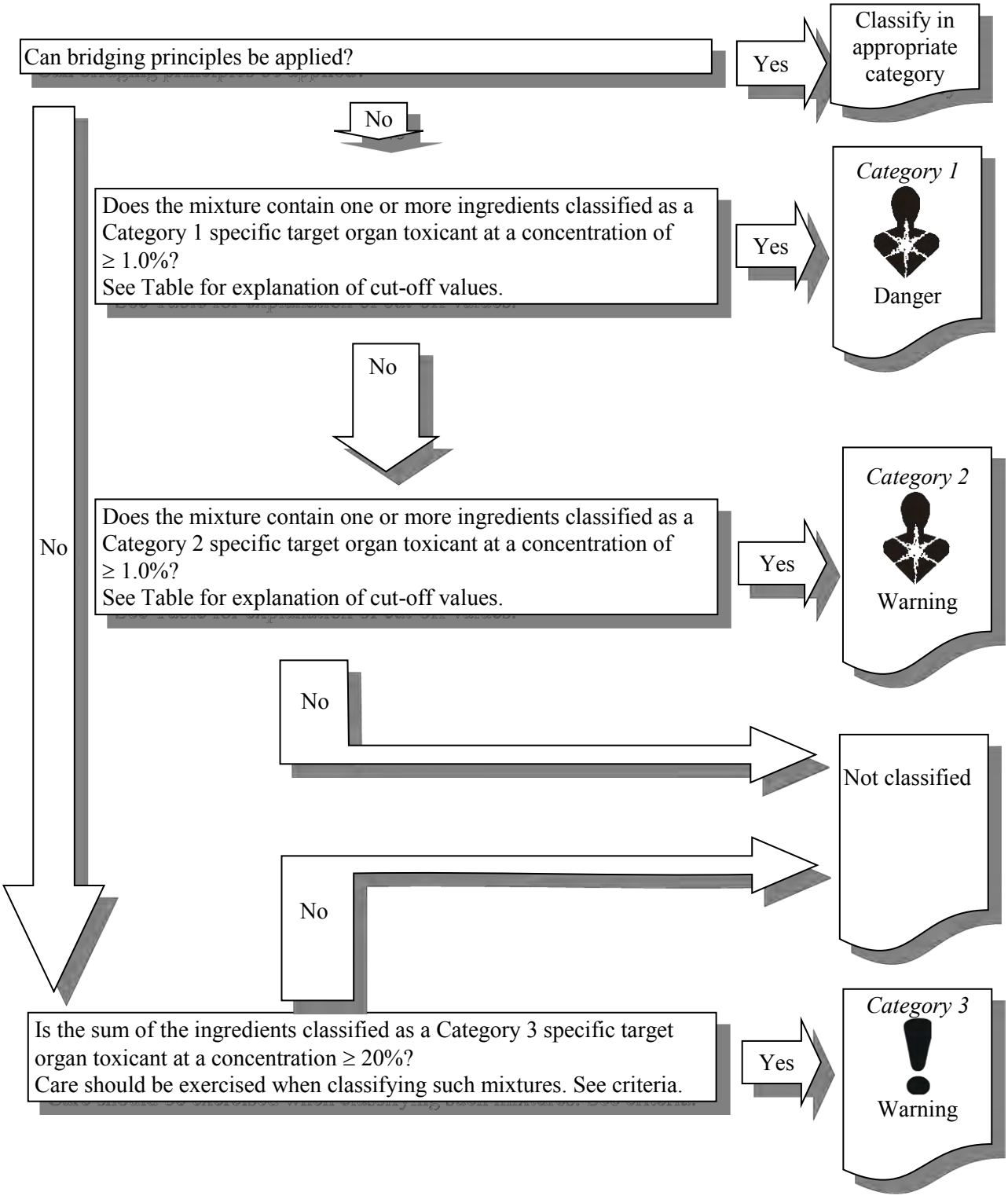
Two decision logics for classifying *specific target organ toxicity – single exposure* are provided. The first decision logic is for substances and tested mixtures. The second decision logic is for classifying mixtures not tested as a whole. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

These decision logics are essentially flowcharts for classifying substances and mixtures regarding specific target organ toxicity – single exposure. They present questions in a sequence that walks you through the classification steps and criteria for classifying specific target organ toxicity – single exposure. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic for specific target organ toxicity – single exposure
Substances and tested mixtures



Decision logic for specific target organ toxicity – single exposure
Mixtures not tested as a whole



Specific Target Organ Toxicity – Single Exposure Classification Examples

The following examples are provided to walk you through the specific target organ toxicity – single exposure classification.

Examples of a substance fulfilling the criteria for classification:

Substance Example #1 **Specific Target Organ Toxicity – Single Exposure**		
Test Data	**HCS 2012 Classification**	**Rationale**
There is broad human experience from many case reports of blindness following oral ingestion. Acute oral toxicity in rats is low (LD50 values > 7,000 mg/kg body weight with no evidence of specific target organ toxicity observed in rats).	STOT – SE Category 1	Fulfills criteria – The classification criteria for STOT-SE Category 1 are fulfilled, as there is clear human evidence of a specific target organ toxicity effect. – The rat is the standard animal species for single exposure tests and is not sensitive as it did not predict the specific target organ toxicity potential seen in humans.

Substance Example #2 **Specific Target Organ Toxicity – Single Exposure**		
Test Data	**HCS 2012 Classification**	**Rationale**
Human experience: There are well-documented case reports of strong neurotoxic effects (peripheral neuropathy; cramps in calves, paresthesia in feet or hands; weak feet, wrist drop, paralysis). Animal data: Serious neurotoxic effects (Paralysis) were observed after single exposure of doses < 200 mg/kg body weight.	STOT–SE Category 1	Fulfills criteria – The classification criteria for STOT-SE Category 1 are fulfilled based on human experience as well as on results of animal studies, with the same target organ toxicity being observed in humans and experimental animals.

Substance Example #3 Specific Target Organ Toxicity – Respiratory Tract Irritation		
Test Data	**HCS 2012 Classification**	**Rationale**
There is broad well-documented human experience on irritating effect to the respiratory system following inhalation.	STOT – SE Category 3 respiratory tract irritation	Fulfills criteria – The classification criteria for respiratory tract irritation STOT Category 3 are fulfilled based on well-documented experience in humans.

Substance Example #4 Specific Target Organ Toxicity – Narcotic Effects		
Test Data	**HCS 2012 Classification**	**Rationale**
In valid animal experiments narcotic effects (transient effect on the nervous system including lethargy, lack of coordination and narcosis) were observed following a single inhalation exposure at ≥ 8 mg/l.	STOT – SE Category 3 Narcotic effects	Fulfills criteria – The classification criteria for narcotic effects STOT Category 3 are fulfilled based on results in an animal experiment.

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 **Specific Target Organ Toxicity – Single Exposure**		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 0.5% Component 2: 3.5%, Category 3 - Respiratory Tract Irritation Component 3: 15%, Category 3 - Narcotic effects Component 4: 15%, Category 3 - Narcotic effects Component 5: 66%	STOT – SE Category 3 Narcotic effects	Respiratory tract irritation and narcotic effects are evaluated separately ∑%Category 3 – Narcotic effects = 15% + 15% = 30% which is > 20%, therefore classify as Category 3 – Narcotic Effects ∑%Category 3 – Respiratory Irritation = 3.5%, which is < 20%, not classified for Respiratory Irritation Expert judgment is necessary. A cut-off value of 20% is appropriate, but the cut-off value at which effects occur may be higher or lower depending on the Category 3 ingredient(s). In this case, the classifiers judged that 30% is sufficient to classify.

Example of a substance not fulfilling the criteria for classification:

Substance Example #5 **Specific Target Organ Toxicity – Single Exposure**		
Data	**HCS 2012 Classification**	**Rationale**
In a study in rats after single exposure at 2,000mg/kg body weight severe liver damage together with mortality was observed in 6/10 animals.	Not classified for STOT – SE	Though specific target organ toxicity was observed in experimental animals, the substance will be classified as Acute Oral Toxicity (Cat 4), since the lethality was due to the target organ toxicity, i.e., liver impairment. The substance would be classified as Acute Oral Toxicity Category 4 as it is assumed that the LD50 is >300 and ≤ 2,000 mg/kg. Thus, classification for STOT single exposure is not required as this would result in double classification for the same effect/mechanism. Death is not generally an effect that supports classification as STOT single exposure.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.8 Specific Target Organ Toxicity-Single Exposure

29 CFR 1910.1200, Hazard Communication, Appendix C Allocation of Label Elements

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

The Organization for Economic Co-operation and Development (OECD). Guidelines for the Testing of Chemicals.

VII.9 Specific Target Organ Toxicity – Repeated or Prolonged Exposure

Introduction

Chemical exposures can potentially result in adverse effects on one or more of the body's target organ systems such as the renal or nervous systems. The HCS provides criteria for the evaluation of data related to a specific target organ or type of effect.

Specific target organ toxicity (STOT) classification addresses chemicals that affect various target organ systems of the body after either a single or repeated exposure. These criteria address those target organ systems that are not covered by the HCS criteria for acute toxicity, skin corrosion/irritation, serious eye damage/eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity and aspiration toxicity. Specific target organ toxicity criteria apply to significant health effects that can impair function, both reversible and irreversible, which can be immediate and/or delayed. Specific target organ toxicity can occur by any route that is relevant for human exposures, i.e., principally oral, dermal or inhalation.

The HCS addresses two different types of STOT hazards: toxicity that occurs after a single exposure to a chemical, and toxicity that occurs after repeated exposures to a chemical. To conform to the HCS, this guidance addresses the two STOT hazard classes separately: STOT – single exposure in Chapter VII.8 and STOT – repeated exposure in Chapter VII.9.

Substances and mixtures shall be classified for either or both single and repeated dose toxicity independently.

Definition and General Considerations

Specific target organ toxicity - repeated exposure (STOT-RE) means specific target organ toxicity arising from repeated exposure to a chemical. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in VII.1 to VII.7 and VII.10 are included. Specific target organ toxicity following a single-event exposure is classified in accordance with Specific Target Organ Toxicity – Single Exposure and is therefore not included here but discussed in the previous chapter, VII.8.

The adverse health effects produced by a repeated exposure include consistent and identifiable toxic effects in humans; or, in experimental animals, toxicologically significant changes which have affected the function or morphology of a tissue/organ, or have produced serious changes to the biochemistry or hematology of the organism, and these changes are relevant for human health. Human data is the primary source of evidence for this hazard class.

Assessment shall take into consideration not only significant changes in a single organ or biological system but also generalized changes of a less severe nature involving several organs.

Specific target organ toxicity can occur by any route that is relevant for humans, i.e., principally oral, dermal or inhalation.

The classification criteria for specific organ systemic toxicity – repeated exposure are organized as criteria for substances Categories 1 and 2 and criteria for mixtures.

Classification Criteria for Substances

Substances shall be classified as STOT - RE by expert judgment on the basis of the weight of all evidence available, including the use of recommended guidance values which take into account the duration of exposure and the dose/concentration which produced the effect(s). Substances shall be placed in one of two categories, depending upon the nature and severity of the effect(s) observed.

Figure VII.9.1. Hazard categories for specific target organ toxicity following repeated exposure

Category	Criteria
Category 1	**Substances that have produced significant toxicity in humans, or that, on the basis of evidence from studies in experimental animals can be presumed to have the potential to produce significant toxicity in humans following repeated or prolonged[17] exposure** Substances are classified in Category 1 for STOT-RE on the basis of: (a) reliable and good quality evidence from human cases or epidemiological studies; or, (b) observations from appropriate studies in experimental animals in which significant and/or severe toxic effects, of relevance to human health, were produced at generally low exposure concentrations. Guidance dose/concentration values are provided below to be used as part of weight-of-evidence evaluation.
Category 2	**Substances that, on the basis of evidence from studies in experimental animals can be presumed to have the potential to be harmful to human health following repeated or prolonged exposure** Substances are classified in Category 2 for STOT-RE on the basis of observations from appropriate studies in experimental animals in which significant toxic effects, of relevance to human health, were produced at generally moderate exposure concentrations. Guidance dose/concentration values are provided below in order to help in classification. In exceptional cases, human evidence can also be used to place a substance in Category 2.

[17] Significant toxic effects observed in a 90-day repeated-dose study conducted in experimental animals.

Note: The primary target organ/system shall be identified where possible, and where this is not possible, the substance shall be identified as a general toxicant. The data shall be evaluated and, where possible, shall not include secondary effects (e.g., a hepatotoxicant can produce secondary effects in the nervous or gastro-intestinal systems).

Specific considerations for classification of substances as specific target organ toxicity – repeated exposure

Classification is determined by expert judgment, on the basis of the weight of all evidence available.

Weight-of-evidence of all available data, including human incidents, epidemiology, and studies conducted in experimental animals is used to substantiate specific target organ toxic effects that merit classification.

The relevant route(s) of exposure by which the classified substance produces damage shall be identified.

The information required to evaluate specific target organ toxicity comes either from repeated exposure in humans, (e.g., exposure at home, in the workplace or environmentally), or from studies conducted in experimental animals. The standard animal studies in rats or mice that provide this information are 28-day, 90-day or lifetime studies (up to 2 years) that include hematological, clinico-chemical and detailed macroscopic and microscopic examination to enable the toxic effects on target tissues/organs to be identified. Data from repeat dose studies performed in other species may also be used. Other long-term exposure studies, e.g., for carcinogenicity, neurotoxicity or reproductive toxicity, may also provide evidence of specific target organ toxicity that could be used in the assessment of classification.

In most cases chemicals with human evidence of target organ toxicity will be classified in Category 1. Only in exceptional cases, based on expert judgment, it may be appropriate to place certain substances with human evidence of target organ toxicity in Category 2: (a) when the weight of human evidence is not sufficiently convincing to warrant Category 1 classification, and/or (b) based on the nature and severity of effects. However, the following considerations should be kept in mind when applying this concept. Dose/concentration levels in humans shall not be considered in the classification. Additionally, any available evidence from animal studies shall be consistent with the Category 2 classification criteria. In other words, if there are also animal data available on the substance that warrant Category 1 classification, the chemical shall be classified as Category 1.

Effects considered to support classification for Categories 1 and 2

Classification is supported by reliable evidence associating repeated exposure to the substance with a consistent and identifiable toxic effect.

Evidence from human experience/incidents is usually restricted to reports of adverse health consequences, often with uncertainty about exposure conditions, and may not provide the scientific detail that can be obtained from well-conducted studies in experimental animals.

Therefore, evidence from appropriate studies in experimental animals can furnish much more detail, in the form of clinical observations and macroscopic and microscopic pathological examination; this can often reveal hazards that may not be life-threatening but could indicate functional impairment. Consequently, all available evidence, including evidence relevant to human health, must be taken into consideration in the classification process. Relevant toxic effects in humans and/or animals include, but are not limited to:

(a) Morbidity resulting from repeated or long-term exposure. Morbidity or death may result from repeated exposure, even to relatively low doses/concentrations, due to bioaccumulation of the substance or its metabolites, or due to overwhelming of the de-toxification process by repeated exposure;

(b) Significant functional changes in the central or peripheral nervous systems, or other organs or other organ systems, including signs of central nervous system depression and effects on special senses (e.g., sight, hearing and sense of smell);

(c) Any consistent and significant adverse change in clinical biochemistry, hematology, or urinalysis parameters;

(d) Significant organ damage that may be noted at necropsy and/or subsequently seen or confirmed at microscopic examination;

(e) Multi-focal or diffuse necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity;

(f) Morphological changes that are potentially reversible but provide clear evidence of marked organ dysfunction (e.g., severe fatty change in the liver); and

(g) Evidence of appreciable cell death (including cell degeneration and reduced cell number) in vital organs incapable of regeneration.

Effects considered <u>not</u> to support classification for Categories 1 and 2

Effects may be seen in humans and/or animals that do not justify classification. Such effects include, but are not limited to:

(a) Clinical observations or small changes in body weight gain, food consumption or water intake that may have some toxicological importance but that do not, by themselves, indicate “significant” toxicity;

(b) Small changes in clinical biochemistry, hematology or urinalysis parameters and/or transient effects, when such changes or effects are of doubtful or of minimal toxicological importance;

(c) Changes in organ weights with no evidence of organ dysfunction;

(d) Adaptive responses that are not considered toxicologically relevant; and

(e) Substance-induced species-specific mechanisms of toxicity, i.e., demonstrated with reasonable certainty to be not relevant for human health.

Guidance values to assist with classification based on the results obtained from studies conducted in experimental animals for Categories 1 and 2

In studies conducted in experimental animals, reliance on observation of effects alone, without reference to the duration of experimental exposure and dose/concentration, omits a fundamental concept of toxicology, i.e., all substances are potentially toxic, and what determines the toxicity is a function of the dose/concentration and the duration of exposure. In most studies conducted in experimental animals the test guidelines use an upper limit dose value.

In order to help reach a decision about whether a substance shall be classified or not, and to what degree it shall be classified (Category 1 vs. Category 2), dose/concentration "guidance values" are provided in the below table for consideration of the dose/concentration which has been shown to produce significant health effects. The principal argument for proposing such guidance values is that all chemicals are potentially toxic and there has to be a reasonable dose/concentration above which a degree of toxic effect is acknowledged. Repeated-dose studies conducted in experimental animals are designed to produce toxicity at the highest dose used in order to optimize the test objective and so most studies will reveal some toxic effect at least at this highest dose. What is therefore to be decided is not only what effects have been produced, but also at what dose/concentration they were produced and how relevant is that for humans.

Thus, in animal studies, when significant toxic effects are observed that indicate classification, consideration of the dose/concentration at which these effects were seen, in relation to the suggested guidance values, provides useful information to help assess the need to classify (since the toxic effects are a consequence of the hazardous property(ies) and also the dose/concentration).

The guidance values refer to effects seen in a standard 90-day toxicity study conducted in rats. They can be used as a basis to extrapolate equivalent guidance values for toxicity studies of greater or lesser duration, using dose/exposure time extrapolation similar to Haber's rule for inhalation, which states essentially that the effective dose is directly proportional to the exposure concentration and the duration of exposure. The assessment should be done on a case-by-case basis; for example, for a 28-day study the guidance values below would be increased by a factor of three.

Thus, for Category 1 classification, significant toxic effects observed in a 90-day repeated-dose study conducted in experimental animals and seen to occur at or below the guidance values (C) as indicated in the below table would justify classification.

For Category 2 classification, significant toxic effects observed in a 90-day repeated-dose study conducted in experimental animals and seen to occur within the guidance value ranges as indicated below would justify classification.

Table VII.9.1. Guidance values to assist in Category 1 and 2 classification
(applicable to a 90-day study)

Route of exposure	Units	Guidance values (dose/concentration)	
		Category 1	**Category 2**
Oral (rat)	mg/kg bw/d	C ≤ 10	10 < C ≤ 100
Dermal (rat or rabbit)	mg/kg bw/d	C ≤ 20	20 < C ≤ 200
Inhalation (rat) gas	ppm/6h/d	C ≤ 50	50 < C ≤ 250
Inhalation (rat) vapor	mg/liter/6h/d	C ≤ 0.2	0.2 < C ≤ 1.0
Inhalation (rat) dust/mist/fume	mg/liter/6h/d	C≤ 0.02	0.02 < C ≤ 0.2

Note: “bw” stands for “body weight”, “h” for “hour” and “d” for “day”.

The guidance values and ranges are intended only for guidance purposes, i.e., to be used as part of the weight-of-evidence approach, and to assist with decisions about classification. They are not intended as strict demarcation values.

It is possible that even where a specific profile of toxicity occurs in repeat-dose animal studies at a dose/concentration below the guidance value, e.g., < 100 mg/kg body weight/day by the oral route, the nature of the effect, e.g., nephrotoxicity seen only in male rats of a particular strain known to be susceptible to this effect, may result in the decision not to classify. Conversely, a specific profile of toxicity may be seen in animal studies occurring at above a guidance value, e.g., ≥ 100 mg/kg body weight/day by the oral route, and in addition there is supplementary information from other sources, e.g., other long-term administration studies, or human case experience, which supports a conclusion that, in view of the weight of evidence, classification is prudent.

Other considerations when classifying using animal data

When a substance is characterized only by use of animal data, the classification process must include reference to dose/concentration guidance values as one of the elements that contribute to the weight-of-evidence approach.

Evidence in humans

When well-substantiated human data are available showing a specific target organ toxic effect that can be reliably attributed to repeated exposure to a substance, the substance shall be classified. Positive human data, regardless of probable dose, predominates over animal data. Thus, if a substance is unclassified because specific target organ toxicity observed was considered not relevant or significant to humans, if subsequent human incident data become available showing a specific target organ toxic effect, the substance shall be classified.

Non-test data

A substance that has not been tested for specific target organ toxicity shall, where appropriate, be classified on the basis of data from a scientifically validated structure activity relationship and expert judgment-based extrapolation from a structural analogue that has previously been classified together with substantial support from consideration of other important factors such as formation of common significant metabolites.

Classification criteria for mixtures

Mixtures are classified using the same criteria as for substances, or alternatively as described below. As with substances, mixtures may be classified for specific target organ toxicity following single exposure, repeated exposure, or both.

The approach to classifying mixtures for specific target organ toxicity – repeated exposure incorporates the tiered approach (i.e., stepwise procedure based on a hierarchy).

Tier 1: Classification of mixtures when data are available for the complete mixture

When reliable and good evidence from human experience or appropriate animal studies is available for the mixture as a whole, then the mixture can be classified by use of a weight-of-evidence approach using the same criteria as specified for substances. Specifically for mixtures, care should be exercised in evaluating data such that the dose, duration of exposure, observation or analysis, do not render the results inconclusive. If test data for the mixture is not available then the classifier should consider application of the criteria in Tier 2 or Tier 3 below, as appropriate.

Tier 2: Classification of mixtures when data are not available for the complete mixture - bridging principles

Where the mixture itself has not been tested to determine its specific target organ toxicity, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazards of the mixture, these data can be used in accordance with the below bridging principles.

All six bridging principles are applicable to the specific target organ toxicity – repeated exposure hazard class:

- Dilution,
- Batching,
- Concentration of mixtures,
- Interpolation within one toxicity category,
- Substantially similar mixtures,
- Aerosols.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential specific target organ toxicity-repeated exposure hazard.

Dilution

If a tested mixture is diluted with a diluent which has the same or a lower toxicity classification as the least toxic original ingredient and which is not expected to affect the specific target organ toxicity of other ingredients, then the new diluted mixture may be classified as equivalent to the original tested mixture.

Batching

The specific target organ toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the specific target organ toxicity of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures

If in a tested mixture of STOT-RE Category 1, the concentration of a specific target organ toxic ingredient is increased, the resulting concentrated mixture should be classified in STOT-RE Category 1 without additional testing.

Interpolation within one toxicity category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in the same STOT-RE category, and where untested mixture C has the same specific target organ toxicologically active ingredients as mixtures A and B but has concentrations of specific target organ toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in the same STOT-RE category as A and B.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Data on toxicity for A and C are available and substantially equivalent, i.e., they are in the same hazard category and are not expected to affect the specific target organ toxicity of B.

If mixture (i) or (ii) is already classified by testing, then the other mixture can be classified in the same hazard category.

Aerosols

An aerosol form of a mixture may be classified in the same hazard category as the tested, non-aerosolized form of the mixture for oral and dermal specific target organ toxicity provided the added propellant does not affect the toxicity of the mixture on spraying. Classification of aerosolized mixtures for specific target organ toxicity by the inhalation route should be considered separately.

If appropriate data is not available to apply the above bridging principles then the classifier should consider application of the criteria in Tier 3.

Tier 3: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

The approach to classifying a mixture for specific target organ toxicity in Tier 3 is to use a cut-off/concentration limit.

Where there is no reliable evidence or test data for the specific mixture itself, and the bridging principles cannot be used to enable classification, then classification of the mixture is based on the classification of the ingredient substances. In this case, the mixture shall be classified as a specific target organ toxicant (specific organ specified), following repeated exposure when at least one ingredient has been classified as a Category 1 or Category 2 specific target organ toxicant and is present at or above the appropriate cut-off value/concentration limit specified in the below table for Categories 1 and 2, respectively.

Table VII.9.2. Cut-off values/concentration limits of ingredients of a mixture classified as a specific target organ toxicant—repeated exposure that would trigger classification of the mixture as Category 1 or 2

Ingredient Classified as:	Cut-off/concentration limits triggering classification of a mixture as:	
	Category 1	**Category 2**
Category 1 Target organ toxicant	≥ 1.0%	
Category 2 Target organ toxicant	-	≥ 1.0%

Note that the additivity approach does NOT apply when classifying mixtures for STOT-RE categories 1 and 2.

Care shall be exercised when toxicants affecting more than one organ system are combined that the potentiation or synergistic interactions are considered, because certain chemicals can cause target organ toxicity at < 1% concentration when other ingredients in the mixture potentiate their toxic effect.

Mixtures containing from 1% to less than 10% of Category 1 STOT-RE ingredients may be classified as Category 2 STOT-RE under the limited following circumstances. The criteria allow for the classification of mixtures under the criteria as used for substances. Where the classification of the ingredients is based on animal data only the use of the guidance values in Tables VII.9.1 and VII.9.2 is appropriate as a part of the total weight-of-evidence approach. It may be appropriate, in light of the guidance values, to classify a mixture containing from 1% to less than 10% of Category 1 STOT-RE substances as a Category 2 STOT-RE hazard, where warranted by the weight of evidence. Such a classification must be consistent with all of the criteria in 29 CFR 1910.1200 A.9.2 ("Classification Criteria for Substances"), including consideration of the severity of the effect observed. However, OSHA would not accept a determination not to classify a mixture based on this approach.

Classification Procedure and Guidance

Test data

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical. Data generated in accordance with internationally recognized scientific principles, are acceptable under HCS 2012.

Examples of scientifically validated test methods

There are a number of scientifically validated methods that can provide information to evaluate specific target organ toxicity:

- OECD Test Guideline 407 Repeated dose 28-day oral toxicity study in rodents
- OECD Test Guideline 410 Repeated dose dermal toxicity: 21/28-day study
- OECD Test Guideline 412 Repeated dose inhalation toxicity: 28-day or 14-day study
- OECD Test Guideline 408 Repeated dose 90-day oral toxicity study in rodents
- OECD Test Guideline 411 Subchronic dermal toxicity: 90-day study
- OECD Test Guideline 452 Chronic toxicity studies
- OECD Test Guideline 424 Neurotoxicity study in rodents

The 28-day studies provide information on toxicological effects arising from exposure to the chemical during a relatively limited period of the animal's life span. The 90-day studies provide information on general toxicological effects arising from subchronic exposure (a prolonged period of the animal's life span) covering post-weaning maturation and growth well into adulthood, on target organs and on potential accumulation of the substance. Chronic toxicity studies provide information on toxicological effects arising from repeated exposure over a prolonged period of time covering the major part of the animal's life span.

The STOT-RE guidance values refer to 90-day toxicity studies conducted in rats. They can be extrapolated to develop equivalent guidance values for toxicity studies of greater or lesser duration.

Classification procedure

Classification for STOT-RE is based on findings of "significant" or "severe" toxic effects. Significant effects mean changes which clearly indicate functional disturbance or morphological changes which are toxicologically relevant. Severe effects are generally more profound or serious than significant effects and are of a considerably adverse nature with substantial impact on health. Both factors have to be evaluated by weight of evidence and expert judgment.

Where the same target organ toxicity of similar severity is observed after single and repeated exposure to a similar dose, it may be concluded that the toxicity is essentially an acute (i.e., single exposure) effect with no accumulation or exacerbation of the toxicity with repeated exposure. In such a case classification with STOT-SE only would be appropriate.

Considerations

The STOT criteria are applied independently for STOT-SE and STOT-RE. Substances and mixtures can be classified into both hazard classes and either Category 1 or Category 2 for each hazard class, as well as the additional STOT-SE Category 3 where respiratory tract irritation and/or narcotic effects are evaluated separately.

If the chemical is classified into more than one STOT hazard class and/or category, then all relevant classifications should be communicated on the Safety Data Sheet in Section 2 and all hazard statements should be communicated along with the specific affected organs on the label.

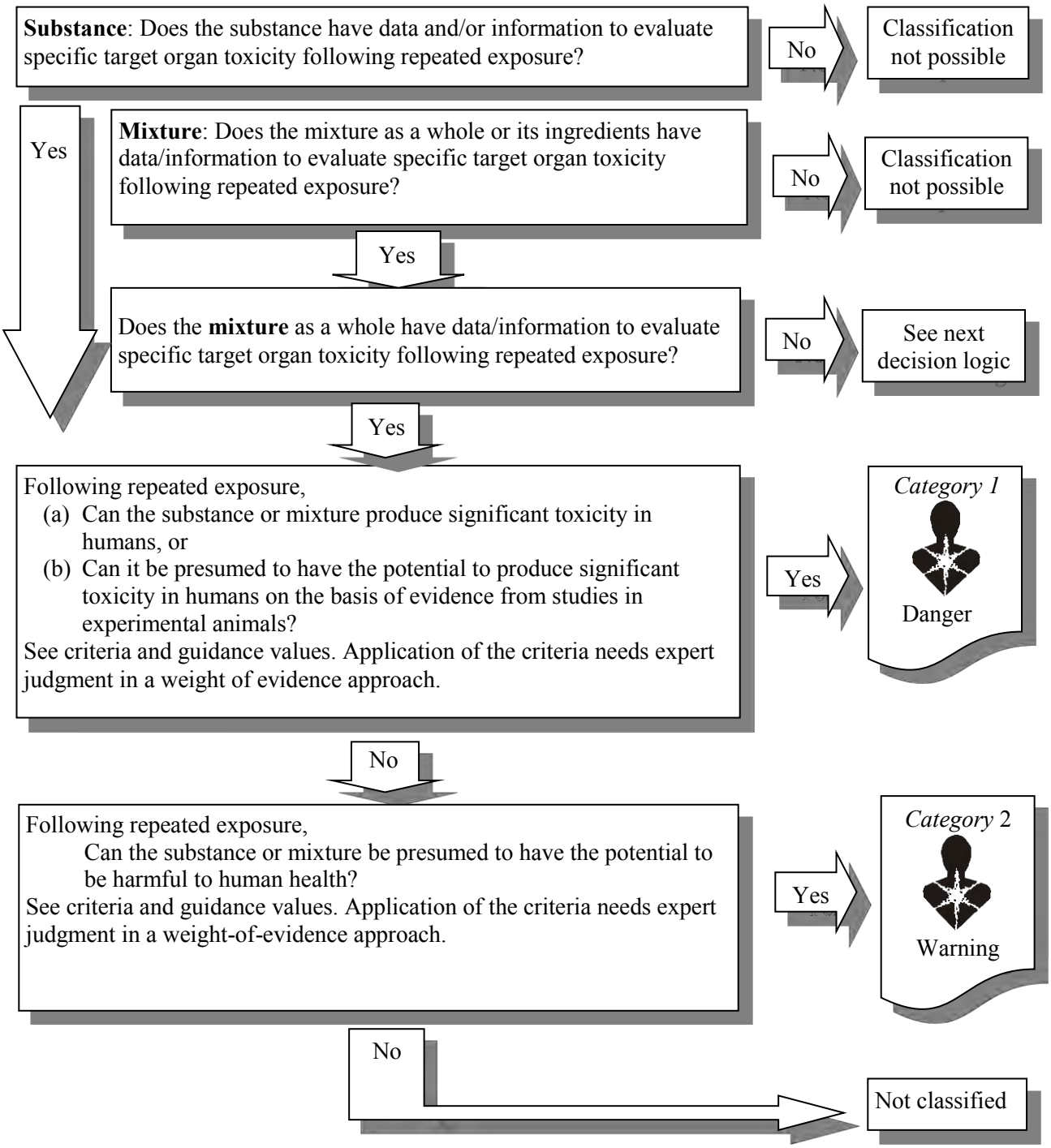
The specific target organ(s) should be identified for both substances and mixtures whenever known. All known specific target organs should be identified for mixtures classified by any of the three tiers. If the mixture is classified on the basis of ingredients, then the target organs effects from the ingredients should be identified. This information should be provided on SDSs and labels.

Decision Logic

Two decision logics for classifying *specific target organ toxicity – repeated exposure* are provided. The first decision logic is for substances and tested mixtures. The second decision logic is for classifying mixtures not tested as a whole. The decision logics are provided as additional guidance. It is strongly recommended that the person responsible for classification study the criteria before and during use of the decision logic.

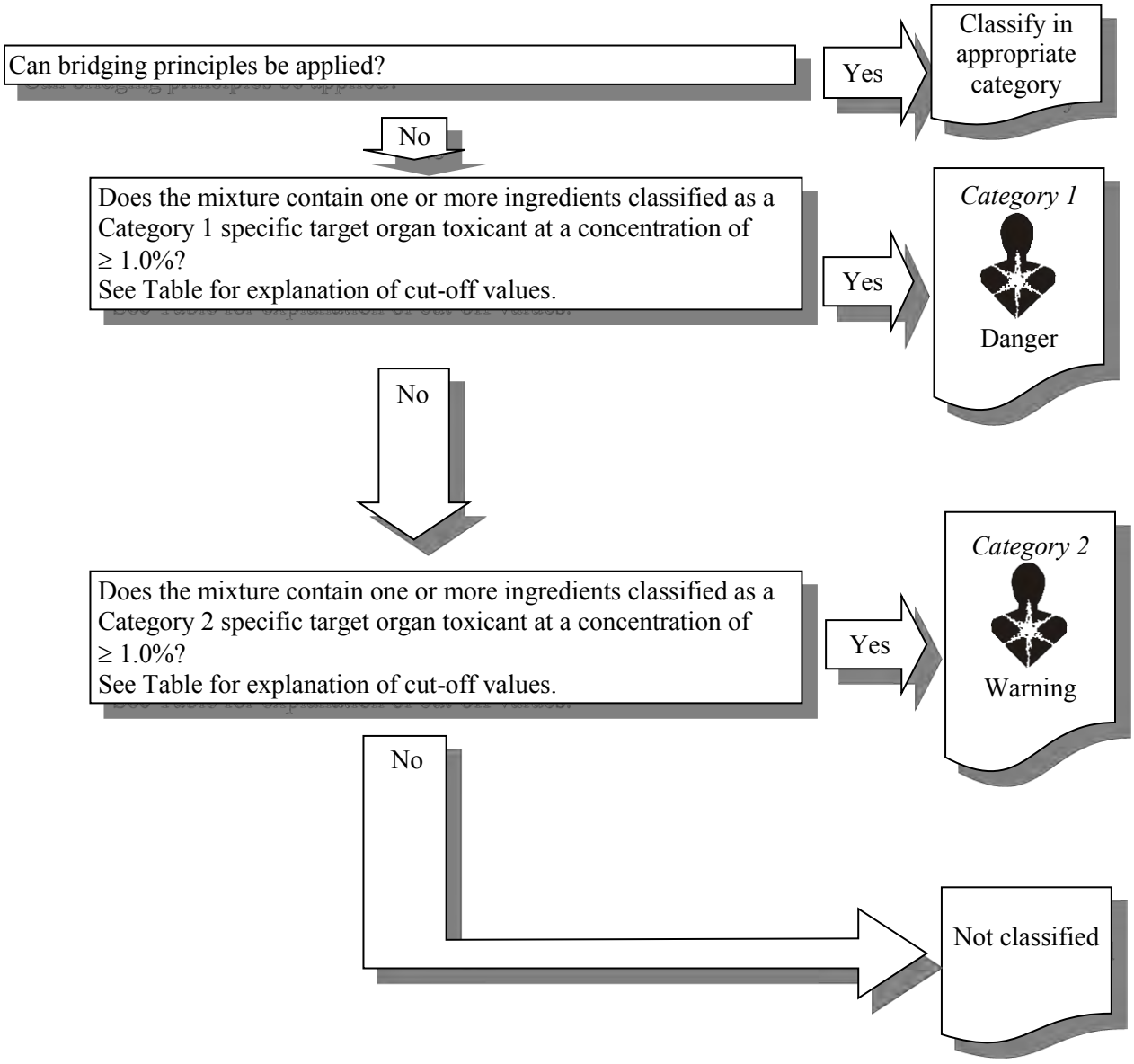
These decision logics are essentially flowcharts for classifying substances and mixtures regarding specific target organ toxicity – repeated exposure. They present questions in a sequence that walks you through the classification steps and criteria for classifying specific target organ toxicity – repeated exposure. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic for specific target organ toxicity – repeated exposure
Substances and tested mixtures



(Cont'd on next page)

Decision logic for specific target organ toxicity – repeated exposure
Mixtures not tested as a whole



Specific Target Organ Toxicity – Repeat Exposure Classification Examples

The following examples are provided to walk you through specific target organ toxicity – repeat exposure classification.

Example of a substance fulfilling the criteria for classification:

Substance Example #1 Specific Target Organ Toxicity – Repeated Exposure		
Test Data	**HCS 2012 Classification**	**Rationale**
Human evidence including "hemolytic anemia, a decrease in white blood cell count" (ACGIH (7th, 2001)), and evidence from animal studies including "a decrease in mean corpuscular hemoglobin, hemoglobin concentrations, red blood cell count and hematocrit levels," and "adrenal degeneration" (MOE Risk Assessment Vol. 3 (2004)).	STOT – RE Category 1 (adrenal, blood system)	Fulfills criteria – The classification criteria for STOT-RE Category 1 are fulfilled. – The effects on experimental animals were observed at dosing levels within the guidance value ranges for Category 1

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 Specific Target Organ Toxicity –Repeated Exposure		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 0.5% Component 2: 3.5%, Category 1 - Liver Component 3: 5%, Category 2 – Kidney Component 4: 7%, Category 1 – Lungs	STOT – RE Category 1 (liver, lungs) and STOT – RE Category 2 (kidney)	Fulfills criteria – Mixture contains 3.5% of a STOT Category 1 target organ toxicant (Ingredient 2), which is ≥ 1.0% so the mixture meets the Category 1 criteria. – Mixture contains 5% of a STOT Category 2 target organ toxicant (Ingredient 3), which is ≥ 1.0% so the mixture meets the Category 2 criteria.

Mixture Example #1 Specific Target Organ Toxicity –Repeated Exposure		
Data	**HCS 2012 Classification**	**Rationale**
Component 5: 66%		– Mixture contains 7% of a STOT Category 1 target organ toxicant (Ingredient 4), which is ≥ 1.0% so the mixture meets the Category 1 criteria. – In this case the mixture is classified into more than one category so the most severe category is used.

References

29 CFR 1910.1200, Hazard Communication, Appendix A.8 Specific Target Organ Toxicity-Repeated or Prolonged Exposure

29 CFR 1910.1200, Hazard Communication, Appendix C Allocation of Label Elements

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

VII.10 Aspiration Hazard

Introduction

A review of the medical literature on chemical aspiration reveals that some hydrocarbons (petroleum distillates) and certain chlorinated hydrocarbons have been shown to pose an aspiration hazard in humans.

Aspiration is initiated at the moment of inspiration, in the time required to take one breath, as the causative material lodges at the crossroad of the upper respiratory and digestive tracts in the throat. Aspiration toxicity includes severe acute effects such as chemical pneumonia, varying degrees of pulmonary injury or death following aspiration.

Aspiration of a substance or mixture can also occur due to vomiting following ingestion. This may have consequences for labeling, particularly where, due to acute toxicity, a recommendation may be considered to induce vomiting after ingestion. However, if the substance/mixture also presents an aspiration toxicity hazard, the recommendation to induce vomiting may need to be modified.

Definition and General Considerations

Aspiration means the entry of a liquid or solid chemical directly through the oral or nasal cavity, or indirectly from vomiting, into the trachea and lower respiratory system.

Although the definition of aspiration includes the entry of solids into the respiratory system, classification according to the criteria for Category 1 is intended to apply to liquid chemicals only.

Classification Criteria for Substances

A substance which is an aspiration hazard shall be classified in a single category based on the criteria described below.

Table VII.10.1. Criteria for Aspiration Toxicity

Category	Criteria
1 Chemicals known to cause human aspiration toxicity hazards or to be regarded as if they cause human aspiration toxicity hazard	A substance shall be classified in Category 1: (a) If reliable and good quality human evidence indicates that it causes aspiration toxicity (See note); or (b) If it is a hydrocarbon and has a kinematic viscosity ≤ 20.5 mm^2/s, measured at 40°C.

Note: Examples of substances included in Category 1 are certain hydrocarbons, turpentine and pine oil.

Classification of aerosol/mist products

Aerosol and mist products are usually dispensed in containers such as self-pressurized containers, trigger and pump sprayers. The key to classifying these products is whether a pool of product is formed in the mouth, which then may be aspirated. If the mist or aerosol from a pressurized container is fine, a pool may not be formed. On the other hand, if a pressurized container dispenses product in a stream, a pool may be formed that may then be aspirated. Usually, the mist produced by trigger and pump sprayers is coarse and, therefore, a pool may be formed that then may be aspirated. Classification is then to be considered. When the pump mechanism may be removed and contents are available to be swallowed, the classification of the product should also be considered.

Classification criteria for mixtures

The approach to classifying mixtures for the aspiration hazard incorporates the tiered approach (i.e., stepwise procedure based on a hierarchy).

Tier 1: Classification of mixtures when data are available for the complete mixture

A mixture can be classified into Category 1 based on reliable and good quality human evidence using the same criteria used for substances. If test data for the mixture is not available then the classifier should consider the application of the criteria in Tier 2 or 3, as appropriate.

Tier 2: Classification of mixtures when data are not available for the complete mixture-bridging principles

Where the mixture itself has not been tested to determine its aspiration toxicity, but there are sufficient data on **BOTH** the individual ingredients **AND** similar tested mixtures to adequately characterize the hazard of the mixture, these data can be used in accordance with the following bridging principles.

Only the following bridging principles are applicable to Aspiration Category 1 for the Aspiration hazard class:

- Dilution,
- Batching,
- Concentration of mixtures,
- Interpolation within one toxicity category, and
- Substantially similar mixtures.

The application of bridging principles ensures that the classification process uses the available data to the greatest extent possible in characterizing the potential aspiration hazard.

Dilution

If a tested mixture is diluted with a diluent that does not pose an aspiration toxicity hazard, and which is not expected to affect the aspiration toxicity of other ingredients or the mixture, then the new diluted mixture may be classified as equivalent to the original tested mixture. However, the concentration of aspiration toxicant(s) should not drop below 10%.

Batching

The aspiration toxicity of a tested production batch of a mixture can be assumed to be substantially equivalent to that of another untested production batch of the same commercial product, when produced by or under the control of the same manufacturer, unless there is reason to believe there is significant variation such that the aspiration toxicity, reflected by viscosity or concentration, of the untested batch has changed. If the latter occurs, a new classification is necessary.

Concentration of mixtures

If a tested mixture is classified in Aspiration Category 1, and the concentration of the ingredients of the tested mixture that are in Aspiration Category 1 is increased, the resulting untested mixture should be classified in Aspiration Category 1 without additional testing.

Interpolation within one toxicity category

For three mixtures (A, B and C) with identical ingredients, where mixtures A and B have been tested and are in Aspiration Category 1, and where untested mixture C has the same aspiration toxicologically active ingredients as mixtures A and B but has concentrations of aspiration toxicologically active ingredients intermediate to the concentrations in mixtures A and B, then mixture C is assumed to be in Aspiration Category 1 like A and B.

Substantially similar mixtures

Given the following:

(a) Two mixtures: (i) A + B;
(ii) C + B;

(b) The concentration of ingredient B is essentially the same in both mixtures;

(c) The concentration of ingredient A in mixture (i) equals that of ingredient C in mixture (ii);

(d) Aspiration toxicity for A and C is substantially equivalent, i.e., they are in Aspiration Category 1 and are not expected to affect the aspiration toxicity of B.

If mixture (i) or (ii) is already classified based on the aspiration hazard substance criteria, then the other mixture can be assigned the same hazard category.

If appropriate data is not available to apply the above bridging principles then the classifier should consider application of the criteria in Tier 3.

Tier 3: Classification of mixtures when data are available for all ingredients or only for some ingredients of the mixture

If there are not sufficient data to apply the bridging principles then the third tier calls for classifying the mixture using a summation method. The sum of classified ingredients must be ≥ 10% and the mixture's kinematic viscosity must be less than or equal to 20.5 mm^2/s measured at 40°C.

Category 1 Criteria

A mixture will be classified in Category 1 when the sum of the concentration of Category 1 ingredients ≥ 10% *and* the mixture has a kinematic viscosity ≤ 20.5 mm^2/s, measured at 40° C.

Special consideration has been given to mixtures which separate into two or more distinct layers. In the case of a mixture which separates into two or more distinct layers, the entire mixture is classified as Category 1 if in any distinct layer the sum of the concentration of Category 1 ingredients ≥ 10 %, *and* the layer has a kinematic viscosity ≤ 20.5 mm^2/s, measured at 40° C.

The relevant ingredients of a mixture are those which are present in concentrations ≥ 1%.

Classification Procedure and Guidance

There is no requirement in the HCS to test a chemical to classify its hazards. The HCS requires collecting and evaluating the best available existing evidence on the hazards of each chemical.

While a methodology for determination of aspiration hazard in animals has been utilized, it has not been standardized. Positive experimental evidence with animals can only serve as a guide to possible aspiration toxicity in humans. Particular care must be taken in evaluating animal data for aspiration hazards.

Classification procedure

To assess the aspiration hazard of a chemical, identify the data relevant for aspiration. The aspiration classification criteria include:

- reliable and good quality human evidence indicating aspiration toxicity; or
- the chemical is a hydrocarbon and has a kinematic viscosity ≤ 20.5 mm^2/s, measured at 40° C.

Data can be found in literature, on SDSs, or be determined by testing, which is not required by the HCS.

In classification the data are compared to the criteria for Aspiration Hazard Category 1. For mixtures follow the above three-tier approach.

The aspiration classification criteria refer to kinematic viscosity. The following provides the conversion between dynamic and kinematic viscosity:

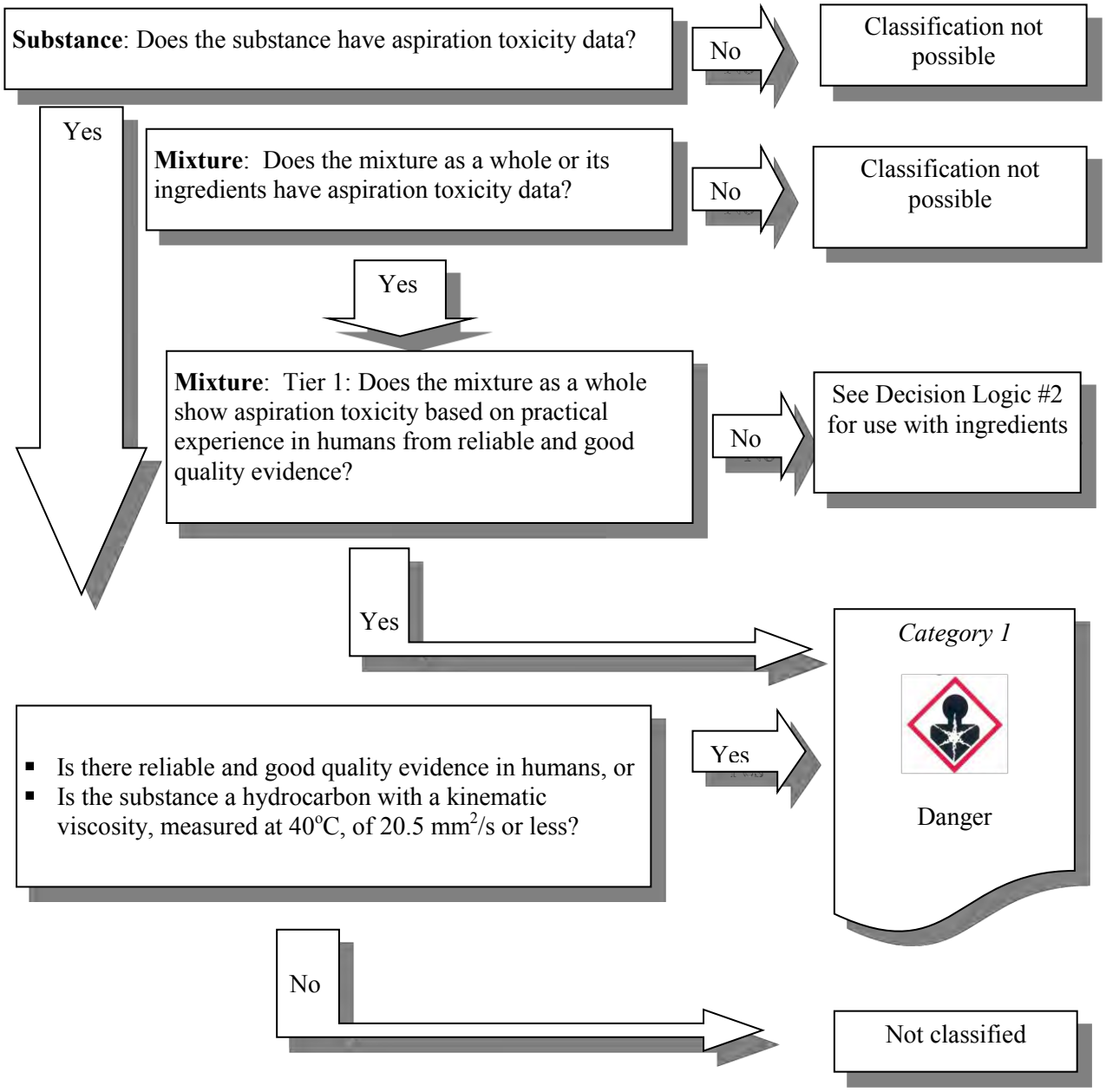
$$\frac{\text{Dynamic viscosity}(mPa \cdot s)}{\text{Density}(g/cm^3)} = \text{Kinematic viscosity}(mm^2/s)$$

Decision Logic

Two decision logics for classifying *aspiration toxicity* are provided. The first decision logic is for substances and mixtures with data on the mixture as a whole. Use the second decision logic for classifying mixtures not tested as a whole.

These decision logics are essentially flowcharts for classifying substances and mixtures regarding the aspiration hazard. They present questions in a sequence that walks you through the classification steps and criteria for classifying aspiration toxicity. Once you answer the questions provided, you will arrive at the appropriate classification.

Decision logic #1 for aspiration toxicity – Substances and tested mixtures



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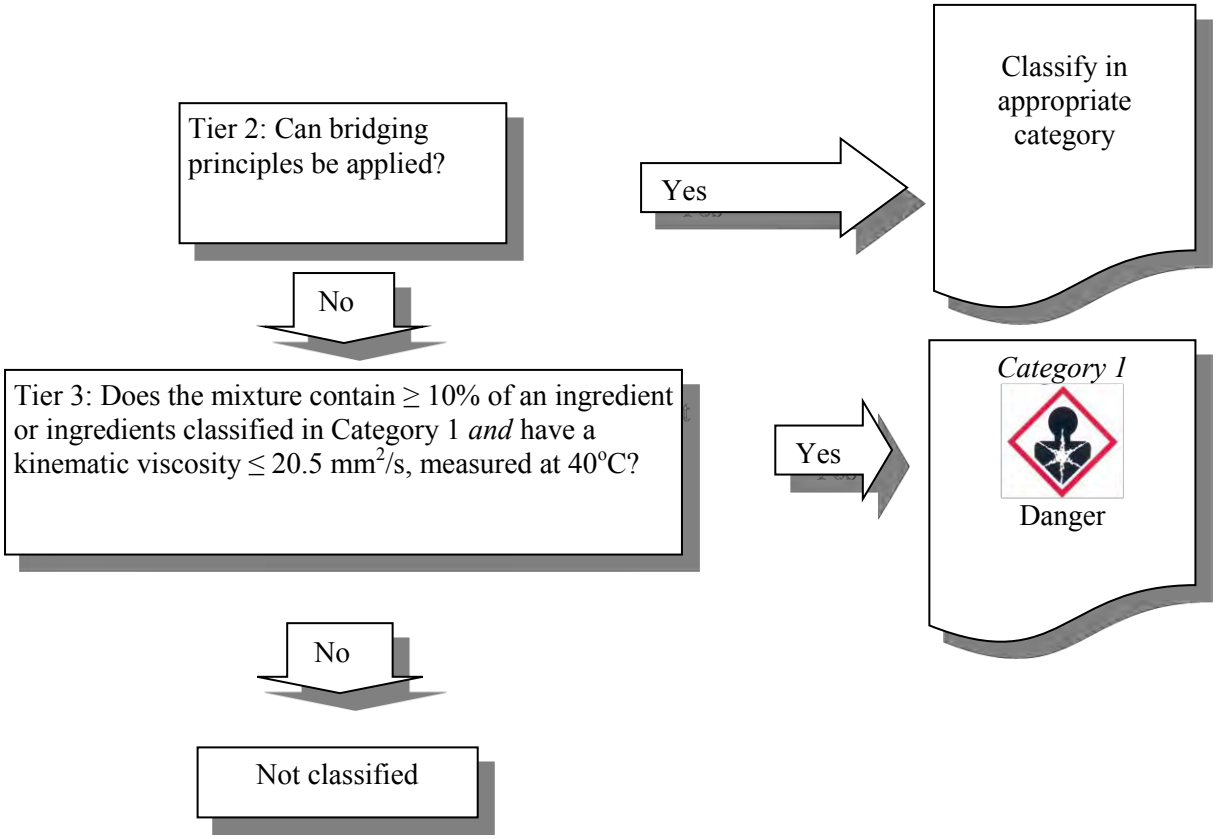
Decision logic #2 for aspiration toxicity – Mixtures not tested as a whole



Aspiration Classification Examples

The following examples are provided to walk you through the aspiration calculation and classification processes.

Example of a substance fulfilling the criteria for classification:

Substance Example #1 Aspiration Hazard		
Test Data	**HCS 2012 Classification**	**Rationale**
The material is a hydrocarbon and has a kinematic viscosity of 0.74mm^2/s at 25℃. Case reports of human symptoms "May cause pulmonary edema if inhaled and chemical pneumonia if swallowed." (ATSDR (2001)).	Aspiration Category 1	Fulfills criteria – it is a hydrocarbon and has a kinematic viscosity ≤ 20.5 mm^2/s, measured at 40°C. – with hydrocarbons, as the temperature increases, the kinematic viscosity decreases. Therefore, in this example if we increase the temperature to 40°C, we would expect the viscosity to be lower than 0.74mm^2/s, which would still fulfill the criteria of ≤ 20.5 mm^2/s, measured at 40°C. Also based on the description in reports of human symptoms, the Aspiration Category 1 criteria are fulfilled

Example of a mixture fulfilling the criteria for classification:

Mixture Example #1 Aspiration Hazard		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 2: 20%, Aspiration Category 1	Aspiration Category 1	Material is a hydrocarbon Fulfills additive threshold criteria Aspiration Calculation:

Mixture Example #1 Aspiration Hazard		
Data	**HCS 2012 Classification**	**Rationale**
Component 3: 28%, Aspiration Category 1 *Mixture data:* Material is a hydrocarbon Kinematic Viscosity @ 40ºC (104ºF) = 10 mm^2/s		Σ % Category 1 ≥ 10% 20% + 28% = 48% Fulfills viscosity criteria Kinematic viscosity ≤ 20.5 mm^2/s @ 40° C 10 mm^2/s < 20.5 mm^2/s Aspiration Category 1 criteria are fulfilled

Example of a mixture not fulfilling the criteria for classification:

Mixture Example #2 Aspiration Hazard		
Data	**HCS 2012 Classification**	**Rationale**
Component data: Component 1: 8%, Aspiration Category 1 Component 4: 7%, Aspiration Category 1 *Mixture data:* Material is a hydrocarbon Kinematic Viscosity @ 40ºC (104ºF) = 25 mm^2/s	Not classified for aspiration hazard	Material is a hydrocarbon Fulfills additive threshold criteria Aspiration Calculation: Σ % Category 1 ≥ 10% 8% + 7% = 15% Does not fulfill viscosity criteria Kinematic viscosity ≤ 20.5 mm^2/s @ 40° C 25 mm^2/s > 20.5 mm^2/s Aspiration Category 1 criteria are NOT fulfilled

References

29 CFR 1910.1200, Hazard Communication, Appendix A.10 Aspiration Hazard.

29 CFR 1910.1200, Hazard Communication, Appendix C Allocation of Label Elements.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

VII.11 Simple Asphyxiants

Introduction

An *asphyxiant* is a vapor or gas that can cause unconsciousness or death by suffocation due to lack of oxygen. Asphyxiants can be either chemical asphyxiants or simple asphyxiants. Chemical asphyxiants cause suffocation by either preventing the uptake of oxygen in the blood or by preventing the normal oxygen transfer from the blood to the tissues or within the cell itself. Simple asphyxiants are inert gases or vapors which are harmful to the body when they become so concentrated that they reduce oxygen in the air (normally about 21 percent) to dangerous levels (19.5 percent or less). When the concentration of a particular gas increases, the fraction of inspired oxygen decreases, causing decreased oxygen in the blood. A decrease in the fraction of inspired oxygen to less than 19.5% causes inadequate oxygen supply within minutes after exposure to a simple asphyxiant, and may result in unconsciousness or death.

Asphyxiation is a well-known hazard in the workplace. Simple asphyxiants frequently contribute to industrial accidents involving loss of life and are of particular concern for those who work in confined spaces, as these gases are colorless and odorless and offer no warning properties.

Definition and General Considerations

Simple asphyxiant means a substance or mixture that displaces oxygen in the ambient atmosphere, and can thus cause oxygen deprivation in those who are exposed, leading to unconsciousness and death.

Simple asphyxiants are of particular concern in enclosed spaces. Some examples of simple asphyxiants include: nitrogen, helium, neon, argon, krypton, and xenon. These gases are well-known simple asphyxiants from experience in the workplace. Evaluation of other gases as simple asphyxiants requires expert judgment to evaluate evidence such as human experience, information from similar substances, and other pertinent data.

References

29 CFR 1910.1200, Hazard Communication, Paragraph C.

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements.

VIII. CLASSIFICATION OF PHYSICAL HAZARDS

Introduction

The physical hazards presented by chemicals often cause harm to workers by exposing them to fire or explosions. Classification of the physical hazards is based on data found in available literature, as a result of a calculation, or through testing using specified test methods. The Hazard Communication Standard does not require the testing of chemicals -- only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, then most chapters specify test methods to be used for the given physical hazard. Each chapter also explains the purpose of each test method, as appropriate, should you choose to conduct the test or have a recognized testing laboratory conduct the analysis for you.

Selection of Hazard Classes

Once the chemical manufacturer, importer, or classifier has collected the data, the data and test results are compared to the classification criteria. The decision logic included for each physical hazard in this guidance document can be used to identify the appropriate hazard class and category of the chemical. The decision logic is essentially a flowchart for classifying chemicals of the specific hazard. It presents questions in a sequence that considers the classification steps and criteria to classify the hazard in the appropriate hazard class and category.

As mentioned throughout this document, many hazardous chemicals have more than one physical hazard and/or health hazard and each hazard must be presented on the label and SDS, as specified in HCS Appendix C, Allocation of Label Elements, and HCS Appendix D, Minimum Information for an SDS. Note that classification of a chemical for one hazard class does not preclude classification of the same chemical for other hazards, unless it is specified otherwise.

Classification Examples

The United Nations Institute of Training and Research (UNITAR) developed several classification examples for physical hazards. These examples are used in each physical hazard section to aid in the understanding of how to apply the decision logics for classification. The examples in each physical hazard section are specific to the given hazard class.

VIII.1 Explosives

Introduction

Explosive chemicals are unstable materials which can release enough energy or force to damage the surrounding area. Explosive chemicals are separated into two types. One type consists of material capable of detonations, that is, reactions that occur at a velocity greater than the speed of sound (for example, nitroglycerine and TNT). The other type consists of materials, usually mixtures, that burn rapidly but at a velocity that is less than the speed of sound (this is called a deflagration). Examples of this second type of explosive include mixtures of natural gas and air, liquid propane (LP) gases and air, or gasoline vapors and air black powder or rocket fuels.

Explosions differ from fire by the rate at which high temperature gases are produced and the physical containment of the burning gases. When high temperature gases build up extremely quickly, there can be such a sudden release of energy from the gases that it creates a shock wave or explosion. Confining the build-up of high-pressure gases to a drum or vessel, which prevents venting of the gases, may promote an increase in the pressure within the restricted volume until an explosion occurs. This is the principle behind some munitions that confine high-pressure gases until the pressure exceeds the strength of the casing.

Most explosives have a chemical structure that contains both oxidizing and fuel functional groups. Examples of functional groups contained in explosives are azides, dizonium, and styphnate. While the presence of such functional groups suggests explosive capability, it is usually necessary to confirm this hazard through experimental studies.

Classification of materials in the explosives hazard class and allocation to the appropriate division is very complex. The classifier should have the necessary expertise and use Part I of the *UN Recommendations on the Transport of Dangerous Goods (UN TDG) Manual of Testing and Criteria* to determine the proper hazard allocation. The HCS classification system almost entirely adopted the *UN TDG Model Regulations*, which is appropriate for transport as well as the storage of packaged explosives.

Definition

An *explosive chemical* is a solid or liquid chemical, which is in itself capable by chemical reaction of producing gas at such a temperature and pressure and at such a speed as to cause damage to the surroundings. Pyrotechnic chemicals are included even when they do not evolve gases.

A *pyrotechnic chemical* is a chemical designed to produce an effect by heat, light, sound, gas, or smoke, or a combination of these, as the result of non-detonative self-sustaining exothermic chemical reactions.

An *explosive item* is an item containing one or more explosive chemicals.

A *pyrotechnic item* is an item containing one or more pyrotechnic chemicals.

An *unstable explosive* is an explosive which is thermally unstable and/or too sensitive for normal handling, transport, or use.

The HCS uses the term "item," instead of the term "article" in the explosives hazard class, because the HCS has an existing and long-standing definition for the term "article."

An *intentional explosive* is a chemical or item which is manufactured with a view to produce a practical explosive or pyrotechnic effect.

The HCS hazard class of explosives includes:

(a) Explosive chemicals;
(b) Explosive items, except devices containing explosive chemicals in such quantity or of such a character that their inadvertent or accidental ignition or initiation does not cause any effect external to the device either by projection, fire, smoke, heat, or loud noise; and
(c) Chemicals and items not included under (a) and (b) above, which are manufactured with the intent to produce a practical explosive or pyrotechnic effect.

Classification Criteria

Chemicals and items of this class are classified as unstable explosives or are assigned to one of the following six divisions depending on the type of hazard they present:

Division 1.1: Chemicals and items which have a mass explosion hazard (a mass explosion is one which affects almost the entire quantity present virtually instantaneously).

Division 1.2: Chemicals and items which have a projection hazard but not a mass explosion hazard.

Division 1.3: Chemicals and items which have a fire hazard and either a minor blast hazard or a minor projection hazard or both, but not a mass explosion hazard, and:

i. Combustion which gives rise to considerable radiant heat; or
ii. Which burn one after another, producing minor blast or projection effects or both.

Division 1.4: Chemicals and items which present no significant hazard: chemicals and items which present only a small hazard in the event of ignition or initiation. The effects are largely confined to the package and no projection of fragments of appreciable size or range is to be expected. An external fire shall not cause virtually instantaneous explosion of almost the entire contents of the package.

Division 1.5: Very insensitive chemicals which have a mass explosion hazard: chemicals, which have a mass explosion hazard but are so insensitive that there is very little probability of initiation or of transition from burning to detonation under normal conditions.

Division 1.6: Extremely insensitive items which do not have a mass explosion hazard: items which contain only extremely insensitive detonating chemicals and which demonstrate a negligible probability of accidental initiation or propagation.

Unstable explosives are those that are thermally unstable and/or are too sensitive for normal handling, transport, and use. Special precautions are necessary.

Classification Procedure and Guidance

To classify an explosive chemical, data on its explosive behavior, thermal stability, and sensitivity are needed.

Available Literature

The manufacturer, importer, or other responsible party may use available scientific literature and other evidence to classify explosives.

As is the case when classifying other physical hazards, the U.S. Department of Transportation (DOT) listings can be used to assist when classifying explosive chemicals (see DOT's Hazardous Materials Table, 49 CFR 172.101). This is especially true if the explosive is transported. In this case, the explosive has already been classified and approved for transport by DOT. Classification of explosives in the HCS generally corresponds to existing explosives assignments that are packaged in authorized DOT transport packaging. Explosives Class 1 is a restricted transportation class. There are generic explosive classifications in 49 CFR 172.101 that may be used to assist in classification. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information. The decision logics presented below also may be used to determine the appropriate hazard classification for explosives.

Test Method

Most explosives that are approved for transport have already undergone testing and assignment to the appropriate explosives hazard class. Testing may be necessary only for those chemicals, mixtures, or items that are new and have not been assigned a transport classification. If you choose to test the substance or mixture, then use of a testing laboratory specializing in the testing of explosives is recommended, as the testing protocol used for explosives is a complex process. Also, if you choose to test the substance or mixture, use the methods identified in Appendix B.1 to 29 CFR 1910.1200, which are described below.

Explosives are either classified as unstable explosives or are assigned to one of the six divisions by using the three-step procedure presented in Part I of the of the Fourth Revised Edition of the *UN TDG Manual of Tests and Criteria*. The test method used for classification of explosives and appropriate hazard division is a complex, three-step procedure.

- The first step, the screening procedure, ascertains whether the substance or mixture has explosive effects (Test Series 1).
- The second step provides an acceptance procedure (Test Series 2 to 4).
- The third step assigns the chemical to a hazard division (Test Series 5 to 7).

Test Series 8 assesses whether an ammonium nitrate emulsion should be classified as an oxidizing liquid (See Appendix B.13 to 29 CFR 1910.1200) or an oxidizing solid (See Appendix B.14 to 29 CFR 1910.1200), or whether it is classifiable as an explosive. The results of this test series may also be used to evaluate the suitability of the chemical or mixture for transport in tanks. Ammonium nitrate emulsions are manufactured precursors for explosives, and when manufactured, are not generally in themselves explosive.

Solid chemicals are classified using tests performed on the chemical as presented and as packaged. If, for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that in which it was tested, and in a form that is considered likely to materially alter the chemical's performance in a classification test, then testing for classification is based the chemical in its new form.

Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the methods, the apparatus used, and analysis of the test results.

Step 1: Screening Procedures

As with other hazardous chemicals, especially those that may be sensitive to mechanical stimuli (such as impact and friction), and to heat and flame, small scale, preliminary tests are suggested to protect laboratory personnel.

Explosive properties are associated with the presence of certain chemical groups in a molecule that can react to produce very rapid increases in temperature or pressure. The screening procedure is aimed at identifying the presence of such reactive groups and the potential for rapid energy release, and is suggested to identify the need for further testing. If the exothermic decomposition energy of organic materials is less than 800 J/g, neither a Series 1 type (a) propagation of detonation test, nor a Series 2 type (a) test of sensitivity to detonative shock is required. If the screening procedure identifies the chemical as a potential explosive or if the chemical contains any known explosives, then the acceptance procedure for explosives is necessary for assignment to a hazard division.

A chemical is **not classified** as explosive if any of the following four conditions apply:

1. There are no chemical groups present in the molecule associated with explosive properties; examples of such groups are provided in Table VIII.1.1 below, extracted from the *UN TDG Manual for Tests and Criteria*, Appendix 6.

   Table VIII.1.1. Examples of Chemical Groups Indicating Explosive Properties in Organic Material.

Structural feature	Examples
C-C unsaturation	Acetylenes, acetylides, 1,2-dienes
C-Metal, N-Metal	Grignard reagents, organo-lithium compounds
Contiguous nitrogen atoms	Azides, aliphatic azo compounds, diazonium salts, hydrazines, sulphonylhydrazides
Contiguous oxygen atoms	Peroxides, ozonides
N-O	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N-halogen	Chloroamines, fluoroamines
O-halogen	Chlorates, perchlorates, iodosyl compounds

   or

2. The substance contains chemical groups associated with explosive properties that include oxygen, and the calculated oxygen balance is less than −200.

   The oxygen balance is calculated for the chemical reaction:

   $$C_xH_yO_z + [x + (y/4)-(z/2)]\ O_2 \leftrightarrow x\ CO_2 + (y/2)\ H_2O$$

   using the formula:

   oxygen balance = -1600 [2x +(y/2) -z] / molecular weight; or

3. The organic substance or a homogenous mixture of organic substances contains chemical groups associated with explosive properties, but the exothermic decomposition energy is less than 500 J/g and the onset of exothermic decomposition is below 500 °C (932 °F). The exothermic decomposition energy may be determined using a suitable calorimetric technique; or

4. For mixtures of inorganic oxidizing chemicals with organic material(s), the concentration of the inorganic oxidizing chemical is:

    i. less than 15%, by mass, if the oxidizing substance is assigned to Category 1 or 2;
    ii. less than 30%, by mass, if the oxidizing substance is assigned to Category 3.

Step 2: Acceptance Procedure

This overview of the explosives test procedures and methods is designed to help classifiers understand the intent of the various tests. OSHA urges caution when performing these tests; a laboratory specializing in explosives testing always should perform them.

Refer to the UN TDG Manual of Tests and Criteria *for a complete description of the methods, the apparatus used, and analysis of the test results.*

The acceptance procedure is used to determine whether a chemical is a candidate for the explosives hazard class or is an unstable explosive. The acceptance procedure should be applied to any chemical or mixture of chemicals containing any known explosives. Although the acceptance procedure includes Test Series 2 through 4, Test Series 1 is included in the explanation below. If the chemical is known to be designed and intended for use in manufacturing explosives, then tests 1 and 2 can be skipped and analysis can begin with Test Series 3. The classification criteria originally were designed for transportation and take into account the chemical as presented and as packaged. However, as mentioned above, if the same chemical is to be presented in a physical form different from that in which it was tested, and in a form that is considered likely to materially alter the chemical's performance (i.e., under normal conditions of use or in foreseeable emergencies) in a classification test, then testing for classification must be based on the chemical in its new form.

- *Test Series 1* is intended to answer the question "Is it an explosive substance/mixture?" (See box 4 of Figure VIII.1.2). This series includes three types of tests to assess possible explosive effects. The tests determine the propagation of detonation, the effect of heating under confinement, and the effect of ignition under confinement. Although four tests are explained in the *UN TDG Manual of Tests and Criteria*, only three are recommended: the UN gap test, the Koenen test, and the time/pressure test.
- *Test Series 2* is intended to answer the question "Is the substance /mixture too insensitive for acceptance into this Class?" (See box 6 of Figure VIII.1.2). This series also includes three types of tests to assess possible explosive effects. The tests determine the sensitivity to shock, the effect of heating under confinement, and the effect of ignition under confinement. The three recommended tests are the same as those for Test Series 1.
- *Test Series 3* is intended to answer the questions "Is the substance / mixture thermally stable?" and "Is the substance/mixture too dangerous in the form in which it was tested?" (See boxes 10 and 11 of Figure VIII.1.2). This test series includes four types of tests to determine sensitiveness to impact, sensitiveness to friction (including impacted friction),

thermal stability of a substance, and response of the substance to fire. Although there are eleven tests identified in this test series and explained in the *UN TDG Manual of Tests and Criteria*, only four are recommended: the BAM Fallhammer, BAM friction apparatus, thermal stability test at 75 °C, and the small-scale burning tests.

- *Test Series 4* is intended to answer the question "Is the item, packaged item or packaged substance too dangerous?" (See box 16 of Figure VIII.1.2). This test series includes two types of tests to determine the thermal stability for items, and the danger from dropping. All three of the tests in this series explained in the *UN TDG Manual of Tests and Criteria* are recommended: the thermal stability test for unpackaged items and packaged items, steel tube drop test for liquids, twelve-meter drop test for items, packaged items and packaged substances.

Step 3: Procedure for Hazard Assignment

This set of procedures assigns the chemical, mixture, or item to one of the six divisions in this hazard class. The assignment depends on the type of hazard presented and applies to all chemicals, mixtures, and/or items that are candidates for the explosives hazard class. If testing is conducted, then the chemical should be assigned to the division that corresponds to the test results to which the chemical, or item as offered for supply and transport, has been subjected (that is, the testing and classification includes the chemical, mixture, or item's packaging).

The test methods used for assignment to a division are grouped into three test series – numbered Test Series 5 to Test Series 7 – designed to provide the information necessary to answer the questions in the decision logic presented in Figure VIII.1.3, "Procedure for assignment to a division in the class of explosives."

- *Test Series 5* is intended to answer the question "Is it a very insensitive explosive substance with a mass explosion hazard?" The results of this test series also determine if a substance may be assigned to Division 1.5. (See box 21 of Figure VIII.1.3) This test series includes three types of tests: a shock test to determine the sensitivity to intense mechanical stimulus, thermal tests to determine the tendency of transition from deflagration to detonation, and a test to determine if a substance, when in large quantities, explodes when subjected to a large fire. Although there are five tests identified in test series 5, only three are recommended: the cap sensitivity test, USA DDT test, and the external fire test for Division 1.5.
- The results from *Test Series 6* tests are used to assign a substance, mixture, or item to Division 1.1, 1.2, 1.3 or 1.4 (see boxes 26, 28, 30, 32, and 33 of Figure VIII.1.3). The results also are used to determine if the substance, mixture, or item is assigned to Compatibility Group S of Division 1.4, and whether the chemical or mixture should be excluded from the explosives hazard class (see boxes 35 and 36 of Figure VIII.1.3). This test series includes four types of tests on the item as packaged, including tests on:
    - a single package to determine if there is mass explosion of the contents,

- packages of an explosive substance or explosive items, or non-packaged explosive items, to determine whether an explosion is propagated from one package to another or from a non-packaged item to another,
- packages of an explosive substance or explosive items, or non-packaged explosive items, to determine whether there is a mass explosion or a hazard from dangerous projections, radiant heat and/or violent burning or any other dangerous effect when involved in a fire, and
- an unconfined package of explosive items to which special provision 347 of Chapter 3.3 of the *UN TDG Model Regulations* applies, to determine if there are hazardous effects outside the package arising from accidental ignition or initiation of the contents.

All four of the tests for test series 6 are recommended: the single package test, stack test, external fire (bonfire) test, and the unconfined package test.

- *Test Series 7* is intended to answer the question "Is it an extremely insensitive explosive item?" (See box 40 of Figure VIII.1.3.) The results of this test series also determine if an item is assigned to Division 1.6. There are ten types of tests in this test series; the first six tests listed below establish if the chemical is an extremely insensitive detonating substance (EIDS), and the last four types of tests determine if an item containing an extremely insensitive detonating substance may be assigned to Division 1.6. The tests determine:

  - sensitivity to intense mechanical stimulus,
  - sensitivity to shock,
  - sensitivity of the explosive substance to deterioration under the effect of an impact,
  - the degree of reaction of the explosive substance to impact or penetration resulting from a given energy source,
  - the reaction of the explosive substance to an external fire when the material is confined,
  - the reaction of the explosive substance in an environment in which the temperature is gradually increased to 365 °C,
  - the reaction to an external fire of an item that is in the condition as presented for transport,
  - the reaction of an item in an environment in which the temperature is gradually increased to 365 °C,
  - the reaction of an item to impact or penetration resulting from a given energy source, and
  - whether a detonation of an item will initiate a detonation in an adjacent, like item.

There are twelve tests in Test Series 7, ten of which are recommended and are listed below. As mentioned above, the first six tests are for chemicals, while the last four tests are for items.

- EIDS cap test
- EIDS gap test
- Friability test
- EIDS bullet impact test
- EIDS external fire test
- EIDS slow cook-off test
- 1.6 article external fire test
- 1.6 article slow cook-off test
- 1.6 article bullet impact test
- 1.6 article stack test

Test Series 8 is intended to answer the question "Is the substance a candidate for "ammonium nitrate emulsion or suspension or gel, intermediate for blasting explosives (ANE)?". Three types of tests are included in this series to determine the thermal stability, sensitivity to intense shock, and the effect of heating under confinement. Three tests are recommended: the thermal stability test for ammonium nitrate emulsions (ANE), the ANE gap test, and the Koenen test.

Compatibility Groups

For the purposes of transport and storage, compatibility groups are also assigned to explosives. These groups identify the necessary controls to prevent hazardous conditions for explosives transported or stored together. There are thirteen compatibility groups: A, B, C, D, E, F, G, H, J, K, L, N, and S. In the Hazard Communication Standard, there are specific labeling requirements for Division 1.4 explosives assigned to compatibility group S (See Appendix C.4.14 to 29 CFR 1910.1200). Additional information about compatibility groups and their assignment can be found in Section 2.1.2 of the *UN TDG Model Regulations,* and Chapters 49 CFR 177.50 – 52 and 49 CFR 178.848 of the U.S. DOT regulations.

Classification Procedure

Explosives are classified according to the classification principles given in the decision logic and the results of test series 1 through 7.

The explosives classification procedure uses the following four decision logics. Once you have collected the data, compare it to the criteria for explosives. Follow the logic paths presented in the decision logics (or flowcharts) in Figures VIII.1.1, VIII.1.2, VIII.1.3, and VIII.1.4 to identify the appropriate classification for explosives. Figure VIII.1.1 presents the overall scheme of the procedure for classifying a chemical, mixture, or item in the explosives hazard class (Class 1 for transport). Figure VIII.1.2 presents the overall scheme to answer questions associated with the results of Test series 1 through 4. Figure VIII.1.3 presents the logic for assigning a chemical, mixture, or item to a division in the explosives hazard class. Figure VIII.1.4 presents the logic for classification of an ammonium nitrate emulsion, suspension, or gel. The reference to B.1.1.2 (b) in Figure VIII.1.3 refers to Appendix B to 29 CFR 1910.1200.

Figure VIII.1.1. Overall scheme of the procedure for classifying a chemical, mixture, or item in the class of explosives (Class 1 for transport).

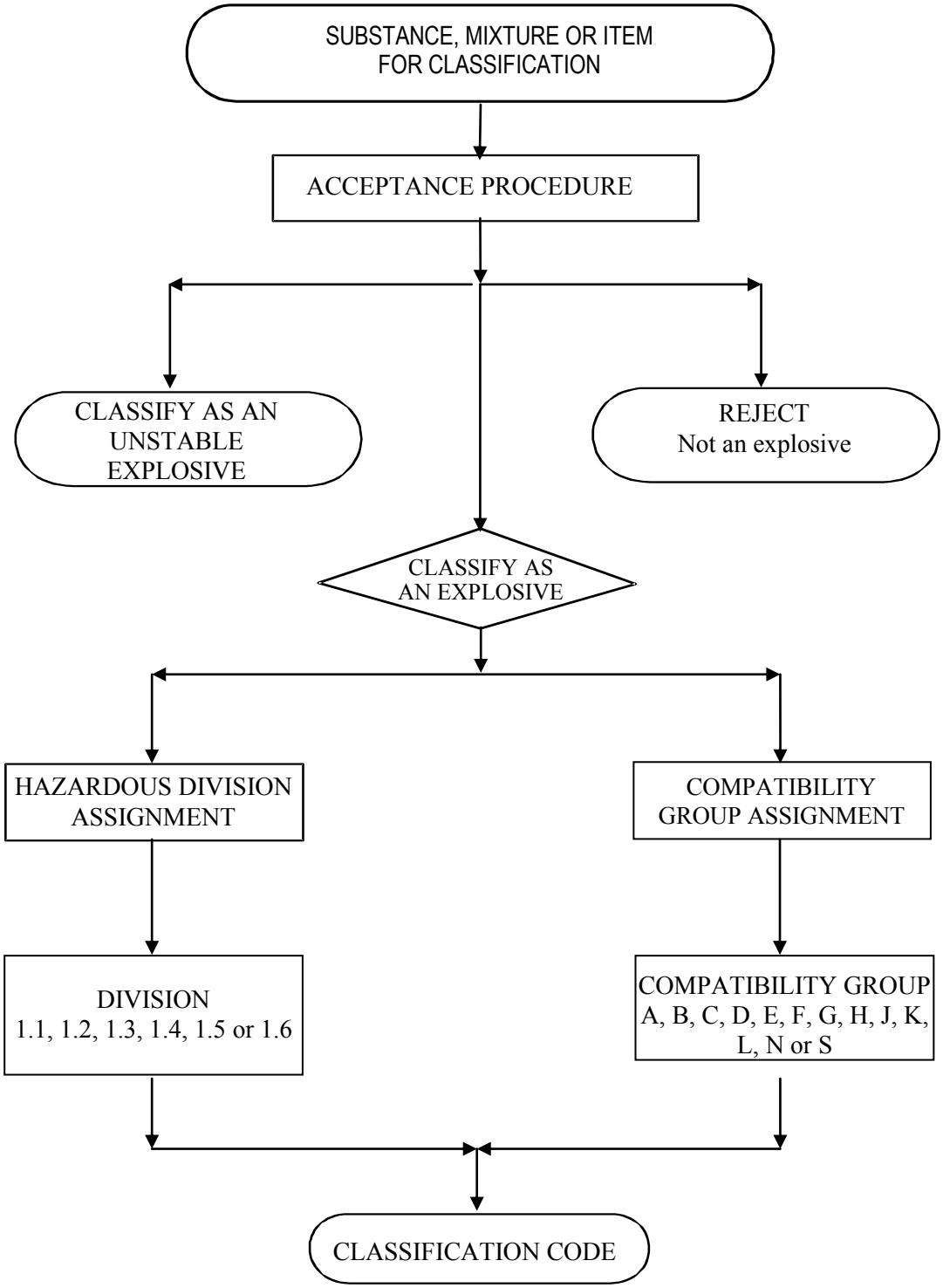
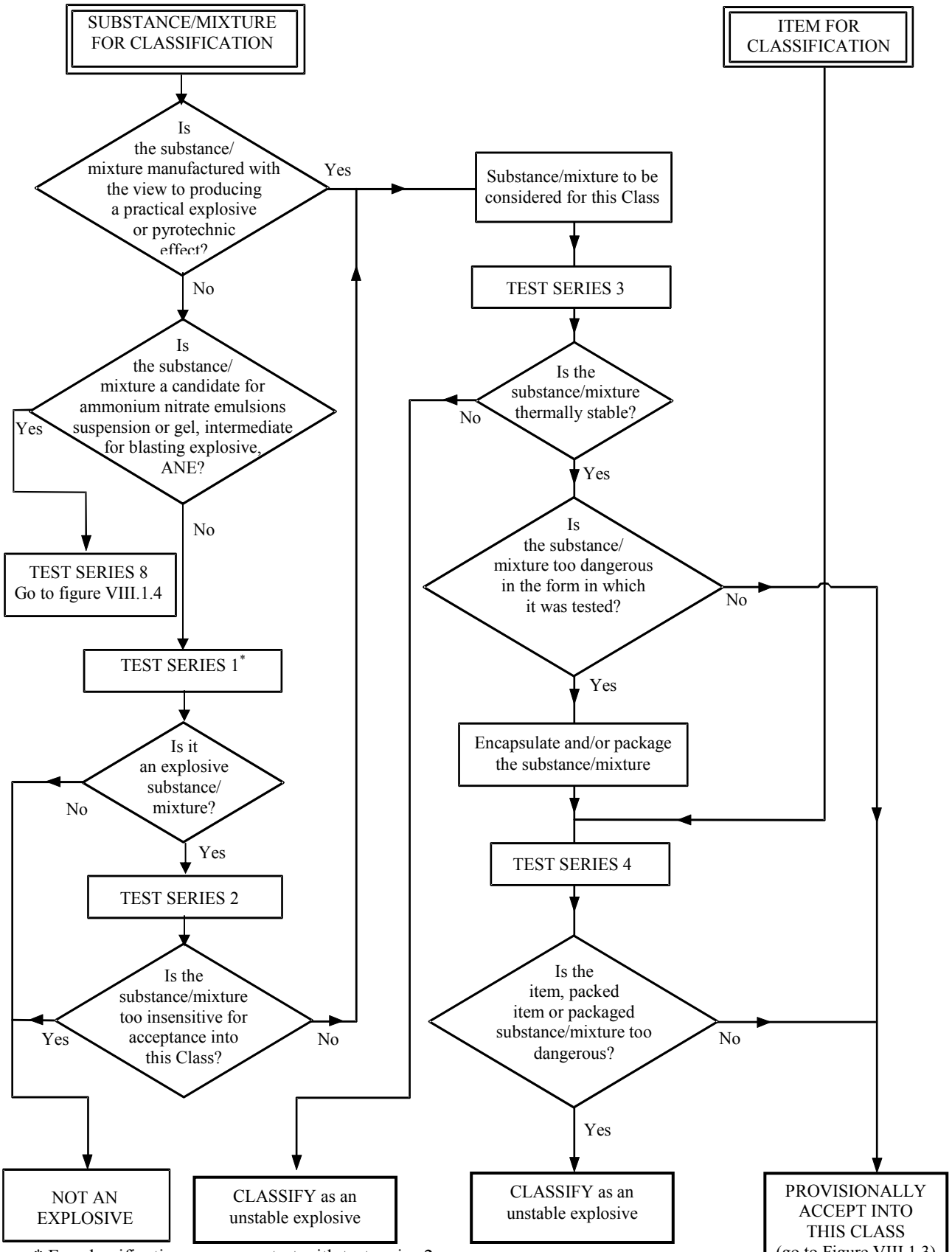


Figure VIII.1.2. Procedure for provisional acceptance of a substance, mixture, or item in the class of explosives (Class 1 for transport).



* For classification purposes start with test series 2

Figure VIII.1.3. Procedure for assignment to a division in the class of explosives (Class 1 for transport).

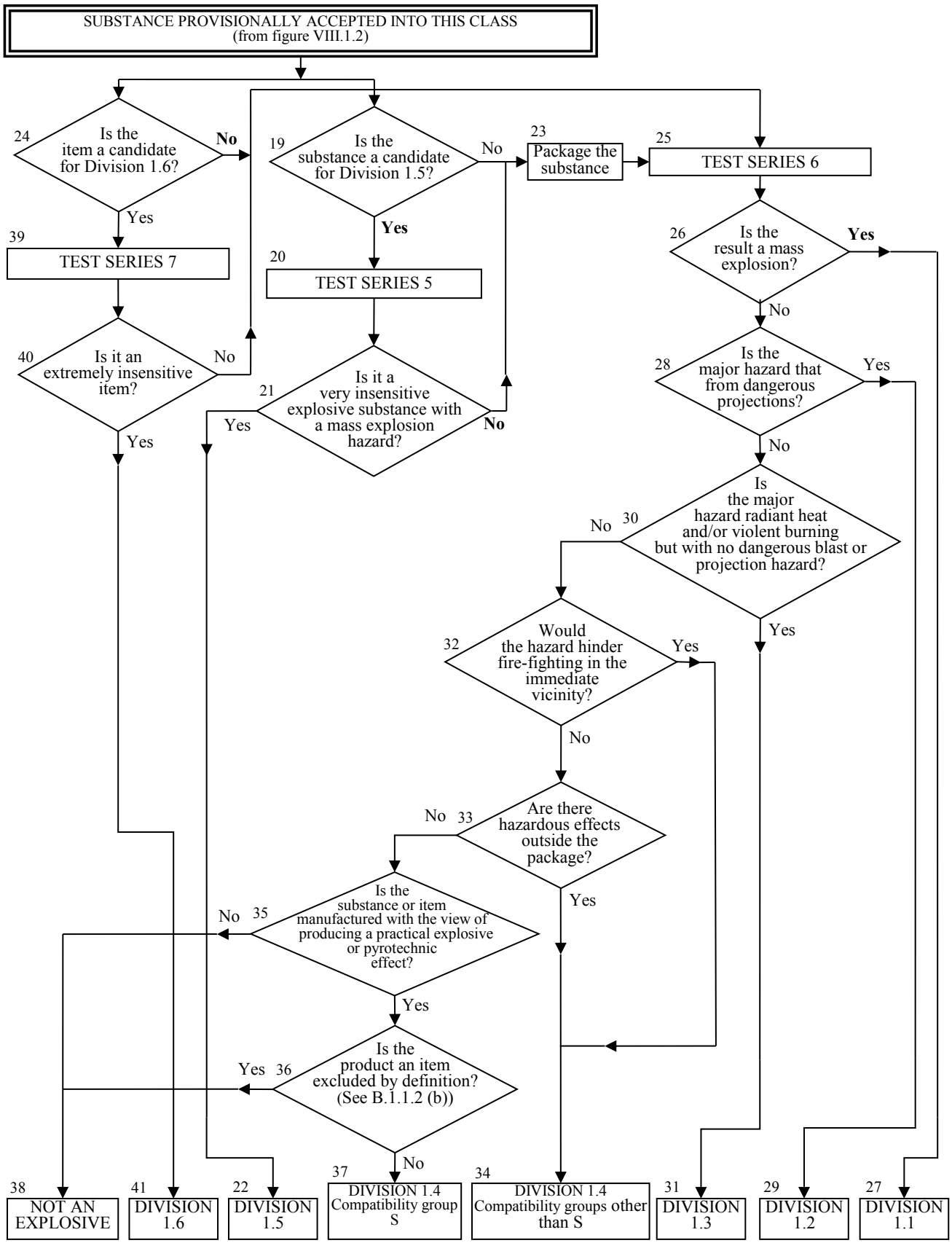
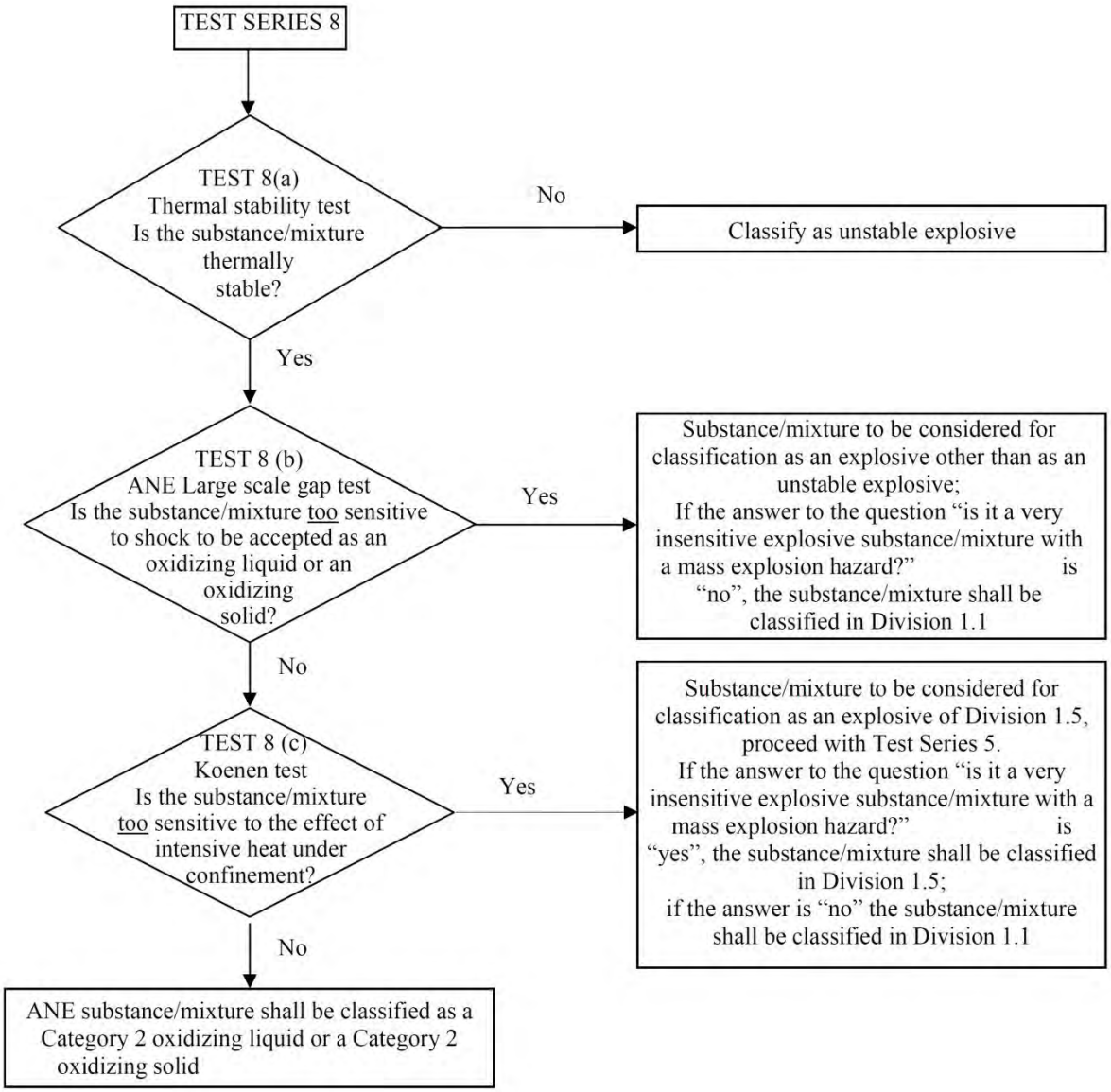


Figure VIII.1.4. Procedure for the classification of ammonium nitrate emulsion, suspension, or gel (ANE).



Explosives Classification Example

The following example is provided to illustrate the classification process and use of the decision logic for explosives. Note that the example includes the use and analysis of test data for explanatory purposes.

A solid, hexanitrostilbene, that is manufactured with the intent of producing a practical explosive and that has chemical groups associated with explosive properties is tested according to the UN tests below to determine if it meets the explosive criteria.

The test methods for determining the classification and division of explosives are performed using the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, Part I, Test Series 1 to 8. The tests are designed to provide the information necessary to answer the questions in the decision logics for explosives. There is a three-step process for determining the classification and division of Explosives: a screening procedure, an acceptance procedure, and an assignment to a hazard division. More details on the classification are found in the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*.

The Explosives Screening Procedure aims to identify the presence of reactive groups and the potential for rapid energy release. If the screening procedure identifies the material as a potential explosive, the Class 1 Acceptance Procedure should be applied.

Known data

- A powder manufactured with the intent of producing a practical explosive and which has chemical groups associated with explosive properties.
- Composition: 96% Hexanitrostilbene

Test Results

Test Series 1 and 2 are not conducted because the powder is manufactured to produce a practical explosive. These two test series need not be performed, since both tests are designed to determine if a material being tested exhibits explosive properties, and whether it is too insensitive to be accepted as an explosive.

Test Series 3: Is the powder thermally stable?

- For determining the thermal stability of the powder, the thermal stability: 75 °C/48-hour test is conducted.
  RESULT: "–", (or "negative") indicating the powder is thermally stable.

- To determine if the powder is too dangerous for transport in the form in which it was tested, two tests are conducted.
  - For determining sensitiveness to impact, the BAM Fallhammer test is conducted.

RESULT: Limiting impact energy 5 Joules (J); the result is considered "–" (or "negative"), indicating the powder is not too dangerous in the form tested.

- For determining sensitiveness to friction (including impacted friction), the BAM friction test is conducted.
  RESULT: Limiting load > 240 Newtons (N); the result is considered "–" (or "negative"), indicating the powder is not too dangerous in the form tested.

CONCLUSIONS: The powder is provisionally accepted into the Explosives Class.

Test Series 4 is not conducted when following the decision logic – the powder is not too dangerous for transport.

Test Series 5: Is it a very insensitive explosive substance with a mass explosion hazard?

- To determine if the powder, in large quantities, explodes when subjected to a large fire [External fire test for Division 1.5]
  RESULT: The powder explodes; the result is considered "+" (or "positive"), indicating the powder is not classified as Division 1.5.

- Based on the results above, neither the shock test (to determine the sensitivity to intense mechanical stimulus), nor the thermal test (to determine the tendency for transition from deflagration to detonation) is performed. The need for testing is waived.

CONCLUSIONS: No, the powder is NOT a very insensitive explosive substance with a mass explosion hazard.

Test Series 6: Is the result a mass explosion?

- To determine the effect of initiation in the package, a test is conducted on a single package to determine if there is mass explosion of the contents.
  RESULT: detonation, crater

- To determine the effect of propagation, a test is conducted on packages of an explosive substance to determine whether an explosion is propagated from one package to another.
  RESULT: detonation of the whole stack of packages, crater

- Based on the results above, the test to determine whether there is a mass explosion or a hazard from dangerous projections, radiant heat and/or violent burning or any other dangerous effect when involved in a fire is not conducted. The need for testing is waived.

CONCLUSIONS: Yes, there is a mass explosion hazard. The powder is assigned to Explosives, Division 1.1.

Test Series 7 is not conducted as the powder is not an item.

Test Series 8 is not conducted as the powder is not a candidate for ammonium nitrate emulsions suspension or gel, intermediate for blasting explosive.

Decision/Rationale

To classify an explosive, the classifier would screen the substance, mixture or item for classification as an explosive, use the information gathered from the test data, and follow the decision logics for explosives, answering the questions and following the flowchart as illustrated in Figures VIII.1.2 and VIII.1.3 above.

1. To screen an explosive: Does the powder have reactive groups and/or the potential for rapid energy release?
   ANSWER: Yes, this powder contains a nitro group which is a chemical group (associated with explosive properties.

2. To classify an explosive, the classifier follows the decision logics for explosives, answering the questions and following the logic presented in the flowcharts. Beginning with the logic presented in Figure VIII.1.2, Procedure for Provisional Acceptance, and starting with Box 2.

3. Is the powder manufactured with the intent to produce a practical explosive or pyrotechnic effect?
   ANSWER: Yes; go to Box 8 of Figure VIII.1.2, because the powder is to be considered for classification in the Explosives hazard class (that is, Transportation Class 1).

4. Go to Box 9, Test Series 3

5. Go to Box 10, Test Series 3: Is Powder thermally stable?
   RESULT: Using the results from Test series 3: Yes.

6. Go to Box 11, Test Series 3: Is Powder too dangerous in the form in which it was tested?
   RESULT: Using the results from Test series 3: No.

7. Go to Box 18, the powder is Provisionally Accepted into the Explosives hazard class.

8. Exit Figure VIII.1.2, Acceptance Procedure. Go to Figure VIII.1.3, Procedure for Assignment to a Division in the Class of Explosives, and start with Box 24.

9. Is Powder a candidate for Division 1.6?
   ANSWER: No; the powder is not an item. Go to Box 19.

10. Is the powder a candidate for Division 1.5?
    ANSWER: Uncertain, so go to Test Series 5 (Box 20).

11. In Box 21, Test Series 5: Is powder a very insensitive explosive substance with a mass explosion hazard?
    RESULT: No; go to Box 23 (Package the substance), and then to Box 25, Test Series 6.

12. Is the result a mass explosion?
    RESULT: Yes; detonation of a single package with crater and detonation of the whole stack of packages with crater.

13. Go to Box 27 and classify the powder as Explosive, Division 1.1.
    Test Series 1, 2, 4, 7 and 8 are not required for this powder if the classifier follows the test logic.

Resulting Classification

The powder is classified as an Explosive, Division 1.1 because it has a mass explosion hazard (a mass explosion is one that affects almost the entire quantity present, virtually instantaneously).

References

29 CFR 1910.1200, Hazard Communication, Appendix B.1, Explosives.

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.2 Flammable Gases

Introduction

Gases that ignite pose a serious safety hazard, especially since most gases are stored in cylinders or other containers. Many of these gases have no odor and their presence cannot be detected without the use of a specific detector. Should a leak occur, the gas often accumulates, forming a pocket of gas. These pockets can accumulate at ground level or towards the room's ceiling, depending on the gas' density. Pockets of certain gases can, in turn, lead to fires or explosions. The gas' container may provide another hazard because, should it explode, the container may become a missile/projectile or send parts of the container in all directions.

Definitions

Flammable gas means a gas having a flammable range with air at 20 °C (68 °F) and a standard pressure of 101.3 kPa (14.7 psi).

Flammable range (often referred to as the explosive range) is the range between the lower and upper flammable limit, expressed in terms of percentage of vapor or gas in air by volume.

The flammable range includes all concentrations of flammable vapor or gas in air, in which a flash will occur or a flame will travel if the mixture is ignited and includes rapid combustion or an explosion.

Classification Criteria

A flammable gas is classified in one of two categories, as shown in Table VIII.2.1.

Table VIII.2.1. Classification criteria for flammable gases.

Category	Criteria
1	Gases, which at 20 °C (68 °F) and a standard pressure of 101.3 kPa (14.7 psi): a) are ignitable when in a mixture of 13% or less by volume in air; or b) have a flammable range with air of at least 12 percentage points regardless of the lower flammable limit.
2	Gases, other than those of Category 1, which, at 20 °C (68 °F) and a standard pressure of 101.3 kPa (14.7 psi), have a flammable range while mixed in air.

Note: Aerosols should not be classified as flammable gases.

Classification Procedure and Guidance

To classify a flammable gas, data are necessary on the flammable range and the percentage of the mixture that ignites in air.

Available Literature

The classifier may use available scientific literature and other evidence to identify the flammable range or the percentage of the mixture that ignites in air for many flammable gases. Appendix B of this document provides a listing of information sources that may prove useful during hazard classification.

In addition, many substances presenting flammable gas hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in flammable gas classifications (see 49 CFR 172.101). The classification of flammable gases in the HCS corresponds to DOT's classification of flammable gases.

As explained in the introduction to Classification of Physical Hazards in this guidance document, the information needed to classify a flammable gas (flammable range and percentage of a mixture that ignites) is the same as that required to assign the chemical to the appropriate hazard class under DOT regulations. When a gas is classified under the DOT regulations as a Class 2, Division 2.1 flammable gas, it is classified under the HCS, as a flammable gas, category 1. However, DOT does not cover HCS Category 2 flammable gases. Therefore, to classify chemicals as Category 2 flammable gases, the necessary information and data must be gathered elsewhere. Refer to the discussion of the interface between the HCS and DOT labeling in Chapter V of this document.

The decision logic presented below should be used to determine the appropriate hazard classification category for a flammable gas under the HCS.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, should you choose to test the substance or mixture, use the test methods identified in Appendix B.2 to 29 CFR 1910.1200, which are described below.

The test method presented in ISO 10156:1996, *Gases and Gas mixtures – Determination of fire potential and oxidizing ability for the selection of cylinder valve outlets* is used for determining whether or not a gas is flammable in air and whether a gas is more or less oxidizing than air. This ISO standard provides both the test method (complete with procedure and necessary testing equipment) and the calculation method.

In most cases, however, the classifier will use a calculation to determine if the gas mixture is flammable or not. As noted above, the calculation to determine flammability of gas mixtures is provided by ISO 10156:1996. Where insufficient data are available to use this method, equivalent validated methods may be used.

The ISO 10156:1996 calculation determines only if the mixture is flammable or not. The calculation does not determine a flammable range, nor does it determine if the mixture is classified as a flammable gas Category 1 or Category 2. Therefore, in the absence of additional information, mixtures determined to be flammable according the calculation method should be classified as a Category 1 flammable gas. When there is a need to distinguish between Category 1 and 2, the lower and the upper explosion limits must be determined by using a suitable test method (e.g., ASTM E 681).

ISO Calculation

The calculation in ISO 10156:1996 uses the criterion that a gas mixture is considered non-flammable in air if:

Criterion: $$\sum_{i}^{n} \frac{V_i\%}{T_{ci}} = \geq 1$$

Formula:

$$\sum_{i}^{n} \frac{V_i\%}{T_{ci}} = \frac{V_1}{T_{c1}} + \frac{V_2}{T_{c2}} + ... + \frac{V_n}{T_{cn}}$$

Where

$V_i\%$	the equivalent flammable gas content
T_{ci}	the maximum concentration of a flammable gas in nitrogen at which the mixture is still not flammable in air
i	the first gas in the mixture
n	the n^{th} gas in the mixture
K_i	the equivalence factor for an inert gas versus nitrogen

In the above equation, both the T_{ci} and K_i values are constants. The T_{ci} values are provided in ISO 10156:1996 Table 2, *Maximum content T_{ci} of flammable gas which, when mixed with nitrogen, is not flammable in air*. The K_i values are a coefficient of equivalency which expresses the terms of an equivalent composition in which all the inert-gas fractions are converted into their nitrogen equivalent. Where a gas mixture contains an inert diluent other than nitrogen, the volume of this diluent is adjusted to the equivalent volume of nitrogen using the equivalency factor for the inert gas K_i. The K_i values are provided in ISO 10156:1996 Table 1, *Coefficients of equivalency, K_i, for inert gases relative to nitrogen*.

Classification Procedure

The necessary data to classify flammable gases includes the following:

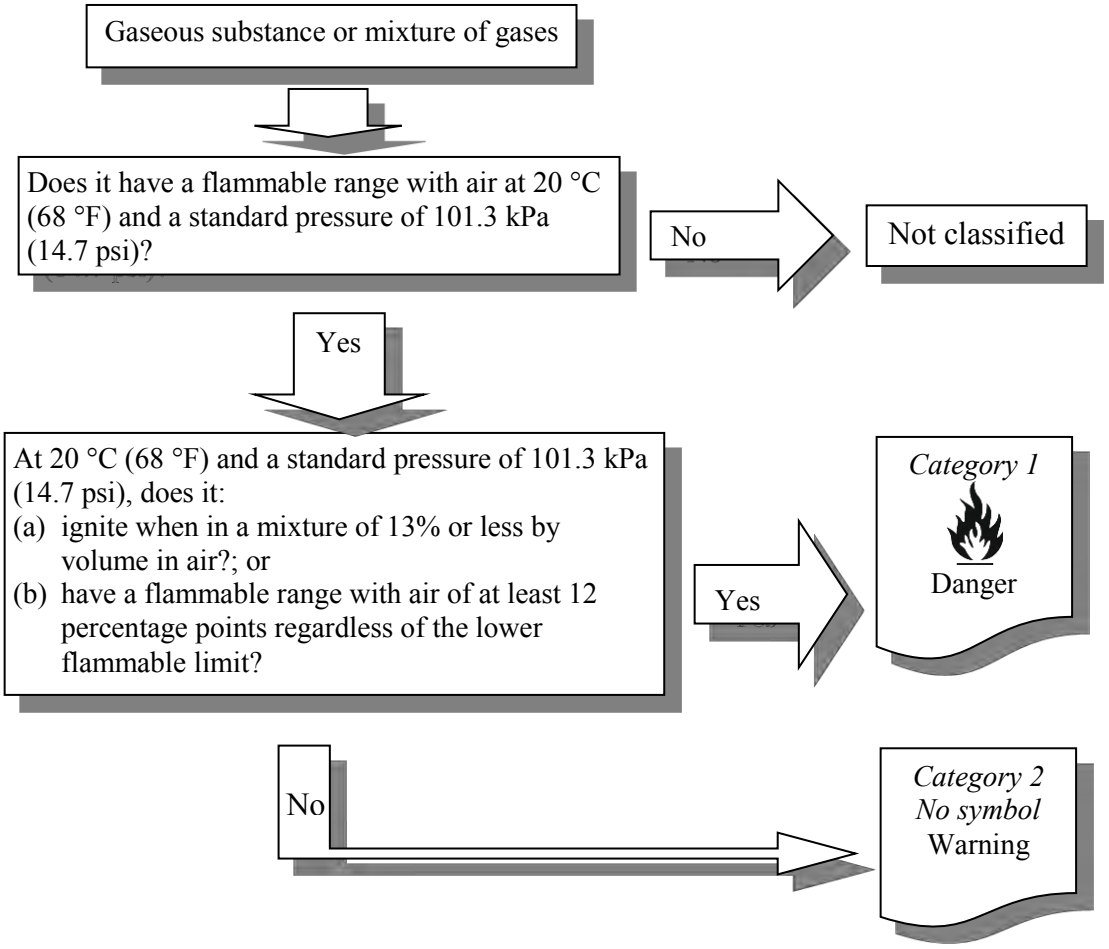
- the flammable range and
- the percentage of the mixture that ignites in air

Classification follows the assessment of data on the flammable range and the percentage of the mixture that ignites in air. Once you have collected the data, compare it to the criteria for flammable gases Category 1 and Category 2, presented in Table VIII.2.1. Follow the logic paths presented in the decision logic (or flowchart) in Figure VIII.2.1, to identify the appropriate classification categories for flammable gases.

Decision logic for classifying flammable gases

The decision logic for classifying flammable gases is provided below.

Figure VIII.2.1. Decision logic for classifying flammable gases.



Flammable Gas Classification Examples

The following examples are provided to illustrate the classification process when data is available for the given chemical.

Example #1: Classification by Calculation According to ISO 10156:1996

When the composition of a material is known, a calculation in ISO 10156:1996, "*Gases and gas mixtures – Determination of fire potential and oxidizing ability for the selection of cylinder valve outlets*," can be used to determine whether a gas mixture that is suspected of being flammable should be classified as a flammable gas. The following example presents the steps to perform this calculation. For the purpose of this example the following gas mixture is used:

2% (H_2) + 6% (CH_4) + 27% (Ar) + 65% (He)

1. Look up the values of T_{ci} and K_i in ISO 10156:

   K_i (Ar) = 0.5
   K_i (He) = 0.5
   T_{ci} H_2 = 5.7%
   T_{ci} CH_4 = 14.3%

2. Calculate the equivalent mixture with nitrogen as balance gas using the K_i figures for the inert gases:

$2\%(H_2) + 6\%(CH_4) + [27\% \times K_i\ (Ar) + 65\% \times K_i\ (He)](N_2) =$
$2\%(H_2) + 6\%(CH_4) + [27\% \times 0.5 + 65\% \times 0.5](N_2) = 2\%(H_2) + 6\%(CH_4) + 46\%(N_2) = 54\%$

3. Adjust the sum of the contents to 100%. The results provide the equivalent flammable gas content (V_i%) values for hydrogen and methane:

$$\frac{100}{54} \text{ x } [2\%(H_2) + 6\%(CH_4) + 46\%(N_2)] = 3.7\%(H_2) + 11.1\%(CH_4) + 85.2\%(N_2)$$

4. Calculate the flammability of the equivalent mixture using the formula in ISO 10156:2010 (shown above) and the V_i% and T_{ci} values for H_2 and CH_4:

$$\sum_i^n \frac{V_i\%}{T_{ci}} = \frac{3.7}{5.7} + \frac{11.1}{14.3} = 1.42$$

5. Compare the answer to the criterion:

$\sum_i^n \frac{V_i\%}{T_{ci}} \geq 1$ Since 1.42 > 1, the mixture is flammable in air. Without additional information, the chemical is classified as a Flammable Gas, Category 1.

Example #2: Classification with Known Data

When the flammability range is known, the classification of the substance can be obtained according to the HCS Flammable Gas Decision Logic.

A gaseous substance that has a known flammability range is suspected of being a flammable gas.

Known data

- Gaseous substance.
- Boiling Point: -42 °C
- Flammable range: 2.2 – 11 % in air at ambient temperature (20 °C) and standard pressure (101.3 kPa)

Decision/Rationale

1. Does the chemical have a flammable range with air at 20 °C and a standard pressure of 101.3 kPa?

   ANSWER: Yes. The chemical has a flammable range of 2.2 – 11% in air.

2. At 20 °C and a standard pressure of 101.3 kPa, does it:

   a) ignite when in a mixture of 13% or less by volume in air?; or

   b) have a flammable range with air of at least 12 percentage points regardless of the lower flammable limit?

   ANSWER: Yes. The chemical is a gaseous substance and ignites at a concentration of <13% at ambient temperature and standard pressure.

Resulting Classification

Since the chemical fulfills the criteria for Flammable Gas, Category 1, it is classified as such.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.2, Flammable Gases.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

International Standards Organization (ISO) 10156:1996 (E), Gases and Gas Mixtures - Determination of Fire Potential and Oxidizing Ability for the Selection of Cylinder Valve Outlets, Second Edition, Feb. 15, 1996.

VIII.3 Flammable Aerosols

Introduction

The analysis as to whether a chemical is a flammable aerosol is usually based upon laboratory testing of the aerosol as emitted from a pressurized container. In practice, most aerosols are mixtures, usually in air, and are primarily propellant formulations of droplets, particles, gases, and/or vapors. Their flammability is highly dependent on the nature of the propellant formulation. Therefore, data obtained from a literature search that does not pertain to the exact mixture of ingredients in the product may not be relevant when determining the flammability of the product and should be used with caution.

Definition

Aerosol means any non-refillable receptacle containing a gas compressed, liquefied or dissolved under pressure, and fitted with a release device allowing the contents to be ejected as particles in suspension in a gas, or as a foam, paste, powder, liquid or gas.

***Receptacle** means a containment vessel for receiving and holding substances or articles, including any means of closing. (Definition from* UN TDG Model Regulations*, Rev. 16)*

Classification Criteria

Aerosols are considered for classification as flammable if they contain any component that is classified as flammable in accordance with the HCS, Appendix B, i.e.:

Flammable gases (See Appendix B.2 to 29 CFR 1910.1200)
Flammable liquids (See Appendix B.6 to 29 CFR 1910.1200)
Flammable solids (See Appendix B.7 to 29 CFR 1910.1200)

Flammable components do not include pyrophoric, self-heating or water-reactive chemicals because such components are never used as aerosol contents. Flammable aerosols do not fall additionally within the scope of flammable gases, flammable liquids, or flammable solids. That is, if a chemical is classified as a flammable aerosol, then it would not be classified additionally as a flammable gas, flammable liquid or flammable solid. However, depending on their contents, flammable aerosols may fall additionally within the scope of other hazard classes (e.g., health hazard or physical hazard classes), and be subject to additional labeling elements.

A flammable aerosol is classified in one of two categories on the basis of its flammable components (see Table VIII.3.1), its chemical heat of combustion and, if applicable, the results of the foam test (for foam aerosols) and the ignition distance test and enclosed space test (for spray aerosols) in the test procedure described below.

Table VIII.3.1. Classification criteria for flammable aerosols.

Category	Criteria
1	Contains ≥ 85% flammable components and the chemical heat of combustion is ≥ 30 kilojoules/gram (kJ/g); OR a) For spray aerosols, in the ignition distance test, ignition occurs at a distance ≥ 75 cm (29.5 in), OR b) For foam aerosols, in the aerosol foam flammability test i. The flame height is ≥ 20 cm (7.87 in) and the flame duration ≥ 2 seconds; OR ii. The flame height is ≥ 4 cm (1.57 in) and the flame duration ≥ 7 seconds
2	Contains > 1% flammable components, or the heat of combustion is ≥ 20 kJ/g; AND a) For spray aerosols, in the ignition distance test, ignition occurs at a distance ≥ 15 cm (5.9 in), OR In the enclosed space ignition test, the i. Time equivalent is ≤ 300 seconds/m^3; OR ii. Deflagration density is ≤ 300 gram/m^3 b) For foam aerosols, in the aerosol foam flammability test, the flame height is ≥ 4 cm and the flame duration is ≥ 2 seconds AND it does not meet the criteria for Category 1.

Note: Aerosols not submitted to the flammability classification procedures found in 29 CFR 1910.1200, Appendix B are classified as extremely flammable (Category 1).

Classification Procedure and Guidance

To classify a flammable aerosol, the following are necessary: data on its flammable components, on its chemical heat of combustion and, if applicable, the results of the aerosol foam flammability test (for foam aerosols) and the results of the ignition distance test and enclosed space test (for spray aerosols).

Available Literature

The classifier may use available literature and other evidence to identify flammable components, the chemical heat of combustion and, if applicable, the results of the aerosol foam flammability

test (for foam aerosols) and the results of the ignition distance test and enclosed space test (for spray aerosols). Appendix B of this document lists information sources that may prove useful during hazard classification.

In addition, many substances presenting flammable aerosol hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in flammable aerosol classifications (see 49 CFR 172.101). Refer to the discussion of the interface between the HCS and DOT labeling presented in Chapter V of this document.

The decision logic presented below should be used to determine the appropriate hazard classification category for flammable aerosols.

Chemical Heat of Combustion (ΔHc)

The chemical heat of combustion (ΔHc), in kilojoules per gram (kJ/g), is the product of the theoretical heat of combustion (ΔHcomb), and a combustion efficiency, usually less than 1.0 (a typical combustion efficiency is 0.95 or 95%).
For a composite aerosol formulation, the chemical heat of combustion is the summation of the weighted heats of combustion for the individual components, as follows:

$$\Delta H_{c\ (product)} = \sum_{i}^{n} [\ w_i\% \times \Delta H_{c(i)}]$$

where:
ΔH_c = chemical heat of combustion (kJ/g)
$w_i\%$ = mass fraction of component i in the product
$\Delta H_{c(i)}$ = specific heat of combustion (kJ/g) of component i in the product

The chemical heats of combustion are found in literature, calculated or determined by tests identified in Appendix B.3 to 29 CFR 1910.1200; these are ASTM D240-02; ISO 13943: 2000 (E/F), Sections 86.1 to 86.3; and NFPA 30B.

Test Methods

As mentioned throughout this guidance document, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, in the case of spray or foam aerosols, information needed for classification may not be readily available and it may be necessary to conduct certain tests. Should you choose to test the substance or mixture, use the test methods identified in Appendix B.3 to 29 CFR 1910.1200, and described below.

Classification Based on Test Methods in the UN TDG Manual of Tests and Criteria

The criteria for flammable aerosols are based on tests described in Part III of the Fourth Revised Edition of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) – Manual of Tests and Criteria*., The Ignition Distance Test, Enclosed Space Ignition Test,

and Aerosol Foam Flammability Test are performed in accordance with sub-sections 31.4, 31.5, and 31.6 of this manual, respectively. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results. The purpose of each test is presented below.

- Ignition Distance Test for Spray Aerosols (*UN TDG Manual of Tests and Criteria*, sub-section 31.4)

  The ignition distance test is the method used to determine the ignition distance of an aerosol spray in order to assess the associated flame risk. This test is applicable to aerosol products that can spray a distance of 15 cm or more.

  Aerosol products with a spray distance of less than 15 cm, such as dispensing foams, mousses, gels and pastes or fitted with a metering valve, are excluded from this test. Aerosol products that dispense foams, mousses, gels or pastes are subject to testing under the aerosol foam flammability test.

- Enclosed Space Ignition Test (*UN TDG Manual of Tests and Criteria*, sub-section 31.5)
  The enclosed space ignition test is the method used to assess the flammability of products emerging from aerosol dispensers due to their propensity to ignite in an enclosed or confined space.

- Aerosol Foam Flammability Test (*UN TDG Manual of Tests and Criteria*, sub-section 31.6)

  The aerosol foam flammability test is the method to determine the flammability of an aerosol spray emitted in the form of a foam, mousse, gel or paste.

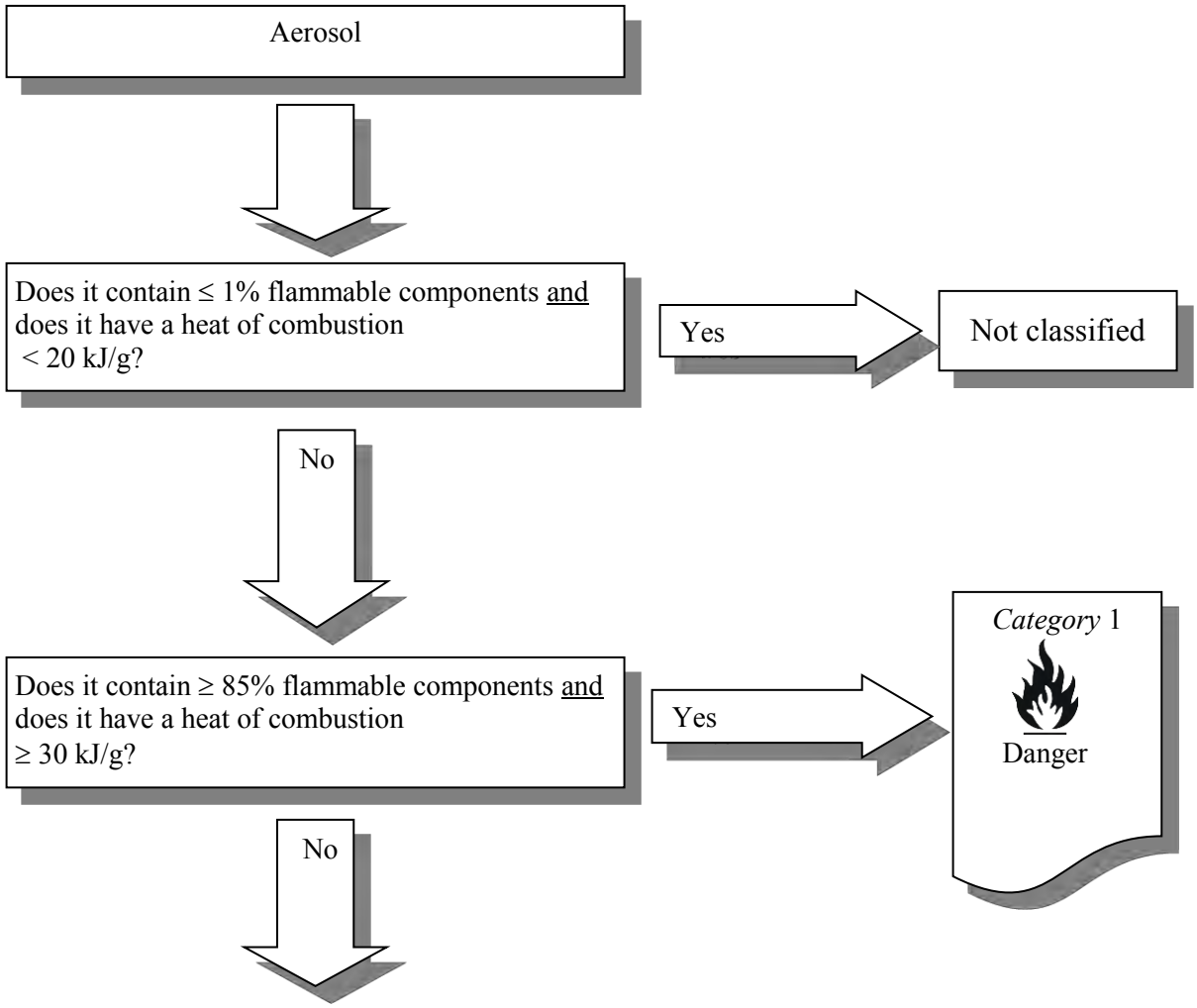
Classification Procedure

The necessary data to classify flammable aerosols includes:

- Amount of flammable components,
- Chemical heat of combustion, and
- Testing results, if applicable, for the aerosol foam flammability test, ignition distance test, and enclosed space test.

Classification follows the assessment of data on the flammable components, on chemical heat of combustion and, if applicable, the results of any testing performed. Once you have collected the data, compare it to the criteria for flammable aerosol category 1 and category 2, presented in Table VIII.3.1. Follow the logic paths presented in the decision logics (or flow charts) in Figures VIII.3.1, VIII.3.2, and VIII.3.3 to identify the appropriate classification categories for flammable aerosols.

Figure VIII.3.1. Decision logic for classifying flammable aerosols.



For the decision logic for spray aerosols, proceed to Figure VIII.3.2.
For the decision logic for foam aerosols, proceed to Figure VIII.3.3.

Figure VIII.3.2. Decision logic for spray aerosols.

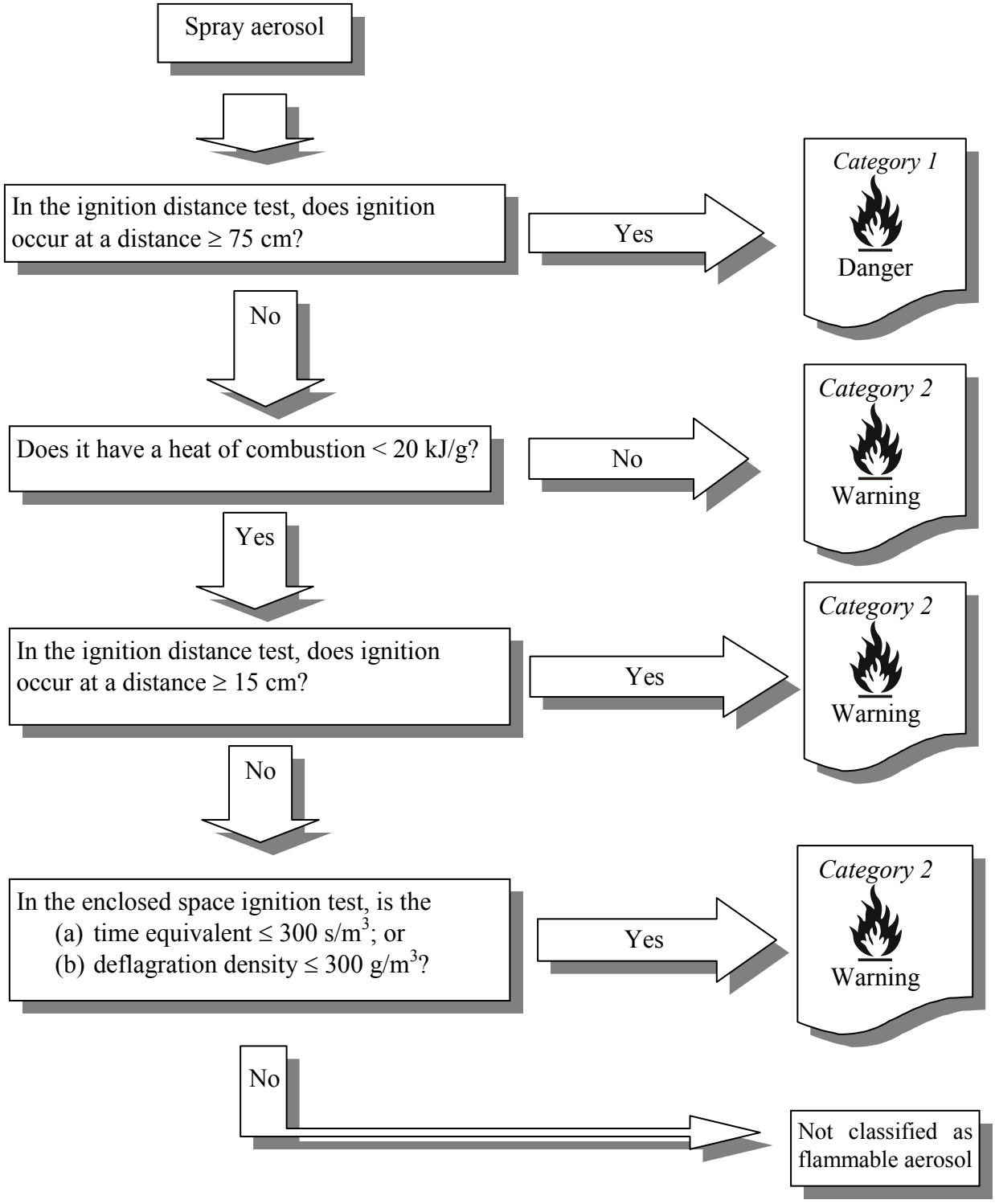
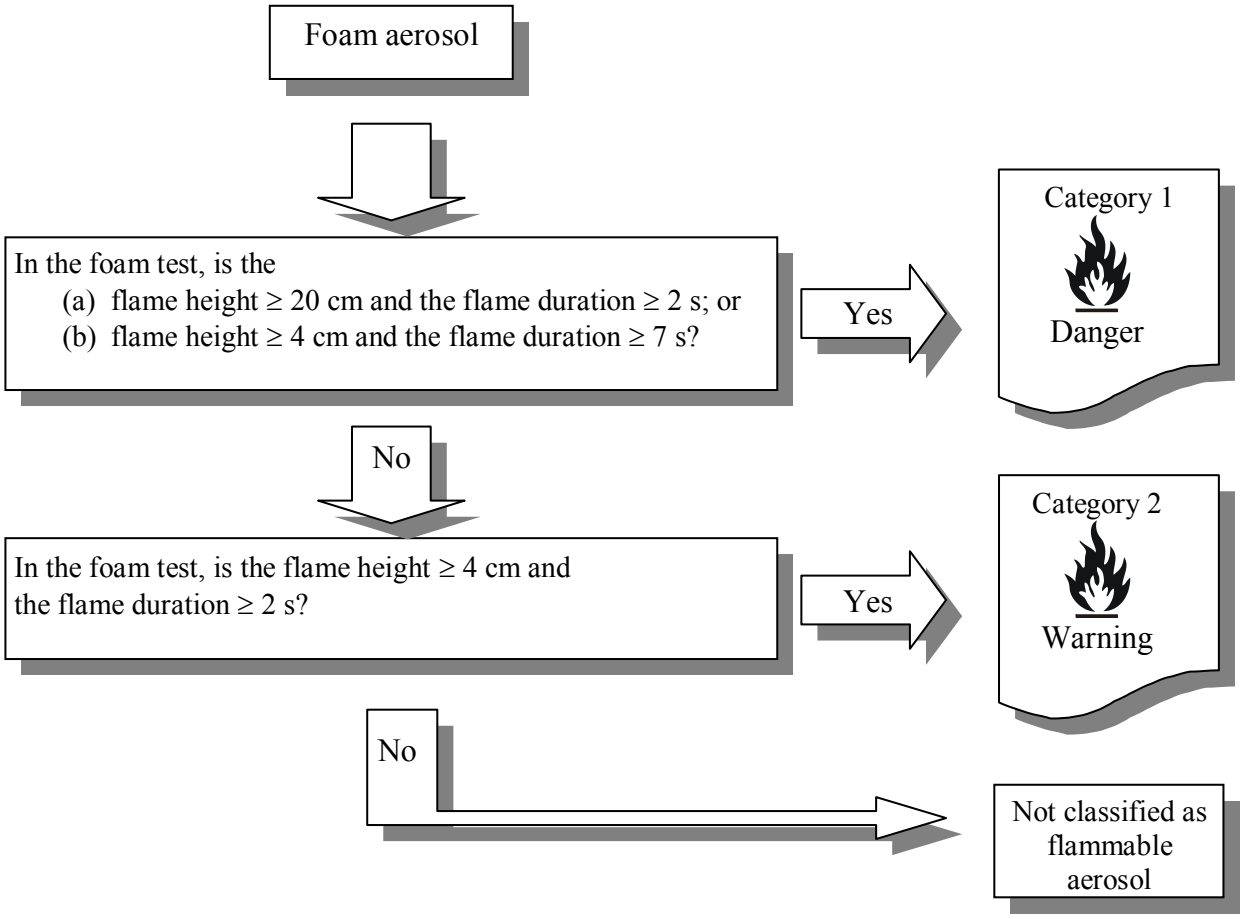


Figure VIII.3.3. Decision logic for foam aerosols.



Flammable Aerosol Classification Examples

Example #1

The following example illustrates the classification process for a chemical suspected of being a flammable aerosol when data on flammable components and on the chemical heat of combustion are known. The classification of the chemical can be determined according to the HCS Flammable Aerosol Decision Logics.

Known data

- The chemical is an aerosol product
- Flammable components:
  Butane/propane = 70% (by mass)
  Ethanol = 25%
- Non-flammable components: 5%
- The chemical heats of combustion [18] (ΔH_c) for gases in the mixture:
  ΔH_c (Butane/propane) = 43.5 kJ/g
  ΔH_c (Ethanol) = 24.7 kJ/g
  ΔH_c (other non-flammable components) = 0 kJ/g

1. Calculate the chemical heat of combustion (ΔH_c) using the formula presented above:

$$\Delta Hc(product) = \sum_{i}^{n} [wi\% \times \Delta Hc(i)]$$

where
ΔH_c is the chemical heat of combustion [kJ/g]
$w_i\%$ is the mass fraction of component i in the product
$\Delta H_{c(i)}$ is the specific heat of combustion [kJ/g] of component i in the product

For this example, the chemical heat of combustion calculation (the summation of the weighted heats of combustion for the individual components) is:

ΔH_c (product) = [$w_i\%$ x $\Delta H_{c(i)}$ for butane/propane] + [$w_i\%$ x $\Delta H_{c(i)}$ for ethanol] + [$w_i\%$ x $\Delta H_{c(i)}$ for the non-flammable components]

ΔH_c (product) = [0.70 x 43.5] + [0.25 x 24.7] + [0.5 x 0] = 30.45 + 6.175 + 0 = 36.6

[18] The chemical heats of combustion can be found in literature, or be calculated or determined by tests (see ASTM D 240, ISO/FDIS 13943:1999 (E/F) 86.l to 86.3 and NFPA 30B).

Decision/Rationale

Using the information gathered, answer the questions posed in the decision logic VIII.3.1, above.

1. Does the chemical contain ≤ 1% flammable components and does it have a heat of combustion < 20 kJ/g?
   ANSWER: No. It has 95% flammable components and the heat of combustion is 36.6 kJ/g.

2. Does the chemical contain ≥ 85% flammable components and does it have a heat of combustion ≥ 30 kJ/g?
   ANSWER: Yes. It has 95% flammable components and the heat of combustion is 36.6 kJ/g.

Resulting Classification

The chemical is classified as a Flammable Aerosol, Category 1, because it contains ≥ 85% flammable components and a heat of combustion ≥ 30 kJ/g.

Example #2

In this example, data on flammable components, the chemical heats of combustion and the results of the ignition distance test and enclosed space test (for spray aerosols) are known. The resulting classification is determined using the HCS Flammable Aerosol Decision Logic VIII.3.1 for aerosols and VIII.3.2 for spray aerosols.

Tests for Flammable Aerosols are located in the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, Part III, Sub-sections 31.4 and 31.5, Ignition distance test and Enclosed space ignition test.

Known data

- Chemical FA2 is a spray aerosol product.
- Flammable components in Chemical FA2:
  Butane/propane: 30%

- Non-flammable components in Chemical FA2: 70%
- The chemical heats of combustion[1] (ΔH_c) for gases in the mixture:
  ΔH_c (Butane/propane) = 43.5 kJ/g
  ΔH_c (other non-flammable components) = 0 kJ/g

Test data/results

Results of the ignition distance test: Ignition occurs at less than 75 cm but more than 15 cm.
Results of enclosed space ignition test: Not conducted
Calculate the chemical heat of combustion[1] (ΔH_c) using the formula presented above:

$$\Delta Hc(product) = \sum_{i}^{n} [wi\% \times \Delta Hc(i)]$$

where
ΔH_c is the chemical heat of combustion [kJ/g]
$w_i\%$ is the mass fraction of component i in the product
$\Delta H_{c(i)}$ is the specific heat of combustion [kJ/g] of component i in the product

For Chemical FA2, the chemical heat of combustion calculation (the summation of the weighted heats of combustion for the individual components) is:

ΔH_c (Chemical FA2) = [$w_i\%$ x $\Delta H_{c(i)}$ for butane/propane] + [$w_i\%$ x $\Delta H_{c(i)}$ for the non-flammable components]

ΔH_c (Chemical FA2) = [0.30 x 43.5] + [0.7 x 0] = 13.05 + 0 = 13.1 kJ/g

Decision/Rationale

1. Does Chemical FA2 contain ≤ 1% flammable components and does it have a heat of combustion < 20 kJ/g?
   ANSWER: No. Chemical FA2 has 30% flammable components and the heat of combustion is 13.1 kJ/g.

2. Does Chemical FA2 contain ≥ 85% flammable components and does it have a heat of combustion ≥ 30 kJ/g?
   ANSWER: No. Chemical FA2 has 30% flammable components and the heat of combustion is 13.1 kJ/g.

3. For spray aerosols, go to decision logic VIII.3.2.

4. In the ignition distance test, does ignition occur at a distance ≥ 75 cm?
   ANSWER: No. Ignition occurs between 75 and 15 cm.

5. Does Chemical FA2 have a heat of combustion < 20 kJ/g?
   ANSWER: Yes. The heat of combustion is 13.1 kJ/g.

6. In the ignition distance test, does ignition occur at a distance ≥ 15 cm?
   ANSWER: Yes. The ignition occurs at less than 75 cm but more than 15 cm.

Resulting Classification

Chemical FA2 is classified as a Flammable Aerosol, Category 2 because it contains < 85% flammable components and has a heat of combustion of 13.1 kJ/g, which is < 20 kJ/g. In the ignition distance test, the ignition occurs at less than 75 cm but more than 15 cm.

Example #3

In this example, data on flammable components, the chemical heats of combustion and the results of the foam test (for foam aerosols) are known. The resulting classification is determined using the HCS Flammable Aerosol Decision Logic VIII.3.1 for aerosols and VIII.3.3 for foam aerosols.

Tests for Flammable Aerosols are in the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, Part III, Sub-section 31.6, Aerosol foam flammability test.

Known data

- Chemical FA3 is a foaming aerosol product.
- Flammable components in Chemical FA3: Butane/propane: 4%;
- Non-flammable components in Chemical FA3: 96%
- The chemical heats of combustion[1] (ΔH_c) for gases in the mixture:
  ΔH_c (Butane/propane) = 43.5 kJ/g
  ΔH_c (other non-flammable components) = 0 kJ/g

Test data/results

Chemical FA3 foam test results: the flame height is less than 4 cm and the flame duration is less than 2 seconds.

Calculate the chemical heat of combustion[1] (ΔH_c) using the formula presented above:

$$\Delta Hc(product) = \sum_{i}^{n} [wi\% \times \Delta Hc(i)]$$

where
ΔH_c is the chemical heat of combustion [kJ/g]
$w_i\%$ is the mass fraction of component i in the product
$\Delta H_{c(i)}$ is the specific heat of combustion [kJ/g] of component i in the product

For Chemical FA3, the chemical heat of combustion calculation (the summation of the weighted heats of combustion for the individual components) is:

ΔH_c (Chemical FA3) = [$w_i\%$ x $\Delta H_{c(i)}$ for butane/propane] + [$w_i\%$ x $\Delta H_{c(i)}$ for the non-flammable components]

ΔH_c (Chemical FA3) = [0.04 x 43.5] + [0.96 x 0] = 1.74 + 0 = 1.7 kJ/g

Decision/Rationale

1. Does Chemical FA3 contain ≤ 1% flammable components and does it have a heat of combustion < 20 kJ/g?
   ANSWER: No. Chemical FA3 has 4% flammable components and the heat of combustion is 1.7 kJ/g.

2. Does Chemical FA3 contain ≥ 85% flammable components and does it have a heat of combustion ≥ 30 kJ/g?
   ANSWER: No. Chemical FA3 has 4% flammable components and the heat of combustion is 1.7 kJ/g.

3. For foam aerosols, go to HCS decision logic VIII.3.3.

4. In the foam test, is
   (a) the flame height ≥ 20 cm and the flame duration ≥ 2 seconds; or
   (b) the flame height ≥ 4 cm and the flame duration ≥ 7 seconds?
   ANSWER: No. In the foam test, the flame height is less than 4 cm and the flame duration less than 2 seconds.

5. In the foam test, is the flame height ≥ 4 cm and the flame duration ≥ 2 seconds?
   ANSWER: No. In the foam test, the flame height is less than 4 cm and the flame duration less than 2 seconds.

Resulting Classification

Chemical FA3 is not classified as a Flammable Aerosol because this foam aerosol contains 4% of flammable components and its chemical heat of combustion equals 1.7 kJ/g. In the foam test, the flame height is less than 4 cm and the flame duration less than 2 seconds. It is not flammable.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.3, Flammable Aerosols.

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.4 Oxidizing Gases

Introduction

An oxidizer is a chemical that brings about an oxidation reaction. In an oxidation reaction, the oxidizer may provide oxygen to the substance being oxidized (in which case the oxidizer has to be oxygen or contain oxygen), or it may receive electrons being transferred from the substance undergoing oxidation (e.g., chlorine is a good oxidizer for electron-transfer purposes, even though it contains no oxygen).

Oxidizers can initiate or greatly accelerate the burning of fuels. The most common oxidizer is atmospheric oxygen. Oxygen-containing chemicals (e.g., nitrous oxide) and halogens (e.g., bromine, chlorine, and fluorine) can also be strong oxidizers. Some chemicals may be oxidizers with such an extremely fast burning ability that they are classified as explosives or blasting agents, rather than oxidizers.

Definition

Oxidizing gas means any gas which may, generally by providing oxygen, cause or contribute to the combustion of other material more than air does.

Gases which cause or contribute to the combustion of other material more than air does means pure gases or gas mixtures with an oxidizing power greater than 23.5% (as determined by a method specified in ISO 10156:1996 or 10156-2:2005, or an equivalent testing method).

Classification Criteria

An *oxidizing gas* is classified in a single category, as shown in Table VIII.4.1.

Table VIII.4.1. Classification criteria for oxidizing gases.

Category	Criteria
1	Any gas which may, generally by providing oxygen, cause or contribute to the combustion of other material more than air does.

Classification Procedure and Guidance

To classify an oxidizing gas, data on the oxidizing potential of the gas are needed. As mentioned throughout this guidance document, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data.

Available Literature

The classifier may use available scientific literature and other evidence to classify a chemical as an oxidizing gas. Appendix B of this document provides a listing of information sources that may prove useful during hazard classification.

In addition, many substances presenting oxidizing gas hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in oxidizing gas classifications (see 49 CFR 172.101). The HCS criteria for classifying oxidizing gases correspond to the DOT Class 5.1, Oxidizer. Refer to the discussion of the interface between the HCS and DOT labeling presented in Chapter V of this document.

The decision logic presented below should be used to determine the appropriate hazard classification category for an oxidizing gas.

Test Method

Although the HCS does not require testing, the oxidizing ability of a gas or gas mixture may be determined by tests or by calculation using the methods identified in Appendix B.4 to 29 CFR 1910.1200, which are:

- ISO 10156:1996, "Gases and gas mixtures – Determination of fire potential and oxidizing ability for the selection of cylinder valve outlets" and
- ISO 10156-2:2005, "Gas cylinders, Gases and gas mixtures. Part 2: Determination of oxidizing ability of toxic and corrosive gases and gas mixtures."
- An equivalent validated method to either of the above.

In most cases, the classifier will use a calculation method to determine if the gas or gas mixture is oxidizing or not. The calculation to determine the oxidizing potential of gas mixtures either may be determined in accordance with ISO 10156:1996, "Gases and gas mixtures – Determination of fire potential and oxidizing ability for the selection of cylinder valves outlets," or through the use of ISO 10156-2:2005, "Gas cylinders, Gases and gas mixtures. Part 2: Determination of oxidizing ability of toxic and corrosive gases and gas mixtures."

However, if the classifier decides to test the gas or gas mixture, use of the test method presented in ISO 10156-2 "Gas cylinders, Gases and gas mixtures. Part 2: Determination of oxidizing ability of toxic and corrosive gases and gas mixtures" is recommended.[19]

The calculation methods are presented and summarized in this guidance document. Should testing be decided on, refer to the ISO methods for details of the procedure and necessary testing apparatus.

[19] ISO does not recommend the testing of a gas mixture by use of the test method presented in ISO 10156:1996, "Gases and gas mixtures – Determination of fire potential and oxidizing ability for the selection of cylinder valves outlets" in certain situations (explained in the scope of this method).

ISO Calculation

The calculation provided in ISO 10156 and ISO 10156-2 uses the criterion that a gas mixture is considered as more oxidizing than air if the oxygen equivalency of the gas mixture is 21% or higher.

Since air contains 20.95% oxygen, oxidizing gases or gas mixtures are considered to contribute to the combustion of other material more than air, if the oxygen equivalency of the gas mixture is greater than or equal to 21%.

Criterion: $C(mixture) = \sum_{i}^{n} Vi\% \times Ci \geq 21$

Formula to calculate the oxidation ability of a gas mixture: $C(mixture) = \sum_{i}^{n} Vi\% \times Ci$

Where	
C(mixture)	the oxidation ability of the mixture
V_i%	the volume percentage of a gas
C_i	the coefficient of oxygen equivalency
i	the first gas in the mixture
n	the n^{th} gas in the mixture

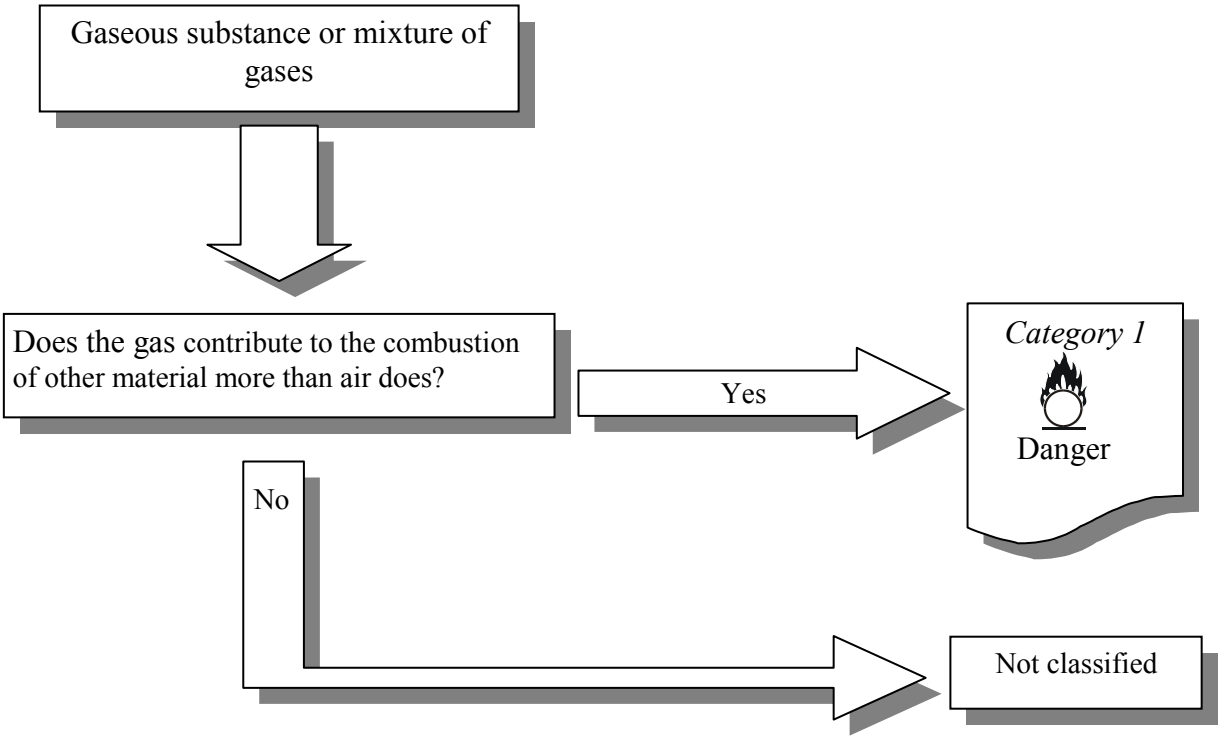
Note: Balance gas (i.e., non-oxidizing gas) is not taken into consideration

- Only the oxidizing gas is considered
- The degree of combustibility in air is considered.

For mixtures containing both flammable and oxidizing components, special calculation methods are described in ISO 10156-2. In the above equation, the value C_i is a constant. The C_i value is found in ISO 10156-2:2005 Table 1, *Coefficients of oxygen equivalency (C_i) of toxic and corrosive gases*.

A decision logic, Figure VIII.4.1, for classifying oxidizing gases is provided below.

Figure VIII.4.1. Decision logic for classifying oxidizing gases.



Oxidizing Gas Classification Example

This example uses the calculation provided in ISO 10156 and ISO 10156-2. The calculation uses the criterion that a gas mixture is considered to be more oxidizing than air if the oxygen equivalency of the gas mixture is 21% or higher.

$$Criterion:\ C(mixture) = \sum_{i}^{n} Vi\% \times Ci \geq 21$$

Formula to calculate the oxidation ability of a gas mixture

$$C(mixture) = \sum_{i}^{n} Vi\% \times Ci$$

Where

C(mixture)	the oxidation ability of the mixture
Vi%	the volume percentage of a gas
Ci	the coefficient of oxygen equivalency (See ISO 10156-2:2005 Table 1, Coefficients of oxygen equivalency (C_i) of toxic and corrosive gases)
i	the first gas in the mixture
n	the n^{th} gas in the mixture

Known data

- The chemical is a gas
- Oxidizing components:
  1.5% fluorine
- Non-oxidizing components:
  98.5 % nitrogen

1. Ascertain the coefficient of oxygen equivalency (Ci) for the oxidizing gases in the mixture, i.e., fluorine, found in ISO 10156-2:2005 Table 1, Coefficients of oxygen equivalency (C_i) of toxic and corrosive gases
   C_i (F_2) = 40

2. Calculate if the gas mixture is oxidizing using the coefficient of oxygen equivalency figures for the oxidizing gases

   Formula: $C(mixture) = \sum_{i}^{n} Vi\% \times Ci$

   C(mixture) = 1.5%(F_2) + 98.5%(N_2) = 40 x 1.5 + 98.5 x 0 = 60

Note: The coefficient of oxygen equivalency (C_i) for non-oxidizing components in a mixture is zero.

Decision/Rationale

Using the information gathered, answer the question posed in the decision logic VIII.4.1, above.

1. Does the gas contribute to combustion of other material more than air does?
   ANSWER: Yes; the oxidation ability of the gas mixture is 60, which is greater than 21.

Resulting Classification

The gas mixture is classified as Oxidizing Gas, Category 1. According to the criterion, the gas mixture is considered more oxidizing than air [60 > 21].

References

29 CFR 1910.1200, Hazard Communication, Appendix B.4, Oxidizing Gases.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

International Standards Organization (ISO) 10156:1996 (E), Gases and Gas mixtures – Determination of fire potential and oxidizing ability for the selection of cylinder valve outlets, February 15, 1996.

International Standards Organization (ISO) 10156-2: 2005(E), Gas cylinders, Gases and gas mixtures. Part 2: Determination of oxidizing ability of toxic and corrosive gases and gas mixtures, August 1, 2005.

VIII.5 Gases under Pressure

Introduction

All gases under pressure are potentially hazardous since they are under great pressure inside a container. Accidental rupture of the container and the rapid release of the pressurized gas can result in injury to persons and damage to objects in the vicinity. Not only can the gas be released with great force, but the force of the release may propel the container for a long distance. In addition to the mechanical hazard from the pressure or propelled container, other hazards may exist from the released gas. Therefore, the hazard from some gases under pressure may be strictly mechanical (e.g., compressed air); others may present other types of hazards, such as being flammable (e.g., methane and propane) or toxic (e.g., ammonia and chlorine).

Definition

Gases under pressure are gases which are contained in a receptacle at a pressure of 200 kPa (29 psi) (gauge) or more[20], or which are liquefied or liquefied and refrigerated. They comprise compressed gases, liquefied gases, dissolved gases and refrigerated liquefied gases.

In practice, this definition means that gases that are packaged at a pressure less than 200 kPa (29 psi) are not classified as gases under pressure. Being under pressure is not an intrinsic property of the substance.

***Receptacle** means a containment vessel for receiving and holding substances or articles, including any means of closing. (Definition from* UN TDG Model Regulations*, Rev.16)*

***Pressure receptacle** is a collective term that includes cylinders, tubes, pressure drums, closed cryogenic receptacles and bundles of cylinders. (Definition from* UN TDG Model Regulations*, Rev.16)*

Classification Criteria

Gases under pressure are classified, according to their physical state when packaged, in one of four groups, as shown in Table VIII.5.1.

[20] The pressure of these gases is normally measured at 20 °C (68 ºF).

Table VIII.5.1. Classification criteria for Gases under pressure.

Category	Criteria
Compressed gas	A gas which when under pressure is entirely gaseous at -50 °C (-58 °F), including all gases with a critical temperature* ≤ -50 °C (-58 °F).
Liquefied gas	A gas which when under pressure is partially liquid at temperatures above -50 °C (-58 °F). A distinction is made between: (a) High pressure liquefied gas: a gas with a critical temperature* between -50 °C (-58 °F) and +65 °C (149 °F); and (b) Low pressure liquefied gas: a gas with a critical temperature* above + 65 °C (149 °F).
Refrigerated liquefied gas	A gas which is made partially liquid because of its low temperature.
Dissolved gas	A gas which when under pressure is dissolved in a liquid phase solvent.

* *The critical temperature is the temperature above which a pure gas cannot be liquefied, regardless of the degree of compression.*

Classification Procedure and Guidance

The Hazard Communication Standard does not require the testing of chemicals - only the collection and analysis of currently available data.

To classify a gas under pressure, data on its vapor pressure, critical temperature, and its physical state are necessary.

Available Literature

The manufacturer, importer, or other responsible party may use available scientific literature and other evidence to identify the vapor pressure, physical state and critical temperature for many gases under pressure. Appendix B of this document lists information sources that may prove useful during hazard classification.

In addition, most pure gases under pressure presenting compressed gas, liquefied gas, refrigerated liquefied gas, and dissolved gas hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in classifications of gases under pressure (see 49 CFR 172.101). Refer to the discussion of the interface between the HCS and DOT labeling presented in Chapter V of this document.

The decision logic presented below should be used to determine the appropriate hazard classification category for gases under pressure.

Test Method

No test methods are specified for gases under pressure.

Classification Procedure

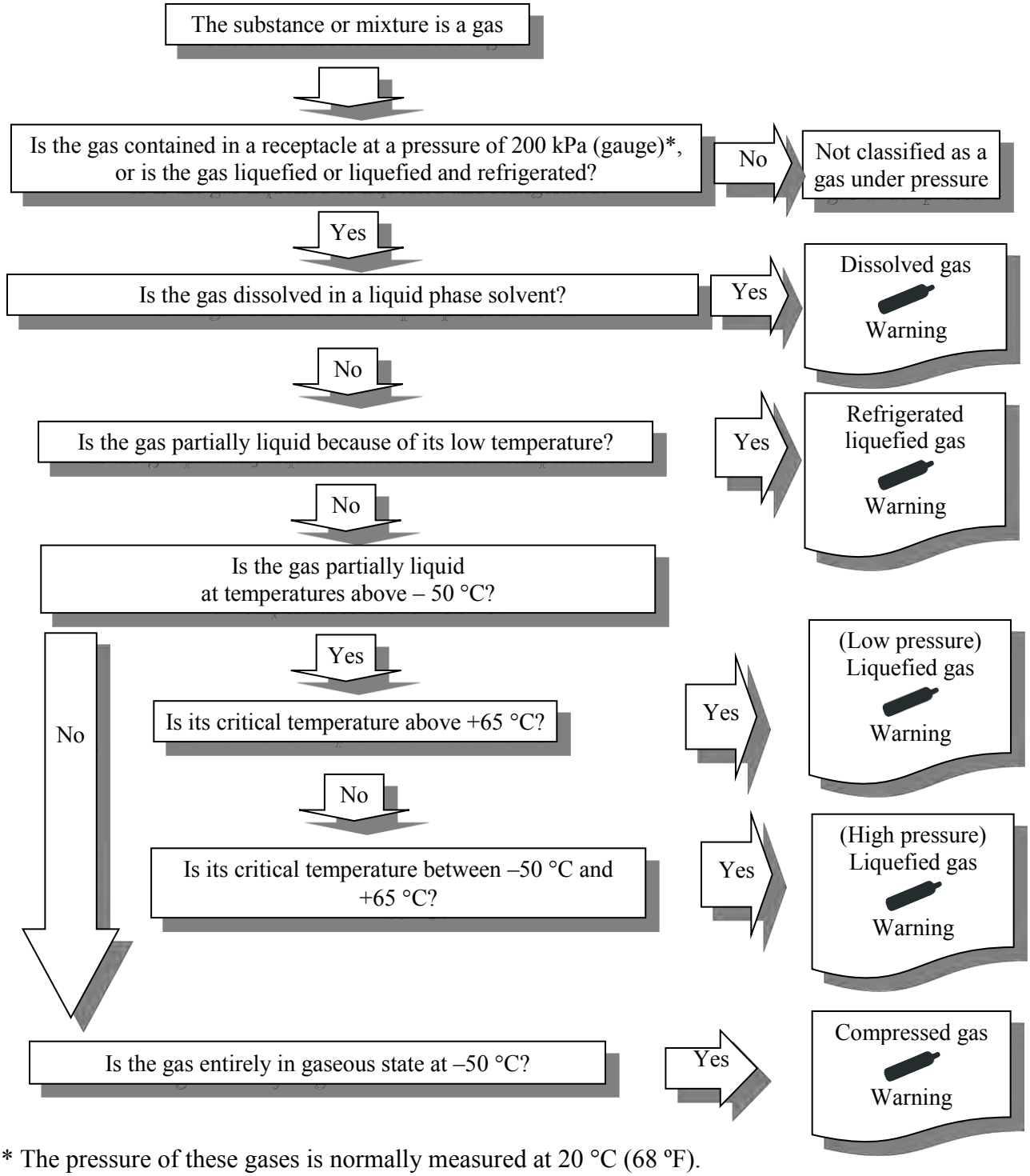
To classify gases under pressure, the data listed below are needed:

(a) The vapor pressure at 50 °C (122 ºF);
(b) The physical state at 20 °C (68 ºF) at standard pressure;
(c) The critical temperature.

Once you have collected the data, compare the data to the criteria for compressed gases, liquefied gases, dissolved gases, and refrigerated liquefied gases, presented in Table VIII.5.1. Follow the logic paths presented in the decision logics (or flowcharts) in Figure VIII.5.1 to identify the appropriate classification for gases under pressure.

Gases under pressure also need to be considered for classification in other hazard classes, such as flammable gases, flammable aerosols, and oxidizing gases, where relevant. In addition, gases considered to be simple asphyxiants should be considered for classification as gases under pressure if they meet the criteria. Simple asphyxiants are those chemicals which displace oxygen in the ambient atmosphere, and can thus cause oxygen deprivation in those who are exposed, leading to unconsciousness and death. Chapter VII.11 of this document presents information on simple asphyxiants).

Figure VIII.5.1. Decision logic for classifying gases under pressure.



* The pressure of these gases is normally measured at 20 °C (68 ºF).

Gases Under Pressure Classification Examples

Compressed Gas Example

The following examples are provided to illustrate the gases under pressure classification process and use of the decision logic.

When the vapor pressure at 50 °C (122 ºF), critical temperature, and physical state at 20 °C (68 ºF) and at standard pressure are known, the classification of the gas can be obtained according to the gases under pressure decision logic.

Known data

- The substance is a gas
- The gas is contained in a receptacle at a pressure of > 200 kPa at 20 °C
- Vapor pressure at 50 °C (122 ºF) is > 410 kPa (4.1 bar)
- Substance when packaged under pressure is entirely gaseous at -50 °C (-58 °F)
- Critical temperature: -240.1 °C

Decision/Rationale

Using the known data, answer the questions posed in the gases under pressure decision logic, Figure VIII.5.1, above.

The substance is a gas (Vapor pressure of the substance at 50 °C is > 410 kPa (4.1 bar).)

1. Is the gas contained in a receptacle at a pressure of 200kPa (psi)[21], or is the gas liquefied or liquefied and refrigerated?
   ANSWER: Yes. The gas is contained in a receptacle at a pressure of ≥200 kPa at 20 °C

2. Is the gas dissolved in a liquid solvent under pressure?
   ANSWER: No.

3. Is the gas partially liquid because of its low temperature?
   ANSWER: No. The substance when packaged is entirely gaseous at -50 ^{o}C

4. Is the gas partially liquid at temperatures above -50 ^{o}C.
   ANSWER: No. The substance when packaged is entirely gaseous at -50 ^{o}C

5. Is the gas entirely in gaseous state at -50 °C?
   ANSWER: Yes.

[21] The pressure of these gases is normally measured at 20 °C (68 ºF).

Resulting Classification

The gas is classified as a compressed gas. A compressed gas is a gas which when packaged under pressure is entirely gaseous at -50 °C; including all gases with a critical temperature ≤ -50 °C.

Liquefied Gas Example

Known data

- Vapor pressure at 50 °C is 290 kPa (2.9 bar)
- Substance is completely gaseous at 20 °C and standard pressure (101.3 kPa)
- Critical temperature: 75.3 °C
- The substance is a gas and contained in a receptacle at a pressure of 200kPa (psi)[22]

Decision/Rationale

Using the known data, answer the questions posed in the gases under pressure decision logic, Figure VIII.5.1, above.

The substance is a gas (completely gaseous at 20 °C and 101.3 kPa)

1. (a) Is the gas contained in a receptacle at a pressure of 200kPa (psi)[5], or is the gas liquefied or liquefied and refrigerated?
   ANSWER: Yes

   (b) Is the substance or mixture completely gaseous at 20 °C and 101.3 kPa?
   ANSWER: Yes.

2. Is the gas dissolved in a liquid solvent under pressure?
   ANSWER: No.

3. Is the gas partially liquid because of its low temperature?
   ANSWER: No

4. Is the critical temperature above +65 °C?
   ANSWER: Yes.

This ends the classification and the decision logic is exited.

[22] The pressure of these gases is normally measured at 20 °C (68 ºF).

Resulting Classification

The gas is classified as liquefied gas and fulfills the low pressure liquefied gas criteria.

The criteria for a low pressure liquefied gas are: A gas which when packaged under pressure is partially liquid at temperatures above -50 °C, and has a critical temperature above +65 °C.

Example for a Substance that is Not Classified

Known data

- Vapor pressure at 50 °C is 200 kPa (2 bar)
- Substance is not completely gaseous at 20 °C and standard pressure (101.3 kPa)

Decision/Rationale

Using the known data, answer the questions posed in the gases under pressure decision logic VIII.5.1, above.

1. (a) Is the vapor pressure at 50 °C greater than 300 kPa (3 bar)?
   ANSWER: No. Vapor pressure at 50 °C is not greater than 300 kPa (3 bar)

   (b) Is the substance or mixture completely gaseous[23] at 101.3 kPa?
   ANSWER: No.

Resulting Classification

The substance is not a gas and therefore is not classified as a gas under pressure.

[23] The pressure of these gases is normally measured at 20 °C (68 ºF).

References

29 CFR 1910.1200, Hazard Communication, Appendix B.5, Gases Under Pressure.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.6 Flammable Liquids

Introduction

The ability of a chemical to either burn or support burning is a potentially dangerous physical hazard. The two primary measures of the ease with which a liquid will burn are the flash point and auto-ignition temperature. The flash point is the lowest temperature at which a liquid will emit sufficient vapors to form an ignitable mixture with air. In contrast, auto-ignition is the characteristic of a material in which it will spontaneously burn without the aid of an ignition source, such as a spark or flame. Many chemicals will burn when ignited, whereas there are only a few that will spontaneously erupt into flames. While no single measure of flammability is sufficient for all purposes, the most commonly found measure in the literature is the flash point. For this reason, the HCS uses flash point in classifying the fire hazard of a chemical liquid.

There are four flammable liquid categories ranging from category 1 extremely flammable liquids and vapors to category 4 combustible liquids. Although the flash point is the criterion used for classification for all hazard categories in this hazard class, the initial boiling point also is used to identify hazard categories 1 and 2. The difference between the flammable liquid categories is the relative ease (temperature) with which the chemical burns or supports burning.

When a chemical flashes, the resulting flame will spread through the vapor from the ignition source to the nearby surface of the liquid. From a practical viewpoint, a flammable liquid Category 1 is potentially more hazardous than a flammable liquid Category 4. A flammable liquid Category 1 presents a fire hazard if present in an open container near an ignition source in an environment in which the temperature is near or below normal room temperature. For a flammable liquid Category 4 to present a fire hazard, it must be above normal room temperature.

Definitions

Flammable liquid is a liquid having a flash point of not more than 93 °C (199.4 °F).

Flash point is the minimum temperature at which a liquid gives off vapor in sufficient concentration to form an ignitable mixture with air near the surface of the liquid, as determined by a specified test method.

Initial boiling point is the temperature of a liquid at which its vapor pressure is equal to the standard pressure (101.3 kPa[24]; 14.7 psi), i.e., the first gas bubble appears. (Definition from GHS, Rev. 3)

[24] *Pascal [Pa]* is the SI Unit (International System of Units) for pressure.
1 Pa = 1 N/m^2 = 10^{-5} bar = 0.75 10^{-2} torr
The letter "k" stands for "kilo": 1 kPa = 1,000 Pa.

Classification Criteria

A flammable liquid is classified in one of four categories on the basis of its flash point and initial boiling point, as presented in Table VIII.6.1.

Table VIII.6.1. Classification criteria for flammable liquids.

Category	Criteria
1	Flash point < 23 °C (73.4 °F) and initial boiling point ≤ 35 °C (95 °F)
2	Flash point < 23 °C (73.4 °F) and initial boiling point > 35 °C (95 °F)
3	Flash point ≥ 23 °C (73.4 °F) and ≤ 60 °C (140 °F)
4	Flash point > 60 °C (140 °F) and ≤ 93 °C (199.4 °F)

Note: Aerosols should not be classified as flammable liquids.

Classification Procedure and Guidance

To classify a flammable liquid, data on its flash point and initial boiling point are necessary.

Available Literature

The classifier may use available scientific literature and other evidence to identify the flash point and initial boiling point for many flammable liquids. The required information may already exist and be well-documented for many flammable liquids.

In addition, many substances presenting flammable liquid hazards have already been classified. The information in the U.S. Department of Transportation's Hazardous Materials Table can be used to assist in flammable liquid classifications (See 49 CFR 172.101). The classification of flammable liquids in the HCS corresponds to DOT's classification of flammable liquids. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Under DOT regulations, flammable liquids are considered Class 3, hazardous materials and are assigned to three packing groups, corresponding to categories 1, 2, and 3 of the HCS. DOT regulations do not include those liquids with a flash point between 60 °C (140 °F) and 93 °C (199.4 °F) in an assigned packing group for Class 3 hazardous materials. Therefore, to classify chemicals as HCS Category 4 flammable gases, the necessary information and data must be gathered elsewhere. The decision logic presented below should be used to determine the appropriate hazard classification category for a flammable liquid.

Test Method

As mentioned throughout this guidance, the HCS does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you decide to test the

substance or mixture, use the methods identified in Appendix B.6 to 29 CFR 1910.1200 and presented below.

Flash Point
To determine the flash point experimentally, information on the viscosity of the liquid is needed to select a suitable method.

The HCS requires that the flash point be determined using any of the following test methods.

- ASTM D56-05, Standard Test Method for Flash Point by Tag Closed Cup Tester
- ASTM D3278-96 (2004) E1, Standard Test Methods for Flash Point of Liquids by Small Scale Closed Cup Apparatus
- ASTM D3828-07a, Standard Test Methods for Flash Point by Small Scale Closed Cup Tester
- ASTM D93-08, Standard Test Methods for Flash Point by Pensky-Martens Closed Cup Tester, or
- Any other method specified in GHS Revision 3, Chapter 2.6.

The GHS Rev. 3 lists the following additional methods for determining the flash point of flammable liquids.

- International standards
  - ISO 1516
  - ISO 1523
  - ISO 2719
  - ISO 13736
  - ISO 3679
  - ISO 3680

- National standards:
  - *Association française de normalisation, AFNOR,* 11, rue de Pressensé. 93571 La Plaine Saint-Denis Cedex
    - French Standard NF M 07 - 019
    - French Standards NF M 07 - 011 / NF T 30 - 050 / NF T 66 - 009
    - French Standard NF M 07 – 036
  - *Deutsches Institut für Normung*, Burggrafenstr. 6, D-10787 Berlin
    - Standard DIN 51755 (flash points below 65 °C)
  - *State Committee of the Council of Ministers for Standardization*, 113813, GSP, Moscow, M-49 Leninsky Prospect, 9
    - GOST 12.1.044-84

Initial Boiling Point

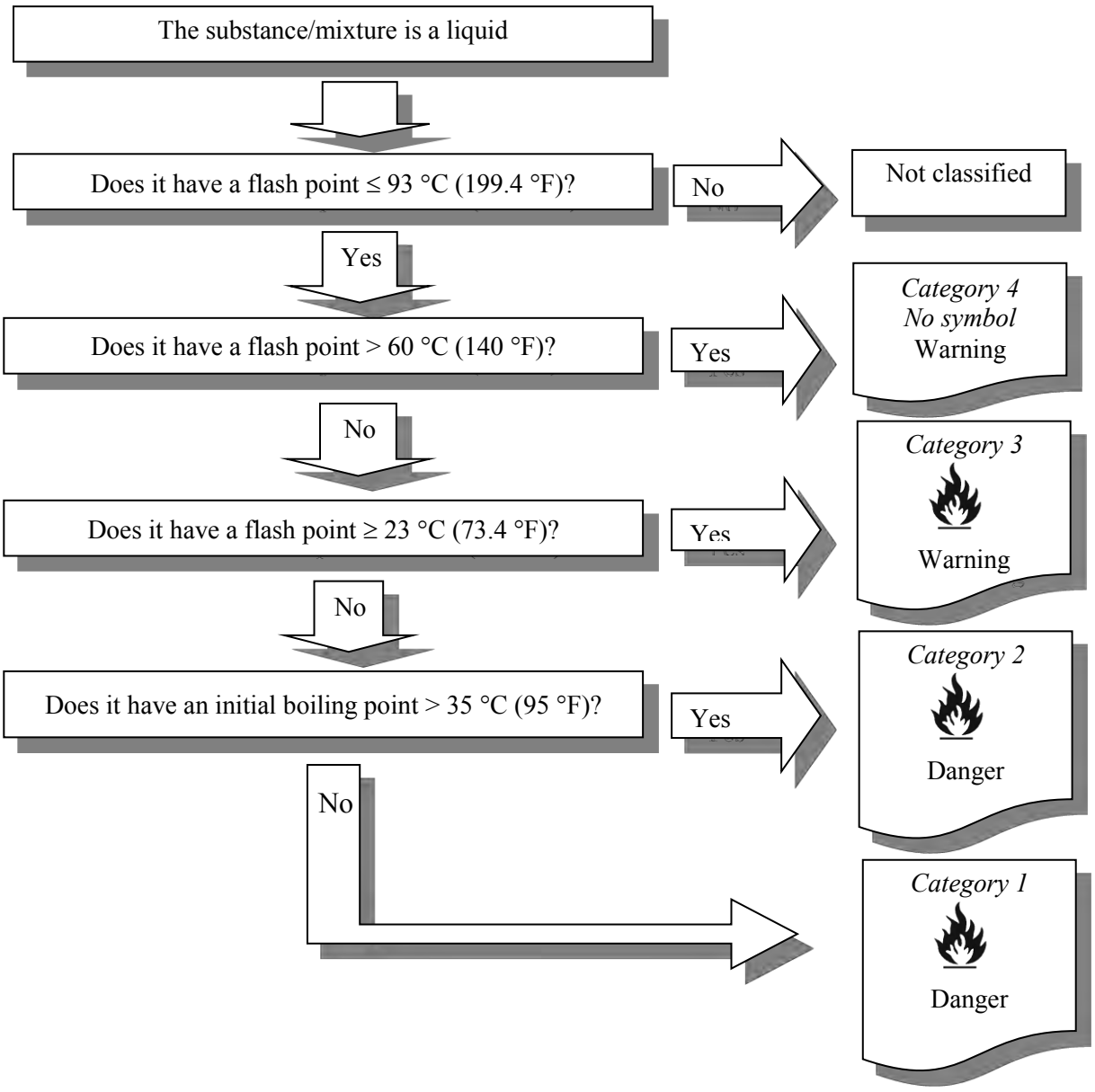
The HCS requires that the initial boiling point be determined using either of the following methods.

- ASTM D86-07a, "Standard Test Method for Distillation of Petroleum Products at Atmospheric Pressure"
- ASTM D1078-05, "Standard Test Method for Distillation Range of Volatile Organic Liquids"

Classification procedure

Once information on the chemical's flash point and initial boiling point (either from available scientific literature or the test results) is gathered, the information is compared to the classification criteria. Follow the logic paths presented in the decision logics in Figure VIII.6.1, to identify the appropriate classification categories for flammable liquids.

Figure VIII.6.1. Decision logic for classifying flammable liquids.



Flammable Liquid Classification Examples

Example

The following example is provided to illustrate the classification process when data are available for the chemical in question. In this case, a liquid is suspected of being a flammable liquid, and has a known flash point and a known initial boiling point. With this information, the classification of the chemical can be determined using the Decision Logic for flammable liquids.

Known data

- Physical state: liquid
- Melting point: -95 ºC
- Initial boiling point: 56 ºC, at standard pressure
- Flash point: -18 ºC (closed cup test)

Decision/Rationale

1. Does the chemical have a flash point ≤ 93 °C?
   ANSWER: Yes. The chemical has a flash point of -18 ºC.

2. Does the chemical have a flash point > 60 °C?
   ANSWER: No. The chemical has a flash point of -18 ºC.

3. Does the chemical have a flash point ≥ 23 °C?
   ANSWER: No. The chemical has a flash point of -18 ºC.

4. Does the chemical have an initial boiling point > 35 °C?
   ANSWER: Yes. The chemical has an initial boiling point of 56 ºC.

Resulting Classification

The chemical fulfills the requirements of a Flammable Liquid, Category 2, because it has a flash point < 23 °C and a boiling point > 35 °C.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.6, Flammable Liquids.

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.7 Flammable Solids

Introduction

The ability of a solid chemical to ignite, to burn rapidly, or for the flame to spread quickly is a potentially dangerous physical hazard. These chemicals can burn so vigorously or persistently that they create a serious fire hazard.

Classification as a flammable solid differentiates between solid chemicals that can be ignited and those that burn rapidly, or whose burning behavior is particularly dangerous. Only solid chemicals whose burning rate exceeds a certain value are classified as flammable solids.

Various solid organic chemicals meet the criteria to be classified as flammable solids. For inorganic solids, classification as a flammable solid is less frequent.

Definition

Flammable solid means a solid which is a readily combustible solid, or which may cause or contribute to fire through friction.

Readily combustible solids are powdered, granular, or pasty chemicals which are dangerous if they can be easily ignited by brief contact with an ignition source, such as a burning match, and if the flame spreads rapidly.

Classification Criteria

A flammable solid is classified in one of two categories based on its burning behavior in the test procedure described below (see Table VIII.7.1).

Table VIII.7.1. Classification criteria for flammable solids.

Category	Criteria
1	Burning rate test: Chemicals other than metal powders: (a) wetted zone does not stop fire; and (b) burning time < 45 seconds or burning rate > 2.2 mm/second Metal powders: Burning time ≤ 5 minutes
2	Burning rate test: Chemicals other than metal powders: (a) wetted zone stops the fire for at least 4 minutes; and (b) burning time < 45 seconds or burning rate > 2.2 mm/second Metal powders: Burning time > 5 minutes and ≤ 10 minutes

Note: Classification of solid chemicals is based on tests performed on the chemical as presented. If, for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that which was tested and which is considered likely to materially alter its performance in a classification test, classification must be based on testing of the chemical in the new form.

Aerosols should not be classified as flammable solids.

Classification Procedure and Guidance

To classify a flammable solid, data on the burning behavior of the chemical is necessary.

Available Literature

The classifier may use available scientific literature and other evidence to identify the burning behavior for many flammable liquids. The required information may already exist and be well-documented for many flammable solids. Many sources, such as those listed in Appendix B, Information Sources to Assist with Hazard Classification, provide chemical data and other information on chemicals.

In addition, many substances presenting flammable solid hazards have already been classified. The information in the U.S. Department of Transportation's Hazardous Materials Table can be used to assist in flammable solid classifications (See 49 CFR 172.101). Under DOT regulations, flammable solids are considered Class 4, Division 4.1 hazardous materials, and are assigned to two packing groups. Flammable solid categories 1 and 2 of the HCS correspond to DOT's Class 4, Division 4.1, Packing Groups II and III. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

The decision logic presented below should be used to determine the appropriate hazard classification category for a flammable solid.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance, use the methods identified in Appendix B. 7 to 29 CFR 1910.1200, which are described below.

Classification based on Test Methods in the UN TDG Manual of Tests and Criteria
The classification of flammable solids is based on tests described in Part III of the Fourth Revised Edition of the *United Nations Recommendations on the Transport of Dangerous Goods(UN TDG) – Manual of Tests and Criteria*, Sub-section 33.2.1, "Test N.1: Test method for readily combustible solids." A summary of this test is presented below.

Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

This test method includes a preliminary screening test and a burning rate test. The method evaluates the ability of a substance to propagate combustion by igniting it to determine the burning time and whether a wetted zone stops the propagation. These tests should only be applied to granular, paste-like, or powdery substances. If in the screening test, the substance does not ignite and propagate combustion by either burning with flame or smoldering, it is not necessary to perform the complete burning rate test, because the substance is not a readily combustible solid as defined in the HCS. However, if propagation occurs and the burning time is less than the time specified in the test, then the full burning rate test should be performed.

Classification Procedure

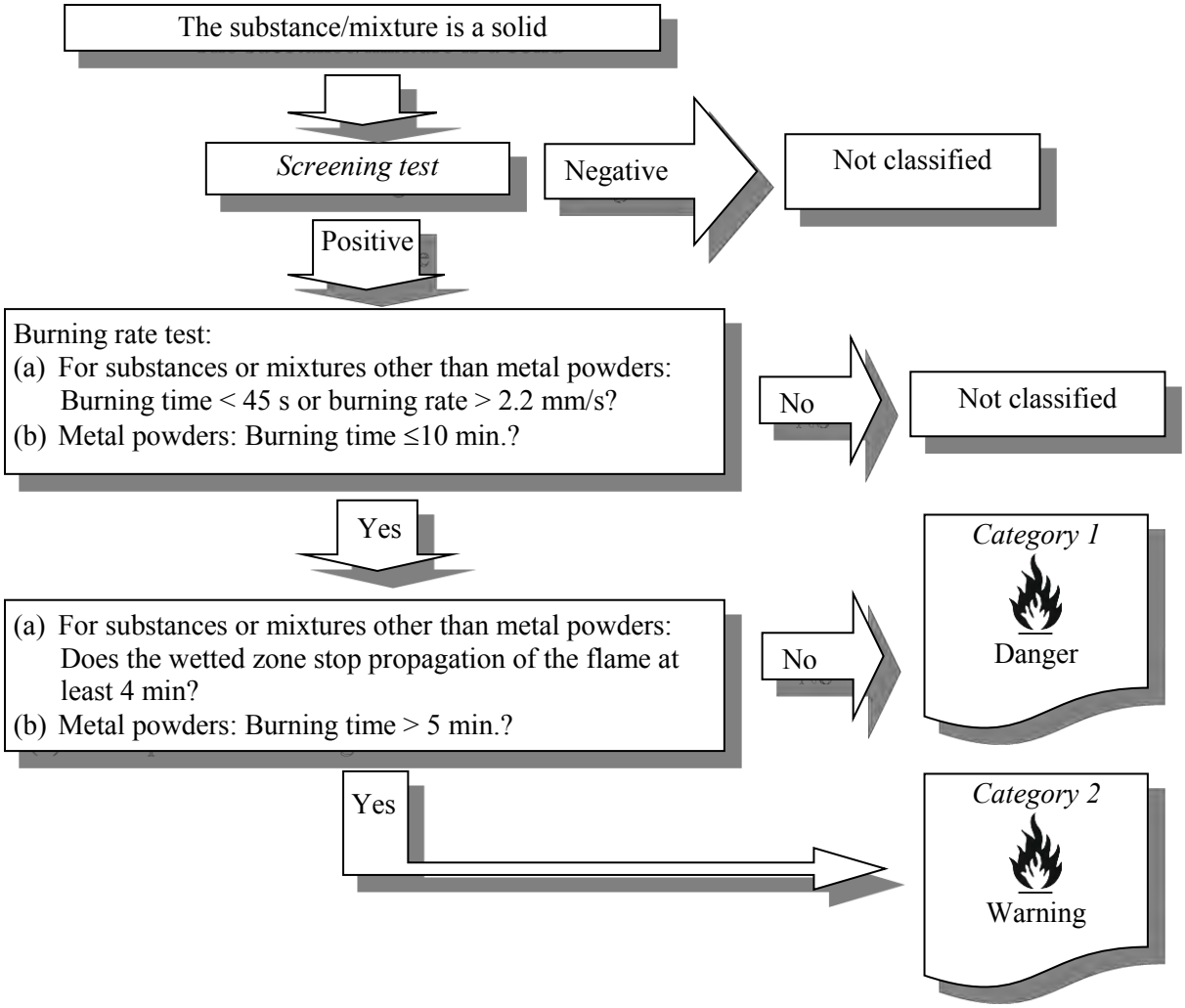
When using the N.1 test results to determine classification, information from both the preliminary screening test and burning rate test is needed. The following information is needed:

- Whether or not the chemical ignites and propagates combustion (Preliminary Screening Test)
- Burning time [seconds] or burning rate [mm/second] (Burning Rate Test)
- Other than metal powders, does the wetted zone stop the propagation of the fire?

Classification is based upon the fastest burning rate and shortest burning time obtained in six test runs, unless a positive result is observed earlier. For substances and mixtures other than metal powders, the category is assigned depending on whether the wetted zone is able to stop the flame.

The results and observation from the Test N.1 are compared to the criteria for flammable solids Category 1 and Category 2 using the decision logic for classifying flammable solids provided in Figure VIII.7.1, below.

Figure VIII.7.1. Decision logic for classifying flammable solids based on Test N.1.



Flammable Solids Classification Example

The following example illustrates the classification process for a chemical suspected of being a flammable solid when there is no existing data, and information from the required test procedure is gathered. An organic solid material is suspected of being a flammable solid, but has no other information to help with the classification process. In this case, the chemical is tested using the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, Part III, Sub-section 33.2.1.4, Test N.1: Test method for readily combustible solids. The procedure consists of two tests: a preliminary screening test and a burning rate test.

Once the test is complete, classification of the chemical can be determined according to the HCS Flammable Solids decision logic.

Known data

Organic solid material, not a metal

Test data results

1. Preliminary screening test results: Burns with an open flame in less than 2 minutes, which is a positive result.

2. Burning rate test results: Burning times for a distance of 100 mm (6 runs): 44 seconds (s); 40 s; 49 s; 45 s; 37 s; 41 s.

3. Wetted zone stops the fire, no re-ignition.

Decision/Rationale

1. Preliminary screening test is performed to determine whether the chemical is a candidate for classification as a flammable solid. The chemical burns with an open flame in less than 2 minutes, so the result is positive.

2. Since the preliminary screening test is positive, a burning rate test is performed.

3. Is the shortest burning time less than 45 s?
   ANSWER: Yes, the shortest burning time was 37 s, indicating the substance is a flammable solid.

4. Does the wetted zone stop the fire?
   ANSWER: Yes, and the chemical does not reignite.

Resulting Classification

The organic solid is classified as a flammable solid, Category 2, based on the outcome of *UN TDG Manual of Tests and Criteria*, Method N.1.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.7, Flammable Solids.

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.8 Self-Reactive Chemicals

Introduction

Self-reactive chemicals display a very wide range of properties. While the most hazardous type of self-reactive chemicals are too dangerous to transport commercially, they can be stored safely with appropriate precautions. The self-reactive classification also includes substances that only decompose slowly at temperatures well above normal storage and transport temperatures [e.g., 75 °C (167 ºF)].

The decomposition of self-reactive chemicals can be initiated by heat, contact with catalytic impurities (e.g., acids, heavy metal compounds, or bases), friction, or impact. The rate of decomposition increases with temperature and varies with the chemical. Decomposition, particularly if no ignition occurs, may result in the evolution of toxic gases or vapors. For certain self-reactive chemicals, the temperature must be controlled, while others may decompose explosively, particularly if confined. This characteristic may be modified by the addition of diluents or by the use of appropriate packagings. Some self-reactive chemicals burn vigorously. Examples of self-reactive chemicals include some compounds of the types listed below:

- Aliphatic azo compounds (-C-N=N-C-);
- Organic azides (-C-N3);
- Diazonium salts (-CN2+Z-);
- N-nitroso compounds (-N-N=O); and
- Aromatic sulphohydrazides (-SO2-NH-NH2).

This list is not exhaustive and chemicals with other reactive groups and some mixtures may have similar properties.

Definition

Self-reactive chemicals are thermally unstable liquid or solid chemicals liable to undergo a strongly exothermic decomposition even without participation of oxygen (air). This definition excludes chemicals classified as explosives, organic peroxides, oxidizing liquids, or oxidizing solids.

A self-reactive chemical is regarded as possessing explosive properties when in laboratory testing the formulation detonates, deflagrates rapidly, or shows a violent effect when heated under confinement.

Deflagration. *Propagation of a reaction zone at a velocity that is less than the speed of sound in the unreacted medium (Definition from NFPA 68).*

Detonation. *Propagation of a combustion zone at a velocity that is greater than the speed of sound in the unreacted medium (Definition from NFPA 68).*

Classification Criteria

Self-reactive chemicals are assigned to one of the seven types, A to G, according to the degree of danger they present. Table VIII.8.1 presents the classification criteria for self-reactive chemicals.

Table VIII.8.1. Classification criteria for self-reactive chemicals.

Self-Reactive Type	Criteria
A	Any self-reactive chemical that can detonate or deflagrate rapidly, as packaged.
B	Any self-reactive chemical possessing explosive properties and which, as packaged, neither detonates nor deflagrates rapidly, but is liable to undergo a thermal explosion in that package.
C	Any self-reactive chemical possessing explosive properties when the chemical as packaged cannot detonate or deflagrate rapidly or undergo a thermal explosion.
D	Any self-reactive chemical which, in laboratory testing, meets the criteria in i, ii, or iii presented below: i. Detonates partially, does not deflagrate rapidly, and shows no violent effect when heated under confinement; or ii. Does not detonate at all, deflagrates slowly, and shows no violent effect when heated under confinement; or iii. Does not detonate or deflagrate at all, and shows a medium effect when heated under confinement.
E	Any self-reactive chemical which, in laboratory testing, neither detonates nor deflagrates at all and shows low or no effect when heated under confinement.
F	Any self-reactive chemical which, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows only a low or no effect when heated under confinement as well as low or no explosive power.

Self-Reactive Type	Criteria
G	Any self-reactive chemical which, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all, and shows no effect when heated under confinement nor any explosive power, provided that it is thermally stable (self-accelerating decomposition temperature is 60 °C (140 °F) to 75 °C (167 °F) for a 50 kg (110 lb.) package), and, for liquid mixtures, a diluent having a boiling point greater than or equal to 150 °C (302 °F) is used for desensitization. If the mixture is not thermally stable or a diluent having a boiling point less than 150 °C (302 °F) is used for desensitization, the mixture is defined as self-reactive chemical TYPE F.

Note: Type G has no hazard communication elements assigned but should be considered for properties belonging to other hazard classes.

Classification Procedure and Guidance

To classify a self-reactive chemical, data on its ability to detonate, deflagrate, and the effect of heating under confinement are needed.

A self-reactive chemical is considered for classification in this class unless:

a) It is classified as an explosive according to Appendix B.1 to 29 CFR 1910.1200;

b) It is classified as an oxidizing liquid or an oxidizing solid according to Appendix B.13 or B.14 to 29 CFR 1910.1200, except that a mixture of oxidizing chemicals which contains 5% or more of combustible organic substances is classified as a self-reactive chemical according to the procedure defined in B.8.2.2 to 29 CFR 1910.1200 (explained below);

c) It is classified as an organic peroxide according to Appendix B.15 to 29 CFR 1910.1200;

d) Its heat of decomposition is less than 300 Joules/gram; or

e) Its self-accelerating decomposition temperature (SADT) is greater than 75 °C (167 °F) for a 50 kg (110 lb.) package.

Self-accelerating decomposition temperature *(SADT) means the lowest temperature at which self-accelerating decomposition may occur with a substance as packaged. (Definition from GHS, Rev. 3)*

Paragraph B.8.2.2 to 29 CFR 1910.1200 explains that mixtures of oxidizing substances, meeting the criteria for classification as oxidizing liquids or oxidizing solids, containing 5% or more of combustible organic substances and which do not meet the criteria explained in (a), (c), (d) or (e), above, are subjected to the self-reactive chemicals classification. Mixtures showing the properties of a self-reactive chemical type B to F are classified as a self-reactive chemical.

The classification procedures for self-reactive chemicals need not be applied if they meet either of the following two criteria:

1. There are no chemical groups present in the molecule associated with explosive or self-reactive properties; examples of such groups are provided in Tables VIII.8.2 and VIII.8.3 below, extracted from the *UN Recommendations on the Transport of Dangerous Goods (UN TDG) Manual for Tests and Criteria, Appendix 6*.

Table VIII.8.2. Examples of Chemical Groups Indicating Explosive Properties in Organic Material.

Structural feature	Examples
C-C unsaturation	Acetylenes, acetylides, 1,2-dienes
C-Metal, N-Metal	Grignard reagents, organo-lithium compounds
Contiguous nitrogen atoms	Azides, aliphatic azo compounds, diazonium salts, hydrazines, sulphonylhydrazides
Contiguous oxygen atoms	Peroxides, ozonides
N-O	Hydroxylamines, nitrates, nitro compounds, nitroso compounds, N-oxides, 1,2-oxazoles
N-halogen	Chloroamines, fluoroamines
O-halogen	Chlorates, perchlorates, iodosyl compounds

Table VIII.8.3. Examples of Chemical Groups Indicating Self-Reactive Properties in Organic Material.

Structural feature	Examples
Mutually reactive groups	Aminonitriles, haloanilines, organic salts of oxidizing acids
S=O	Sulphonyl halides, sulphonyl cyanides, sulphonyl hydrozines
P-O	Phosphites
Strained rings	Epoxides, aziridines
Unsaturation	Olefines, cyanates

or

2. For a single organic substance or a homogeneous mixture of organic substances, the estimated SADT is greater than 75 °C (167 °F) or the exothermic decomposition energy is less than 300 Joules/gram. The onset temperature and decomposition energy may be estimated using a suitable calorimetric technique (See 20.3.3.3 in Part II of the *UN TDG Manual of Tests and Criteria*).

Available Literature

The classifier may use available scientific literature and other evidence to classify self-reactive chemicals. The information needed to classify the chemicals may be found in available literature or through laboratory testing. Should data from laboratory testing be used, the chemical must be tested together with their packages.

In addition, many substances presenting self-reactive chemical hazards have already been classified. The information in the U.S. Department of Transportation's Hazardous Materials Table can be used to assist when classifying self-reactive chemicals (See 49 CFR 172.101). The DOT regulations also provide a list of self-reactive substances in 49 CFR 173.224. Under DOT regulations, the majority of self-reactive chemicals are considered Hazard Class 4 Division 4.1, self-reactive materials. Self-reactive chemicals classified in accordance with the HCS correspond to self-reactive materials classified for transport. Therefore, the labeling requirements for self-reactive materials in the HCS correspond to DOT's Hazard Class 4, Division 4.1, self-reactive materials. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals - only the collection and analysis of currently available data.

However, if you choose to test the substance or mixture, then use methods identified in Appendix B.8 to 29 CFR 1910.1200 and described below.

The classification of self-reactive chemicals is based on tests described in Part II of the Fourth Revised Edition of the *UN TDG Manual of Tests and Criteria*, Sub-sections 20 to 28, Test Series A to H. The methods are designed for testing both self-reactive chemicals and organic peroxides. The decision logic presented below should be used to determine the appropriate hazard classification category for self-reactive chemicals if testing is performed to gather the necessary information.

Self-reactive chemicals are classified into seven types according to the hazard. The tests are performed in two stages. The first stage uses preliminary small scale tests to ascertain the stability and sensitivity of the chemicals and ensure the safety of laboratory workers. During the second stage, classification tests are performed. Note that explosive properties are associated with the presence of certain chemical groups in a molecule that can react to produce very rapid increases in temperature or pressure. The preliminary procedure is aimed at identifying the presence of such reactive groups and the potential for rapid energy release.

A brief summary of these tests is presented below. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

Preliminary procedure

Performing small-scale preliminary tests before attempting to handle larger quantities is essential for ensuring the safety of laboratory workers. The preliminary tests determine the sensitiveness of the chemical to mechanical stimuli (impact and friction), and to heat and flame. Four types of small-scale tests are used to make the preliminary assessment:

(a) A falling weight test to determine sensitiveness to impact;
(b) A friction or impacted friction test to determine the sensitiveness to friction;
(c) A test to assess thermal stability and the exothermic decomposition energy; and
(d) A test to assess the effect of ignition.

The details of these preliminary tests can be found in Part I of the Fourth Revised Edition of the *UN TDG Manual of Tests and Criteria*, Sub-section 13, Test Series 3. Appendix 6 of the *UN TDG Manual of Tests and Criteria* provides additional guidance on screening procedures.

Classification test

The classification of a self-reactive chemical in one of the seven categories, Types A to G, is dependent on its detonation, explosive thermal explosion and deflagrating properties, its response to heating, the concentration and the type of diluent added to desensitize the substance. The classification of a self-reactive chemical as Type A, B or C is also dependent on the type of packaging in which the chemical is tested, as the package affects the degree of confinement to which the chemical is subjected.

Should testing be performed on the chemical, data from self-reactive chemical test series A to H is needed. A brief description of the tests described in the *UN TDG Manual of Tests and Criteria* is presented below.

Test Series A answers the question, "Does the chemical propagate a detonation?" The tests measure the ability of a substance to propagate a detonation by subjecting it to a detonating booster charge under confinement in a steel tube. The test methods include:

- BAM 50/60 steel tube test
- TNO 50/70 steel tube test
- UN gap test
- UN detonation test (the recommended test)

Test Series B answers the question "Can the chemical detonate as packaged for transport?" The tests measure the ability of a chemical to propagate a detonation when packaged for transport by subjecting it to the shock from a detonating booster charge. The test is required only for substances that propagate detonation.

Test Series C answers the question, "Does the chemical propagate a deflagration?" This test series consists of two tests – the time/pressure test, and the deflagration test. Both tests are recommended. The time and pressure test measures the ability of a substance under confinement to propagate a deflagration. The deflagration test measures the ability of a chemical to propagate a deflagration.

Test Series D answers the question, "Does the chemical deflagrate rapidly in package?" The test measures the ability of a chemical to rapidly propagate a deflagration when packaged for transport. The test is required for substances that deflagrate rapidly in a Test Series C test.

Test Series E answers the question, "What is the effect of heating the chemical under defined confinement?" This test series consists of three test methods – the Koenen test, the Dutch pressure test, and the USA pressure test. For self-reactive chemicals, the Koenen test is recommended in combination with one of the other tests. The three tests are described below.

The Koenen test determines the sensitivity of substances to the effect of intense heat under high confinement. The Dutch pressure vessel test and the USA pressure test determine the sensitivity of substances to the effect of intense heat under defined confinement.

Test Series F answers the question, "What is the chemical's explosive power?" Several tests are described in the *UN TDG Manual of Tests and Criteria*, including the Ballistic mortar Mk. IIId test, the Ballistic mortar test, the BAM Trauzl test, the Modified Trauzl test**,** and the High-pressure autoclave. The Modified Trauzl test is the recommended test, measures the explosive power of a chemical, and is used for chemicals being considered for transport in intermediate bulk containers (IBCs) or tank-containers.

Test Series G answers the question, "Can the chemical explode as packaged for transport?" The test series uses two test methods – the thermal explosion test in package, and the accelerating decomposition test in package. The test is needed only for chemicals that show a violent effect in tests involving heating under defined confinement (Test Series E). The thermal explosion test in package is the recommended test and is used to determine the potential for thermal explosion in a package.

Temperature control

In addition to the classification tests, the thermal stability of the self-reactive substances is needed to determine the Self-Accelerating Decomposition Temperature (SADT). There is no relation between the SADT of a self-reactive substance and its classification in one of the seven categories Types A to G. However, the SADT is used to derive safe handling, storage and

transport temperatures (control temperature), and alarm temperature (emergency temperature). Self-reactive substances need to be subjected to temperature control if their SADT is less than or equal to 55 °C (131 ºF).

The *UN TDG Manual of Tests and Criteria*, Part II, Sub-section 28, Test Series H, describes several test methods for determining the SADT, including the United States SADT test, the Adiabatic storage test, the Isothermal storage test, and the heat accumulation storage test. Since there are several test methods presented, the test selected and conducted should be representative of the package, both in size and material. Each test involves either storage at a fixed external temperature and observation of any reaction initiated or storage under near adiabatic conditions and measurement of the rate of heat generation versus temperature.

Self-accelerating decomposition temperature *(SADT) means the lowest temperature at which self-accelerating decomposition may occur with a substance as packaged. (Definition from GHS, Rev. 3)*

Classification Procedure

Self-reactive chemicals are classified according to the classification principles given in the decision logic and the results of test series A to H. In addition, classification may be determined using information provided in available scientific literature. As one can see from the explanations above, the test series are designed to provide the information necessary to answer the questions in the decision logic for self-reactive chemicals, presented in Figure VIII.8.1.

- Test series A includes laboratory tests and criteria concerning propagation of detonation as requested in box 1 of the flowchart.
- Test series B includes a test and criteria concerning the propagation of detonation of the substance as packaged for transport, as requested in box 2 of the flowchart.
- Test series C includes laboratory tests and criteria concerning propagation of deflagration as requested in boxes 3, 4, and 5 of the flowchart.
- Test series D includes a test and criteria concerning the propagation of a rapid deflagration of the substance as packaged for transport, as requested in box 6 of the flowchart.
- Test series E includes laboratory tests and criteria concerning the determination of the effect of heating under defined confinement, as requested in boxes 7, 8, 9, and 13 of the flowchart.
- Test series F includes laboratory tests and criteria concerning the explosive power of substances that are considered for transport in Intermediate Bulk Containers (IBCs) or tanks, or for exemption (see box 11 of the flowchart), as requested in box 12 of the flowchart.
- Test series G includes tests and criteria concerning the determination of the effect of a thermal explosion of the substance as packaged for transport, as requested in box 10 of the flowchart.

- Test series H includes tests and criteria concerning the determination of the self-accelerating decomposition temperature of self-reactive or potentially self-reactive substances.

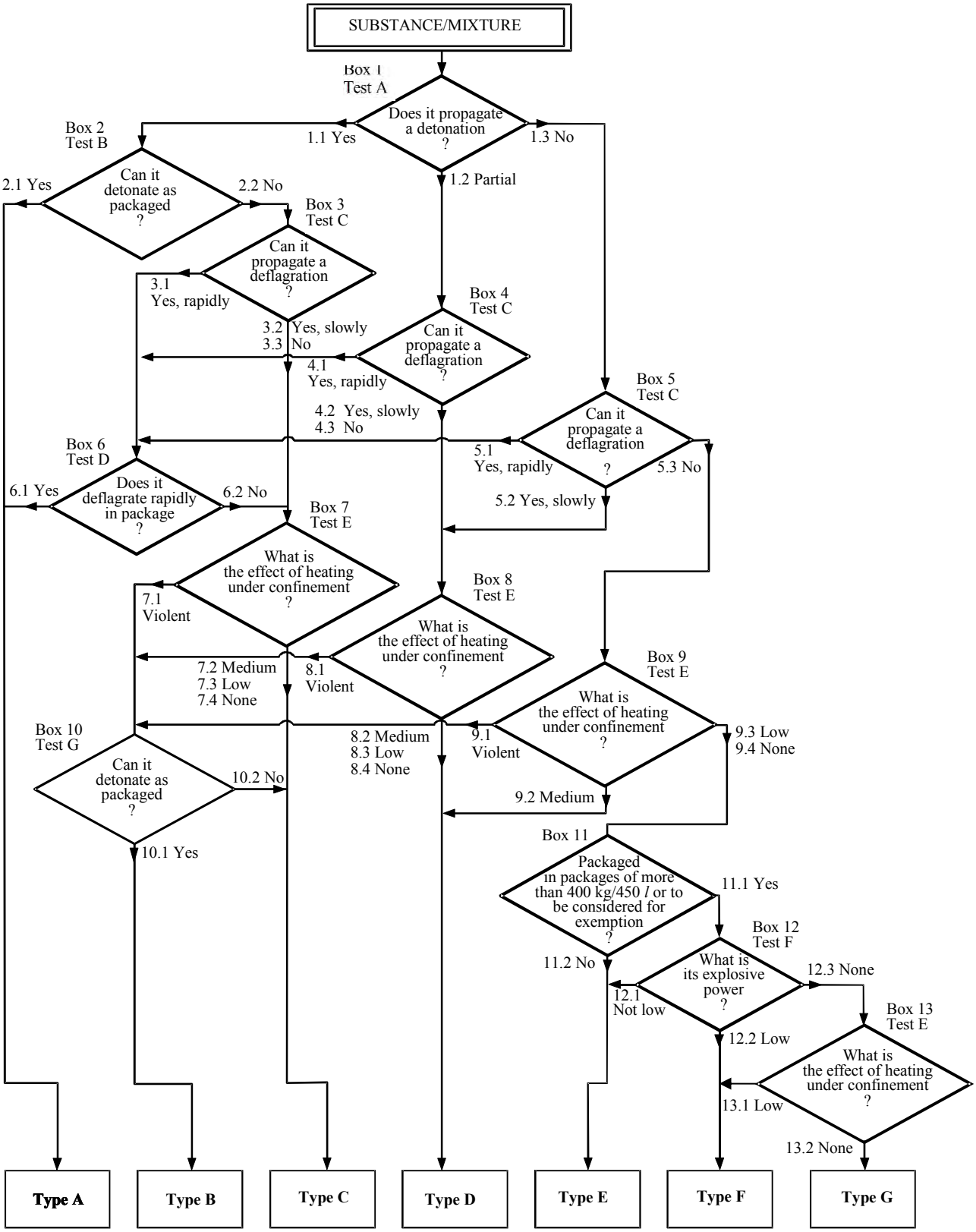
The decision logic for classifying self-reactive chemicals is provided in Figure VIII.8.1. To answer the questions in the decision logic the following information is needed:

- Propagation of detonation
- Propagation of deflagration
- Effect on heating in confinement
- Thermal stability: Self-accelerating decomposition temperature (SADT)

Data from additional tests may also be needed (for example, explosive power, or explosivity as packaged) depending on the circumstances and/or the results of the foregoing tests.

Classification follows the assessment of available data and, if applicable, the results of any testing performed. Once you have collected the data, the data and test results are compared to the classification criteria for self-reactive chemicals types A through G presented in Table VIII.8.1. Follow the logic paths presented in the decision logic (or flowchart) in Figure VIII.8.1 to identify the appropriate classification for self-reactive chemicals.

Figure VIII.8.1. Decision logic for classifying self-reactive chemicals.



Self-Reactive Chemical Classification Example

The following example is provided to illustrate the self-reactive chemicals classification process and use of the decision logic.

A white solid is suspected of being a self-reactive chemical and is tested according to the appropriate UN tests.

The test methods for determining the type of self-reactive chemical are performed using the *UN TDG Manual of Tests and Criteria*, Part II, Test Series A to H. The tests are designed to provide the information necessary to answer the questions in the decision logic for self-reactive chemicals and to apply the principles for classification. In the following example, the results of the tests are assessed in alphanumeric order; however, the tests are performed in the order given in section 20.4.5 of the *UN TDG Manual of Tests and Criteria.*

Known data

- White solid
- Composition: 96% Azodicarbonamide
- Molecular formula: $C_2H_4N_4O_2$
- Apparent density: 945 kg/m^3
- Particle size: < 400 µm

Test results

Test Name	**Observation**	**Result**
Test series A - Detonation propagation [BAM 50/60 steel tube test]	30 cm of tube fragmented, unreacted substance remained in the tube	Partial propagation of detonation (Exit 1.2 of Box 1/Test Decision Logic flowchart)
Test series B - Detonation as packaged	Not applicable	
Test series C - Deflagration propagation [Time/pressure test]	Test conducted on 5 g of sample three times and the time it took for the pressure to rise from 690 kPa to 2,070 kPA was noted (3.0 s, 2.5 s, 2.7 s). Shortest recorded time (2.5 s) is used for result.	Test result/criteria: Yes, slowly, because the time for pressure to rise from 690 kPa to 2,070 kPA is greater than or equal to 30 ms.

Test Name	Observation	Result
Test series C - Deflagration propagation [Deflagration test]	Test conducted two times on 265 cm^3 of sample at 50 °C, and the reaction rate noted for each (0.71 mm/s, 0.65 mm/s). Shortest recorded rate (0.65 mm/s) is used for result.	Test result/criteria: Yes, slowly, because the deflagration rate is less than or equal to 5.0 mm/s and greater than or equal to 0.35 mm/s. Overall result: Yes, slowly (Exit 4.2 of Box 4/Test C Decision Logic flowchart)
Test series D - Deflagration as packaged	Not applicable	
Test series E - Effect of heating under confinement [Koenen test]	Tested 26.0 g of sample. Limiting diameter of 3.5 mm (time to reaction 19.0 s, duration of reaction 22 s)	Test result/criteria: Violent, because the limiting diameter is greater than or equal to 2.0 mm.
Test series E - Effect of heating under confinement [Dutch Pressure Vessel test]	Tested 10.0 g of sample. Limiting diameter of 10.0 mm (time to reaction 110 s, duration of reaction 4 s)	Test result/criteria: Violent, because rupture of the disc with an orifice of 9.0 mm or greater and a sample mass of 10.0 g. Overall result: Violent (Exit 8.1 of Box 8/Test E Decision Logic flowchart)
Test series F - Explosive Power	Not applicable	
Test series G - Detonation as packaged [Thermal explosion test in the package]	Tested 25 kg of substance in packaging type 6HG2. Observed fumes only, no fragmentation of the package.	Test result/criteria: No explosion: No fragmentation or a fragmentation into no more than three pieces shows that the substance does not explode in the package. Exit 10.2 of Box 10/Test G Decision Logic flowchart. Chemical is classified as a self-reactive Type C.

Test Name	Observation	Result
Test series H - Thermal stability [United States SADT test]	Tested 20 liters of substance in packaging type 6HG2 in a test chamber with a capacity of 25 liters. Observed auto-accelerating decomposition at 63°C (145.4ºF) and no auto-accelerating decomposition at 58°C (136.4ºF). The self-accelerating decomposition temperature was identified as 63°C (145.4ºF).	Self-reactive chemicals need to be subjected to temperature control if their SADT is less than or equal to 55 °C (131ºF). This chemical has a SADT of 63°C (145.4ºF). No temperature control is required for this package. Chemical is classified as a self-reactive Type C.

Decision/Rationale

To classify a self-reactive chemical, the classifier follows the decision logic for self-reactive chemicals, answering the questions and following the flowchart:

Box 1, Test Series A

1. Does Substance 15 propagate a detonation?
   RESULT (Test series A): 1.2 Partial

Box 4, Test C

2. Can Substance 15 propagate a deflagration?
   RESULT (Tests series C): 4.2 Yes, slowly

Box 8, Test E

3. What is the effect of heating under confinement?
   RESULT (Tests series E): 8.1 Violent

Box 10, Test G

4. Can it detonate as packaged?
   RESULT (Tests series G): 10.2 No

Tests B, D, F are not required for this chemical, if the classifier follows the test logic.

5. Test H is performed to determine whether the substance requires temperature control measures.
   RESULT (Tests series H): this chemical has a SADT of 63°C (145.4ºF).

Resulting Classification

This chemical is classified as Self-Reactive, Type C: Any self-reactive substance or mixture possessing explosive properties when the chemical as packaged cannot detonate or deflagrate rapidly or undergo a thermal explosion will be defined as self-reactive substance Type C.

This chemical has a SADT of 63 °C (145.4 ºF). No temperature control is required for this package.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.8, Self-Reactive Chemicals.

29 CFR 1910.1200, Hazard Communication, Appendix C, Allocation of Label Elements.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.

NFPA 68, Standard on Explosion Protection by Deflagration Venting, 2013.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.9 Pyrophoric Chemicals

Introduction

Pyrophoric chemicals ignite spontaneously in air without a supplied spark, flame, heat or other ignition source. There are only a few chemicals that have the ability to catch fire without an ignition source when exposed to air. Examples of potential pyrophoric chemicals include alkali metals in elemental form (e.g., lithium, powdered aluminum, magnesium), organometallic compounds (such as lithium hydride, diethyl zinc), or gases (such as diborane, phosphine, and silane). Tests should be performed on the substance or mixture as presented, including how it can reasonably be expected to be used.

This chapter covers all pyrophoric hazard classes, that is, pyrophoric liquids, solids, and gases.

Pyrophoric Liquids

Definition

A *pyrophoric liquid* is a liquid which, even in small quantities, is liable to ignite within five minutes after coming in contact with air.

Classification Criteria

A pyrophoric liquid is classified in a single category, as shown in Table VIII.9.1.

Table VIII.9.1. Classification criteria for pyrophoric liquids.

Category	Criteria
1	The liquid ignites within 5 min. when added to an inert carrier and exposed to air, or it ignites or chars a filter paper on contact with air within 5 min.

Classification Procedure and Guidance

To classify pyrophoric liquids, data on ignition is necessary. The classification procedure for pyrophoric liquids need not be applied when experience in production or handling shows that the chemical does not ignite spontaneously when it comes in contact with air at normal temperatures, i.e., the substance is known to be stable at room temperature for prolonged periods of time (days).

Available Literature

The classifier may use available scientific literature and other evidence to identify the ignition information necessary to classify pyrophoric liquids.

In addition, many substances presenting pyrophoric liquid hazards have already been classified. The information in the U.S. Department of Transportation's Hazardous Materials Table can be used to assist in pyrophoric liquid classifications (See 49 CFR 172.101). The classification of

pyrophoric liquids in the HCS corresponds to DOT's classification for spontaneously combustible materials. Under DOT regulations, pyrophoric liquids are considered Class 4, Division 4.2, hazardous materials and assigned to Packing Group I. Refer to the discussion of the interface between the HCS and DOT labeling in Chapter V of this document for more information.

The decision logic presented below should be used to determine the appropriate hazard classification category for pyrophoric liquids.

Test Methods

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use the methods identified in Appendix B.9 to 29 CFR 1910.1200, which are discussed below.

Classification Based on Test Methods in the UN TDG Manual of Tests and Criteria

The classification of pyrophoric liquids is based on Test N.3, "Test method for pyrophoric liquids," described in Part III, sub-section 33.3.1.5, of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) Manual of Tests and Criteria*, Fourth Revised Edition. The decision logic presented below should be used to determine the appropriate hazard classification for a pyrophoric liquid using the test data. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

The test method for pyrophoric liquids uses a two-part procedure and determines the ability of the liquid a) to ignite when added to an inert carrier and exposed to air, or (b) to char or ignite a filter paper on contact with air.

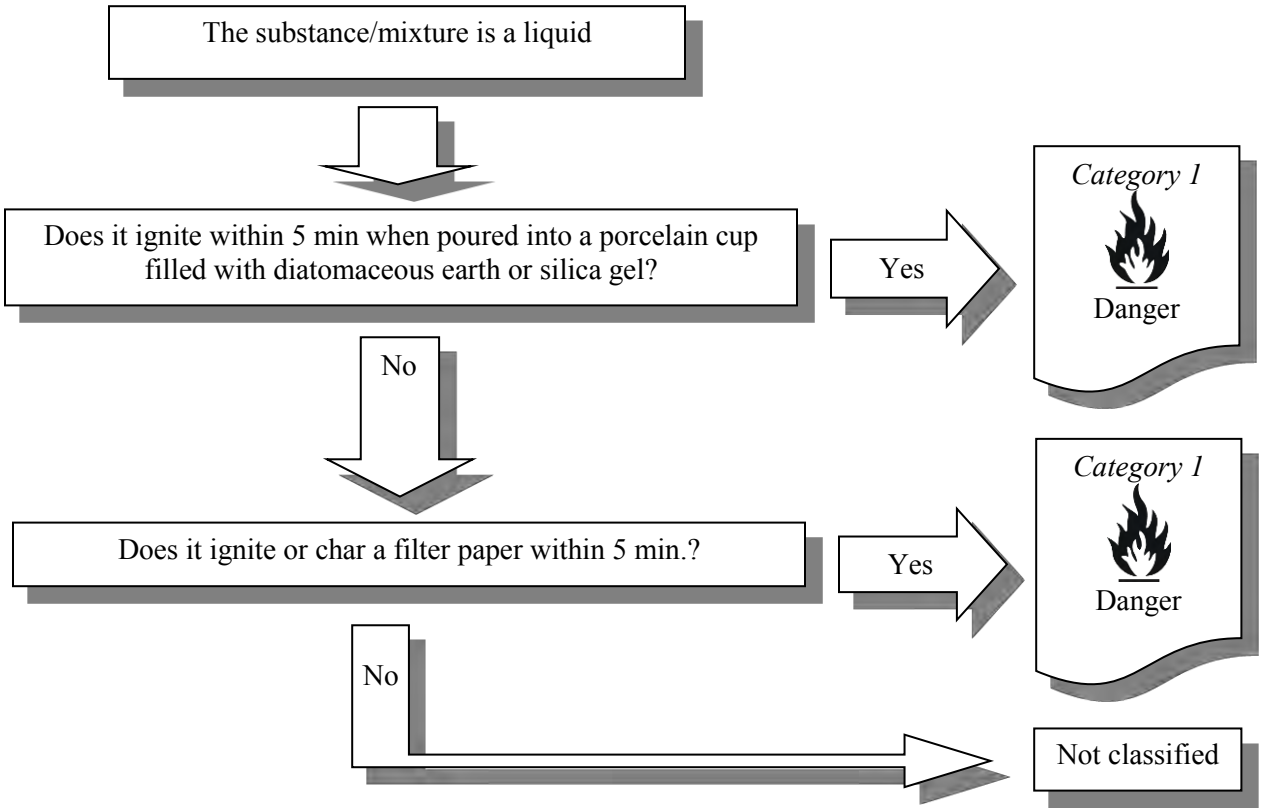
Classification Procedure

The classification procedure is based on the following test data:

- Result of the Test N.3, Procedure (a): ignition in porcelain cup when exposed to air occurs within 5 minutes, or
- Result of the Test N.3, Procedure (b): ignition or charring of a filter paper when in contact to air occurs within 5 minutes

Classification follows the assessment of the ignition or charring data. Once you have collected the data, compare it to the criteria for pyrophoric liquids category 1 presented in Table VIII.9.1. Follow the logic paths presented in the decision logics in Figure VIII.9.1 to identify the appropriate classification categories for pyrophoric liquids.

Figure VIII.9.1. Decision logic for classifying pyrophoric liquids.



Pyrophoric Solids

Definition

A *pyrophoric solid* is a solid which, even at small quantities, is liable to ignite within five minutes after coming into contact with air.

Classification Criteria

A pyrophoric solid is classified in a single category, as shown in Table VIII.9.2.

Table VIII.9.2. Classification criteria for pyrophoric solids.

Category	Criterion
1	The solid ignites within 5 minutes of coming into contact with air.

Classification of solid chemicals is based on tests performed on the chemical as presented. If, for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that which was tested and which is considered likely to materially alter its performance in a classification test, classification must be based on testing of the chemical in the new form. Note that particle size can influence the ability of the chemical to spontaneously ignite.

Classification Procedure and Guidance

To classify pyrophoric solids, data on ignition is necessary. As for pyrophoric liquids, the classification procedure for pyrophoric solids need not be applied when experience in production or handling shows that the chemical does not ignite spontaneously when it comes in contact with air at normal temperatures, i.e., the substance is known to be stable at room temperature for prolonged periods of time (days).

Available Literature

The classifier may use available scientific literature and other evidence to identify the ignition information necessary to classify pyrophoric solids.

In addition, many substances presenting pyrophoric solid hazards have already been classified. The information in the U.S. Department of Transportation's Hazardous Materials Table can be used to assist in pyrophoric solid classifications (See 49 CFR 172.101). The classification of pyrophoric solids in the HCS corresponds to DOT's classification for spontaneously combustible materials. Under DOT regulations, pyrophoric solids are considered Class 4, Division 4.2, hazardous materials and assigned to Packing Group I. Refer to the discussion of the interface between the HCS and DOT labeling in Chapter V of this document for more information.

The decision logic presented below should be used to determine the appropriate hazard classification category for pyrophoric solids.

Test Methods

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use the methods identified in Appendix B.10 to 29 CFR 1910.1200 and described below.

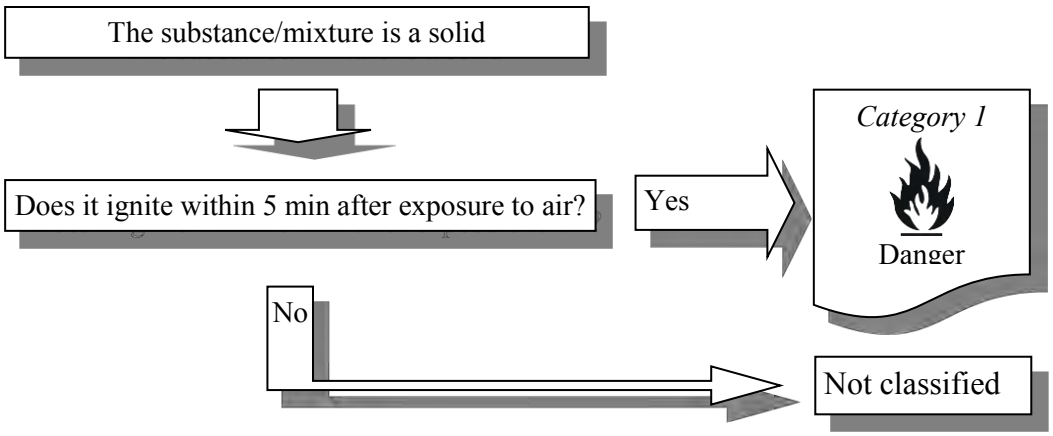
Classification Based on Test Methods in the UN TDG Manual of Tests and Criteria

The classification of pyrophoric solids is based on Test N.2, Test method for pyrophoric solids, described in described in Part III, sub-section 33.3.1.4, of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG), Manual of Tests and Criteria*, Fourth Revised Edition. The test determines the ability of a solid to ignite on contact with air and determines the time of ignition. The decision logic presented below should be used to determine the appropriate hazard classification for a pyrophoric solid using the test data. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

Classification Procedure

Classification follows the assessment of the ignition data. Once you have collected the data, compare it to the criteria for pyrophoric solids category 1 presented in Table VIII.9.2. Follow the logic paths presented in the decision logics (or flowcharts) in Figure VIII.9.2 to identify the appropriate classification categories for pyrophoric solids.

Figure VIII.9.2. Decision logic for classifying pyrophoric solids.



Pyrophoric Gases

Definition

A *pyrophoric gas* is a chemical in a gaseous state that will ignite spontaneously in air at a temperature of 130 °F (54.4 °C) or below.

Classification Criteria

A pyrophoric gas is classified in a single category, as shown in Table VIII.9.3.

Table VIII.9.3. Classification criteria for pyrophoric gases.

Category	Criteria
Pyrophoric Gas	A gas which ignites spontaneously in air at a temperature of 130 ºF (54.4 ºC) or below.

Classification Procedure and Guidance

To classify pyrophoric gases, data on ignition is necessary. The classification procedure for pyrophoric gases need not be applied when experience in production or handling shows that the chemical does not ignite spontaneously when it comes in contact with air at normal temperatures, i.e., the substance is known to be stable at room temperature for prolonged periods of time (days).

Available literature

The classifier may use available scientific literature and other evidence to identify the ignition information necessary to classify pyrophoric gases.

In addition, many substances presenting pyrophoric gas hazards have already been classified. Information in the U.S. Department of Transportation's Hazardous Materials Table can be used to assist in pyrophoric gas classifications (See 49 CFR 172.101). The classification of pyrophoric gases in the HCS corresponds to DOT's classification for flammable gases. Under DOT regulations, pyrophoric gases are considered Class 2, Division 2.1, hazardous materials. The UN special packing instruction P200 is also used by transport for this hazard. Refer to the discussion of the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Test Methods

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, then use of the following test methods is suggested.

Pyrophoric gases are a new hazard class in the United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The test methods listed below may be used when data is not available.

Please refer to these test methods for a complete description of the necessary apparatus and analytical procedure needed to classify a gas as pyrophoric.

- IEC 60079-20-1 ed 1.0 (2010-01)): Explosive atmospheres - Part 20-1: Material characteristics for gas and vapour classification - Test methods and data
- DIN 51794: Determining the ignition temperature of petroleum products

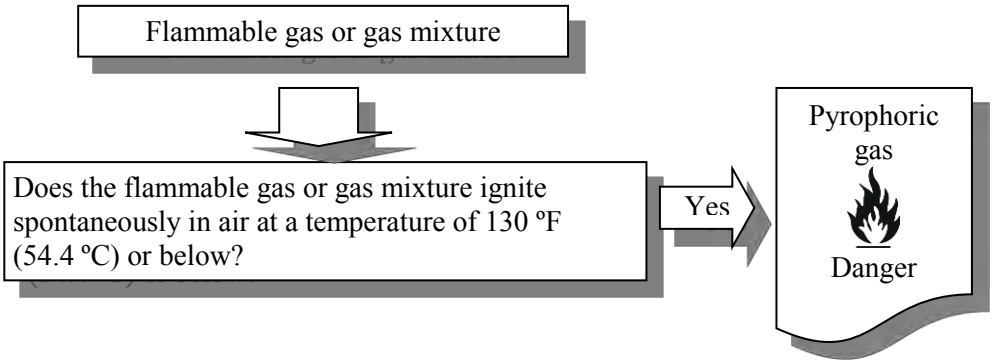
Classification Criteria

Classification follows the assessment of ignition data. Once you have collected the data, compare it to the criteria for pyrophoric gases presented in Table VIII.9.3. Follow the logic paths presented in the decision logic in Figure VIII.9.3 to identify the appropriate classification categories for pyrophoric gases.

However, the classification procedure for pyrophoric gases need not be applied when experience in production or handling shows that the substance does not ignite spontaneously on coming into contact with air at a temperature of 130 ºF (54 ºC) or below. Flammable gas mixtures, that contain more than one percent pyrophoric components, should be classified as a pyrophoric gas unless test data or other evidence supports non-classification.

Expert judgment in the properties and physical hazards of pyrophoric gases and their mixtures should be used in assessing the need for classification of flammable gas mixtures containing one percent or less pyrophoric components. In this case, testing may be considered if expert judgment indicates a need for additional data to support the classification process.

Figure VIII.9.3. Decision logic for classifying pyrophoric gases.



Pyrophoric Chemical Classification Examples

Example #1

The following example illustrates the classification process for a chemical that is suspected of being a pyrophoric liquid, when no information is available and it must be tested. Tests are performed using the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, Part III, Sub-section 33.3.1.5, Test Method N.3: Test method for pyrophoric liquids. This procedure consists of two steps: the inert carrier test, and the filter paper test.

Once the test data is gathered, the classification of the chemical can be determined using the HCS Pyrophoric Liquids Decision Logic.

Test data

Using UN Test N.3, Part III, subsection 33.3.1.5 of the *UN TDG Manual of Tests and Criteria*: Test method for pyrophoric liquids, the liquid is tested.

Step 1: Inert carrier test results:

> Liquid is tested six times on silica gel at room temperature and exposed to air for five minutes. No ignition occurred after six trials. Because of the negative result, and according to the test procedure, the second part of the N.3 test is conducted.

Step 2: Filter paper test results:

> This procedure is performed two times on the liquid. The filter paper is charred in the first test after 5 minutes 15 seconds and in the second test after 4 minutes 45 seconds.

Decision/Rationale

Using the information gathered, answer the questions posed in the pyrophoric liquids decision logic.

1. Does the liquid ignite within 5 minutes when it is poured into a porcelain cup filled with diatomaceous earth or silica gel?
   ANSWER: No. The liquid does not ignite within 5 minutes when poured into a porcelain cup filled with silica gel.

2. Does the liquid ignite or char a filter paper within 5 min?
   ANSWER: Yes. In the second trial, the liquid chars the filter paper within 5 min.

Resulting Classification

The chemical is classified as a Pyrophoric Liquid, Category 1.

Example #2

The following example illustrates the classification process for a chemical that is suspected of being a pyrophoric solid, but no information is available and it must be tested. Tests are performed using the *UN TDG Manual of Tests and Criteria*, Part III, Sub-section 33.3.1.4, Test method N.2: Test method for pyrophoric solids.

Once the test data is gathered, the classification of the chemical can be determined using the HCS Pyrophoric Solids Decision Logic.

Test data

A powder is suspected of being a pyrophoric solid and is tested to determine if the solid ignites when poured from a height of about one meter onto a non-combustible surface. It is observed whether the chemical ignites during dropping or within 5 minutes of settling. This procedure was performed five times with the following results:

> The chemical did not ignite within 5 minutes on the first 4 droppings. However, on the fifth dropping the powder ignited at 4 minutes, 45 seconds after settling.

Decision/Rationale

Using the information gathered, answer the questions posed in the Pyrophoric Solids decision logic.

1. Does the solid chemical ignite within 5 minutes after exposure to air?
   ANSWER: Yes. The solid ignites within 5 minutes of coming into contact with air.

Resulting Classification

The chemical is classified as a Pyrophoric Solid, Category 1, because the solid ignited within 5 minutes of coming into contact with air.

References

29 CFR 1910.1200, Hazard Communication.

29 CFR 1910.1200, Hazard Communication, Appendix B.9, Pyrophoric Liquids.

29 CFR 1910.1200, Hazard Communication, Appendix B.10, Pyrophoric Solids.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.10 Self-Heating Chemicals

Introduction

A chemical that self-heats undergoes a gradual reaction with oxygen (in air) and generates heat. The reaction is not initiated by an outside source. If the rate of heat production exceeds the rate of heat loss, then the temperature of the chemical will rise which, after an induction time, may lead to self-ignition and combustion.

Definition

A *self-heating chemical* is a solid or liquid chemical, other than a pyrophoric liquid or solid, which, by reaction with air and without energy supply, is liable to self-heat; this chemical differs from a pyrophoric liquid or solid in that it will ignite only when in large amounts (kilograms) and after long periods of time (hours or days).

Classification Criteria

A *self-heating chemical* is classified in one of two categories, as shown in Table VIII.10.1.

Table VIII.10.1. Classification criteria for self-heating chemicals.

Category	Criteria
1	A positive result is obtained in a test using a 25 mm sample cube at 140 °C (284 °F).
2	A negative result is obtained in a test using a 25 mm cube sample at 140 °C (284 °F), a positive result is obtained in a test using a 100 mm sample cube at 140 °C (284 °F), and: a) The unit volume of the chemical is more than 3 m^3; or b) A positive result is obtained in a test using a 100 mm cube sample at 120 °C (248 °F) and the unit volume of the chemical is more than 450 liters; or c) A positive result is obtained in a test using a 100 mm cube sample at 100 °C (212 °F).

Note: Although the HCS does not require testing, should testing be performed, then classification of solid chemicals is based on tests performed on the chemical as presented. If, for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that which was tested and which is considered likely to materially alter its performance in a classification test, classification must be based on testing of the chemical in the new form.

Chemicals with a temperature of spontaneous combustion higher than 50 °C (122 °F) for a volume of 27 m^3 are not classified as self-heating chemicals.

Chemicals with a spontaneous ignition temperature higher than 50 °C (122 °F) for a volume of 450 liters (~118.88 gallons) are not classified in Category 1.

Classification Procedure and Guidance

To classify a self-heating chemical, data on how it reacts with air at specified temperatures is necessary.

Even though the definition of this hazard class includes liquids, in general, liquids are not classified as self-heating and the test method is not applicable to liquids.

Available Literature

The classifier may use available scientific literature and other evidence to classify self-heating chemicals. Appendix B of this document provides a listing of information sources that may prove useful during hazard classification.

In addition, some chemicals presenting self-heating chemical hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in classifying self-heating chemicals (See 49 CFR 172.101). The HCS self-heating chemicals category 1 corresponds to DOT Class 4, Division 4.2, Substances Liable to Spontaneous Combustion Packing Group II. HCS self-heating chemicals category 2 corresponds to DOT Class 4, Division 4.2, Substances Liable to Spontaneous Combustion Packing Group III. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

The decision logic presented below should be used to determine the appropriate hazard classification category for a self-heating chemical.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use the methods identified in Appendix B.11 to 29 CFR 1910.1200 and described below.

The classification procedure for self-heating chemicals need not be applied if the results of a screening test can be adequately correlated with the classification test and an appropriate safety margin is applied.

Examples of screening tests are:

a) The Grewer Oven test (VDI guideline 2263, part 1, 1990, Test methods for the Determination of the Safety Characteristics of Dusts) with an onset temperature 80° Kelvin (K) above the reference temperature for a volume of 1 liter; and

b) The Bulk Powder Screening Test (Gibson, N. Harper, D. J. Rogers, R. Evaluation of the fire and explosion risks in drying powders, Plant Operations Progress, 4 (3), 181-189, 1985) with an onset temperature 60° Kelvin (K) above the reference temperature for a volume of 1 liter.

Classification Based on Test Methods in the *UN TDG Manual of Tests and Criteria*

The classification of self-heating chemicals is based on tests described in Part III, Sub-section 33.3.1.6 of the *United Nations Recommendations on the Transport of Dangerous Goods (TDG), Manual of Tests and Criteria*, Test N.4 "Test method for self-heating substances." The test determines the ability of a chemical to undergo oxidative self-heating by exposure to air at temperatures of 100 °C (212 °F), 120 °C (248 °F), or 140 °C (284 °F) in a 25 mm or 100 mm wire mesh cube sample container. Spontaneous ignition or dangerous self-heating are indicated by a 60 °C rise in the oven temperature within 24 hours.

Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

Classification Procedure

Classification of self-heating chemicals is based on information from available literature or the results of the N.4 test. If the N.4 test is performed, then classification is as follows:

Category 1 is assigned to a chemical providing a positive test result using a 25 mm sample cube at an oven temperature of 140 °C (284 °F).

Category 2 is assigned to a chemical providing a positive result using a 100 mm sample cube at 140°C (284°F), providing a negative test result using a 25 mm cube sample at 140 °C (284 °F), **and**:

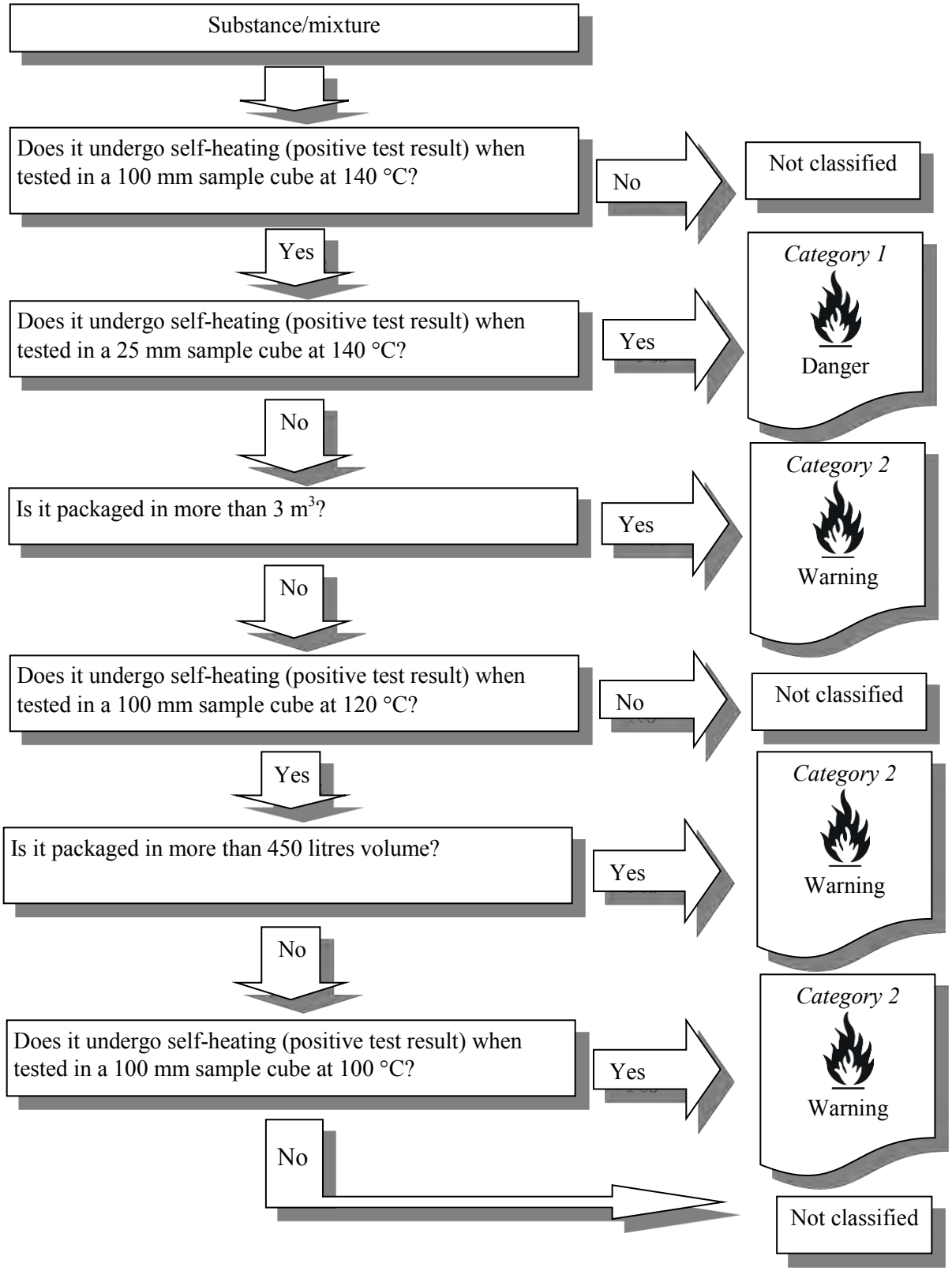
a) The volume of the chemical is more than 3 m^3; or

b) A positive result is obtained in a test using a 100 mm cube sample at 120°C (248°F) and the volume of the chemical is more than 450 liters; or

c) A positive result is obtained in a test using a 100 mm cube sample at 100°C (212°F).

Once the data has been collected, compare the data and test results to the classification criteria for self-heating chemicals presented in Table VIII.10.1. Follow the logic path presented in the decision logic (or flowchart) in Figure VIII.10.1 to identify the appropriate classification categories for self-heating chemicals.

Figure VIII.10.1. Decision logic for classifying self-heating chemicals based on Test N.4.



Self-Heating Chemicals Classification Example

The following example is provided to illustrate the self-heating chemicals decision logic.

Tests are performed using the *UN TDG Manual of Tests and Criteria*, Part III, Sub-section 33.3.1.6, Test method N.4: Test method for self-heating substances.

An inorganic black powder is suspected of being a self-heating substance and is tested according to the above UN test.

Known data

- Inorganic black powder, transported in packages of 400 liters.
- Tested per UN Test method N.4 with the following results:
    - A positive result using a 100 mm sample cube at 140 °C (284 °F).
    - A negative result using a 25 mm sample cube at 140 °C (284 °F).

  According to the procedure, if a positive result is obtained at 140 °C (284 °F) in a 100 mm sample cube, but not in a 25 mm sample cube, then an additional test with the substance in a 100 mm sample cube should be performed based on the packaging and quantity being transported. Below are the results of this addition test:
    - A positive result using a 100 mm sample cube at 120 °C (248 °F).
    - A positive result using a 100 mm sample cube at 100 °C (212 °F).

Decision/Rationale

Using the test data, answer the questions posed in the oxidizing liquid decision logic Figure VIII.10.1, above.

The substance is a powder.

1. Does a 100 mm sample cube undergo self-heating when tested at 140 °C (284 °F)?
   ANSWER: Yes. A positive result was obtained.

2. Does a 25 mm sample cube undergo self-heating when tested at 140 °C (284 °F)?
   ANSWER: No. A negative result was obtained.

3. Is it packaged in more than 3 m^3?
   ANSWER: No. it is transported in packages of 400 liters.

4. Does a 100 mm sample cube undergo self-heating when tested at 120 °C (248 °F)?
   ANSWER: Yes. A positive result was obtained.

5. Is it packaged in more than 450 liters?
   ANSWER: No. it is transported in packages of 400 liters.

6. Does a 100 mm sample cube undergo self-heating when tested at 100 °C (212 °F)?
   ANSWER: Yes. A positive result is obtained using a 100 mm sample cube at 100 °C (212 °F).

Resulting Classification

The chemical is classified as Self-Heating Substance, Category 2.

A positive result is obtained in a test using a 100 mm sample cube at 140 °C, and a negative result is obtained in a test using a 25 mm sample cube at 140 °C, and a positive result is obtained using a 100 mm sample cube at 100 °C. The chemical fulfills the Category 2(c) criteria.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.11, Self-Heating Chemicals.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.11 Chemicals Which, in Contact with Water, Emit Flammable Gases

Introduction

Some chemicals, when in contact with water, may emit flammable gases that can form explosive mixtures with air. Such mixtures are easily ignited by ordinary sources of ignition, for example sparking tools or light bulbs. The resulting blast wave and flames may be hazardous to people and the environment. Sometimes these chemicals are referred to as water-reactive substances.

Definition

Chemicals which, in contact with water, emit flammable gases are solid or liquid chemicals which, by interaction with water, are liable to become spontaneously flammable or to give off flammable gases in dangerous quantities.

Classification Criteria

A *chemical which, in contact with water, emits flammable gases* is classified in one of three hazard categories on the basis of information in available literature or though testing that measures gas evolution and speed of evolution, as described in Table VIII.11.1, below.

Table VIII.11.1. Classification criteria for chemicals which, in contact with water, emit flammable gases.

Category	Criteria
1	Any chemical which reacts vigorously with water at ambient temperatures and demonstrates generally a tendency for the gas produced to ignite spontaneously, or which reacts readily with water at ambient temperatures such that the rate of evolution of flammable gas is equal to or greater than 10 liters per kilogram of chemical over any one minute.
2	Any chemical which reacts readily with water at ambient temperatures such that the maximum rate of evolution of flammable gas is equal to or greater than 20 liters per kilogram of chemical per hour, and which does not meet the criteria for Category 1.
3	Any chemical which reacts slowly with water at ambient temperatures such that the maximum rate of evolution of flammable gas is equal to or greater than 1 liter per kilogram of chemical per hour, and which does not meet the criteria for Categories 1 and 2.

Note: Although the HCS does not require testing, should testing be performed, then classification of solid chemicals is based on tests performed on the chemical as presented. If, for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that which was tested and which is considered likely to materially alter its performance in a classification test, classification must be based on testing of the chemical in the new form.

Classification Procedure and Guidance

To classify a *chemical which, in contact with water, emits flammable gases*, data on how it reacts with water and the evolution rate of the flammable gas is necessary.

Available Literature

The manufacturer, importer, or other responsible party may use available scientific literature and other evidence to classify *chemicals which, in contact with water, emit flammable gases*. Appendix B of this document provides a listing of information sources that may prove useful during hazard classification.

In addition, some substances presenting the hazards from *chemicals which, in contact with water, emit flammable gases* have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in classifying *chemicals which, in contact with water, emit flammable gases* (See 49 CFR 172.101). DOT Hazard Class 4, Division 4.3 substances which in contact with water emit flammable gases, Packing Groups I, II and III correspond directly to the HCS hazard categories 1, 2 and 3, respectively. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

The decision logic presented below may also be used to determine the appropriate hazard classification category for a *chemical which, in contact with water, emits flammable gases*.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance, then use the method identified in Appendix B.12 to 29 CFR 1910.1200 and described below.

The test method for this physical hazard class is used to determine whether the reaction of a chemical with water leads to the development and evolution of a dangerous amount of gases that may be flammable.

The classification procedure for this class need not be applied if:

(a) The chemical structure of the chemical does not contain metals or metalloids;

(b) Experience in production or handling shows that the chemical does not react with water, (e.g., the chemical is manufactured with water or washed with water); or

(c) The chemical is known to be soluble in water to form a stable mixture.

Classification Based on Test Methods in the *UN TDG Manual of Tests and Criteria*

The classification of a chemical which, in contact with water, emits flammable gases is based on tests described in Part III of the Fourth Revised Edition of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) - Manual of Tests and Criteria*. Test Method N.5, "Test method for substances which in contact with water emit flammable gases" is found in Sub-section 33.4.1.4 of the manual. Test method N.5 does not prescribe a specific test apparatus. The test is performed in three steps (each involving contact with water under a different condition). If the chemical identity of the evolved gas is unknown, the gas should be tested for flammability. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method and analysis of the test results.

Classification Procedure

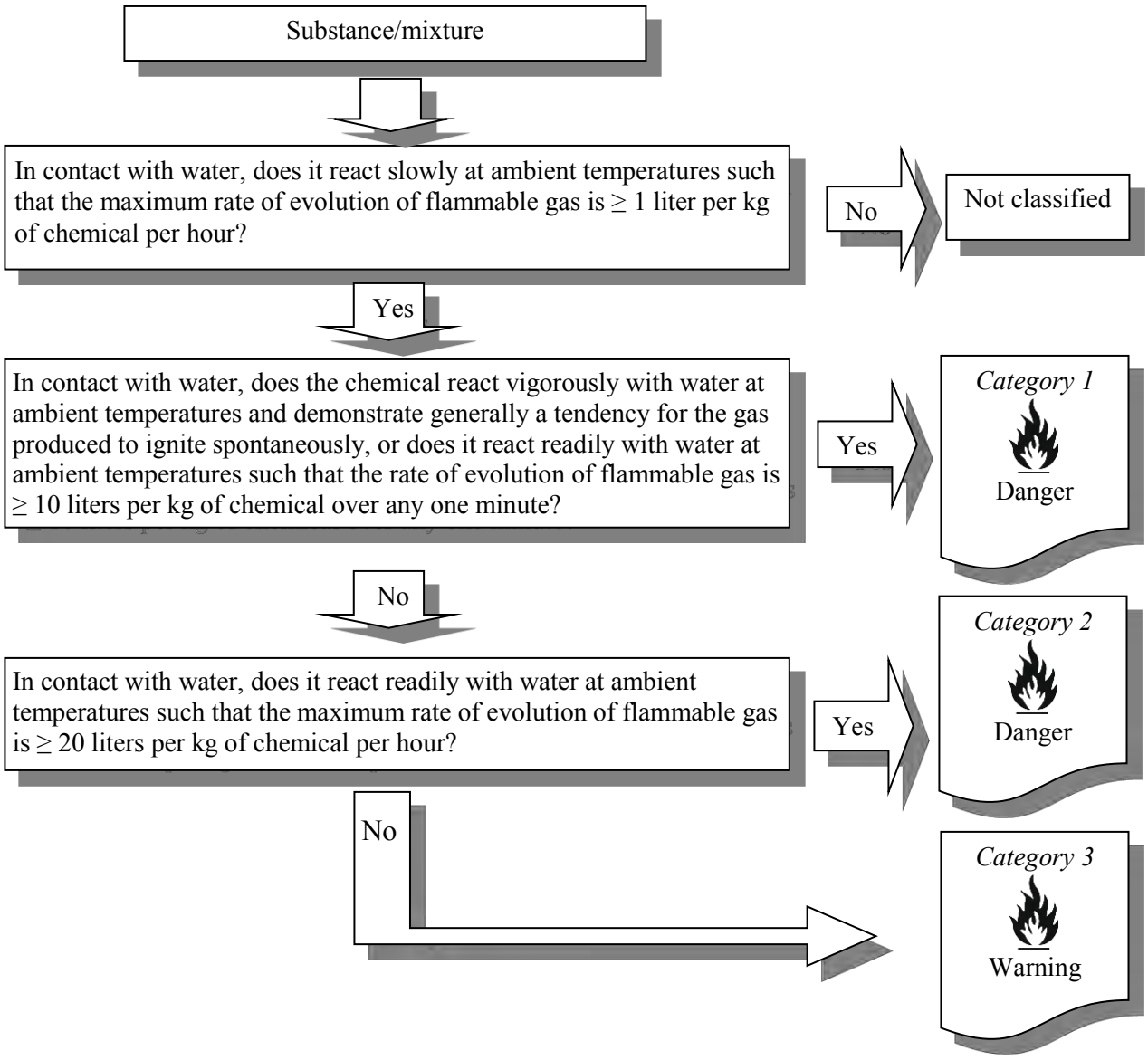
Classification for the physical hazard *chemicals which, in contact with water, emit flammable gases* is based on the maximum rate of evolved flammable gas [Liters flammable gas/kilogram chemical and time].

Should testing be performed, a chemical is assigned to the hazard class *chemicals which, in contact with water, emit flammable gases* when, during testing, contact with water causes the chemical to

- spontaneously ignite in any step of the test procedure; or
- evolution of a flammable gas occurs at a rate ≥1 liter per kilogram of chemical per hour.

Once the data is collected, compare the data and/or test results to the criteria for Category 1, Category 2, and Category 3, presented in Table VIII.11.1. Follow the logic path presented in the decision logic in Figure VIII.11.1 to identify the appropriate classification categories for *chemicals which, in contact with water, emit flammable gases*.

Figure VIII.11.1. Decision logic for classifying chemicals which, in contact with water, emit flammable gases.



Chemicals Which, in Contact with Water, Emit Flammable Gases Classification Example

The following example is provided to illustrate the classification process and decision logic for *chemicals which, in contact with water, emit flammable gases*.

A liquid is suspected of being a *chemical which, in contact with water, emits flammable gas*. The liquid is tested to determine whether any gas is evolved, if spontaneous ignition of the gas occurs, and if there is evolution of flammable gas at a rate greater than 1 liter per kilogram of the chemical per hour.

Tests are performed using the *UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, Part III, Sub-section 33.3.1.4, Test method N.5: "Test method for substances which in contact with water emit flammable gases."

Known data

- Liquid contains an organometallic.
- The chemical reacts slowly with water and emits a gas known to be flammable.
- Chemical was tested for seven hours at ambient temperature per UN Test N.5 "Test method for substances which, in contact with water, emit flammable gases." Test results showed
  - A maximum rate of evolution of 15 liters per kilogram (L/kg) substance per hour of flammable gas.
  - The gas did not spontaneously ignite.

Decision/Rationale

1. When contacted with water, does the chemical react slowly, such that the maximum rate of evolution of flammable gas is ≥ 1 L/kg of chemical per hour?
   ANSWER: Yes

2. When contacted with water, does the chemical react vigorously with water at ambient temperatures and demonstrate generally a tendency for the gas produced to ignite spontaneously, or does it react readily with water at ambient temperatures such that the rate of evolution of flammable gas is ≥ 10 L/kg of chemical over any one minute?
   ANSWER: No

3. When contacted with water, does the chemical react readily at ambient temperatures such that the maximum rate of evolution is ≥ 20 L/kg of substance per hour?
   ANSWER: No. This chemical reacts slowly with water at ambient temperatures such that the maximum rate of evolution of flammable gas is ≥ 1L/kg/hr, and ≤ 20 L/kg/hr and there is no spontaneous ignition.

Resulting Classification

Liquid is classified as a *chemical which, in contact with water, emits flammable gases*, Category 3.

The liquid fulfills the Category 3 criteria: Any chemical which reacts slowly with water at ambient temperatures such that the maximum rate of evolution of flammable gas is equal to or greater than 1 liter per kilogram of chemical per hour, and which does not meet the criteria for Categories 1 and 2.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.12 Chemicals which, in Contact with Water, Emit Flammable Gases.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.12 Oxidizing Liquids and Solids

Introduction

An oxidizer is a chemical that brings about an oxidation reaction that can promote combustion of other materials due to the release of oxygen. Although widely known as "oxidizing materials," their hazards and behavior may be better understood by considering them as "fire enhancing substances." For example, an unclassified solid in contact with an oxidizing material may, upon ignition, behave like a flammable solid.

In an oxidation reaction the oxidizer may provide oxygen to the substance being oxidized (in which case the oxidizer has to be oxygen or contain oxygen), or it may receive electrons being transferred from the substance undergoing oxidation. For example, chlorine is a good oxidizer for electron-transfer purposes, even though it contains no oxygen.

Oxidizers can initiate or greatly accelerate the burning of fuels. The most common oxidizer is atmospheric oxygen. Oxygen-containing chemicals (e.g., hydrogen peroxide) and halogens (e.g., bromine, chlorine, and fluorine) can also be strong oxidizers. Some chemicals may be oxidizers with such an extremely fast burning ability that they are classified as explosives or blasting agents rather than oxidizers. Often the fact that a chemical possesses oxidizing ability can be determined by an examination of its chemical structure. For example, oxidizing substances usually include recognizable functional chemical groups - e.g., perchlorate (ClO_4-), chlorate (ClO_3-), chlorite (ClO_2-), hypochlorite (ClO-), nitrate (NO_3-), nitrite (NO_2-), dichromate (Cr_2O_7), persulfate (S_2O_8), and permanganate (MnO_4).

Because of the similarities of liquid and solid oxidizing chemicals, this chapter provides classification guidance on both. There is a separate chapter on oxidizing gases.

Oxidizing Liquids

Definition

Oxidizing liquid means a liquid which, while in itself not necessarily combustible, may, generally by yielding oxygen, cause, or contribute to, the combustion of other material.

Classification Criteria

To classify a liquid chemical as an oxidizing liquid, information is needed about its ability to increase the burning rate or burning intensity of a combustible substance (fibrous cellulose) when the two are thoroughly mixed.

Oxidizing liquids are assigned to one of three hazard categories based on test results that measure ignition or pressure rise time compared to that of defined (or control) mixtures, as shown in Table VIII.12.1. Pressure rise time is the length of time that it takes the pressure to rise from 690 kilopascals (kPa) to 2,070 kPa.

Table VIII.12.1. Classification criteria for oxidizing liquids.

Category	Criteria
1	Any chemical which, in the 1:1 mixture, by mass, of chemical and cellulose tested, spontaneously ignites; or the mean pressure rise time of a 1:1 mixture, by mass, of chemical and cellulose is less than that of a 1:1 mixture, by mass, of 50% perchloric acid and cellulose.
2	Any chemical which, in the 1:1 mixture, by mass, of chemical and cellulose tested, exhibits a mean pressure rise time less than or equal to the mean pressure rise time of a 1:1 mixture, by mass, of 40% aqueous sodium chlorate solution and cellulose; and the criteria for Category 1 are not met.
3	Any chemical which, in the 1:1 mixture, by mass, of chemical and cellulose tested, exhibits a mean pressure rise time less than or equal to the mean pressure rise time of a 1:1 mixture, by mass, of 65% aqueous nitric acid and cellulose; and the criteria for Categories 1 and 2 are not met.

Classification Procedure and Guidance

To classify a chemical as an oxidizing liquid , data is necessary on how it reacts with air at specified temperatures.

For this hazard class, organic and inorganic chemicals are treated differently. When classifying chemicals suspected of being oxidizing liquids, pre-test evaluations are necessary. For organic chemicals, the classification procedure for oxidizing liquids does not need to be applied if:

(a) the chemical does not contain oxygen, fluorine or chlorine; or
(b) the chemical contains oxygen, fluorine or chlorine and these elements are chemically bonded only to carbon or hydrogen.

For inorganic chemicals, the classification procedure for oxidizing liquids does not need to be applied if the chemical does not contain oxygen or halogen atoms.

Available Literature

The classifier may use available scientific literature and other evidence to classify chemicals as oxidizing liquids. Appendix B of this document provides a listing of sources that may prove useful during hazard classification.

Many chemicals that present oxidizing liquid hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in oxidizing liquid classifications (see 49 CFR 172.101). The HCS criteria for oxidizing liquids category 1, 2 or 3 corresponds to DOT Class 5.1, Oxidizing Substances Packing Group I, II, or III, respectively. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use methods identified in Appendix B.13 to 29 CFR 1910.1200, described below.

Classification Based on Test Methods in the *UN TDG Manual of Tests and Criteria*

The classification of oxidizing liquids is based on tests described in Part III of the Fourth Revised Edition of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) - Manual of Tests and Criteria*. Test O.2, "Test for oxidizing liquids," is performed in accordance with sub-section 34.4.2 of the manual. The test measures the time it takes for the pressure to rise from 690 kilopascals (kPa) to 2,070 kPa, and compares this period with the time taken for the pressure of a similar mixture containing the reference substance and cellulose to rise the same amount.

Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

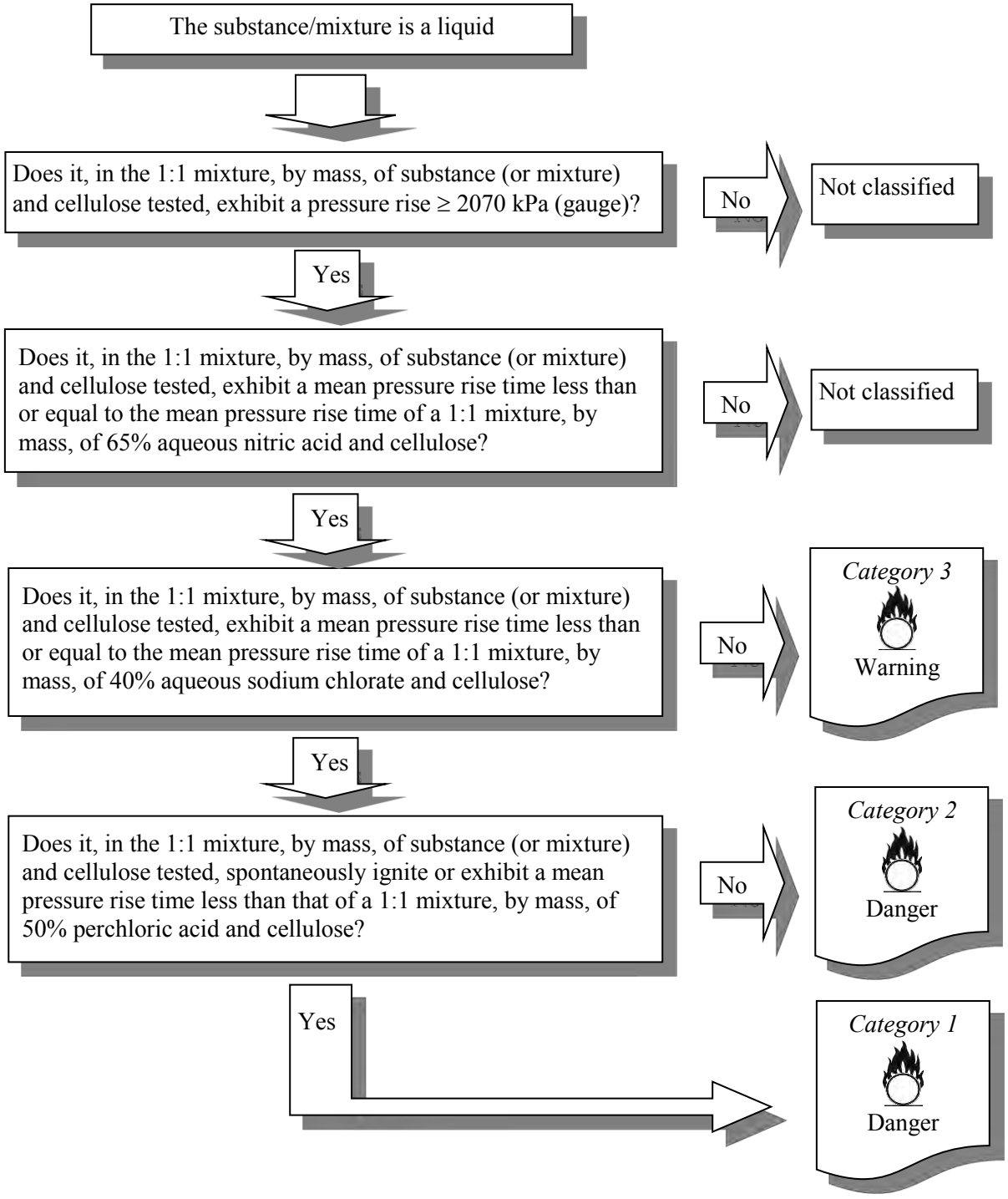
Classification Procedure

Classification of oxidizing liquids is based on the results of Test O.2. You may also find information available from assigned transport packing groups under the DOT regulations to be helpful. The transport packing group assignments coincide with the hazard category assignments for oxidizing liquids.

When test results diverge from known experience in the handling and use of a chemical shows the chemical to be an oxidizing hazard, then professional judgment, based on known experience, takes precedence over test results. When professional judgment is relied upon for classification, the classifier must be able to explain why professional judgment was used instead of the test results.

Figure VIII.12.1 provides a decision logic for classifying oxidizing liquids based on the results from Test O.2 or from available literature.

Figure VIII.12.1. Decision logic for classifying oxidizing liquids.



Oxidizing Solids

Definition

Oxidizing solid means a solid which, while in itself is not necessarily combustible, may, generally by yielding oxygen, cause, or contribute to, the combustion of other material.

Classification Criteria

To classify a solid as oxidizing, data are needed on the potential for a solid chemical to increase the burning rate or burning intensity of a combustible substance (in general, fibrous cellulose) when the two are thoroughly mixed.

Oxidizing solids are assigned to one of three hazard categories on the basis of information from available literature or from test results that measure mean burning time compared to defined mixtures, as shown in Table VIII.12.2.

Table VIII.12.2. Classification criteria for oxidizing solids.

Category	Criteria
1	Any chemical which, in the 4:1 or 1:1 sample-to-cellulose ratio (by mass) tested, exhibits a mean burning time less than the mean burning time of a 3:2 mixture (by mass) of potassium bromate and cellulose.
2	Any chemical which, in the 4:1 or 1:1 sample-to-cellulose ratio (by mass) tested, exhibits a mean burning time equal to or less than the mean burning time of a 2:3 mixture (by mass) of potassium bromate and cellulose and the criteria for Category 1 are not met.
3	Any chemical which, in the 4:1 or 1:1 sample-to-cellulose ratio (by mass) tested, exhibits a mean burning time equal to or less than the mean burning time of a 3:7 mixture (by mass) of potassium bromate and cellulose and the criteria for Categories 1 and 2 are not met.

Note 1: Some oxidizing solids may present explosion hazards under certain conditions (e.g., when stored in large quantities). For example, some types of ammonium nitrate may give rise to an explosion hazard under extreme conditions. The "Resistance to detonation test" (IMO: Code of Safe Practice for Solid Bulk Cargoes, 2005, Annex 3, Test 5) may be used to assess this hazard. When information indicates that an oxidizing solid may present an explosion hazard, the explosive hazard must be indicated on the Safety Data Sheet.

Note 2: Classification of solid chemicals should be based on tests performed on the chemical as presented. If, for example, for the purposes of supply or transport, the same chemical is to be presented in a physical form different from that which was tested and which is considered likely to materially alter its performance in a classification test, then classification is based on testing of the chemical in the new form.

Classification Procedure and Guidance

To classify an oxidizing solid, data is needed on its potential to increase the burning rate or burning intensity of a combustible substance.

Organic and inorganic chemicals are treated differently during classification; that is, an organic chemical should not be classified as an oxidizing solid if:

(a) the chemical does not contain oxygen, fluorine or chlorine; or
(b) the chemical contains oxygen, fluorine or chlorine and these elements are chemically bonded only to carbon or hydrogen.

In addition, inorganic chemicals that do not contain oxygen or halogen atoms are not oxidizing solids, and should not be classified as such.

Available Literature

The classifier may use available scientific literature and other evidence. Appendix B of this document provides a list of sources that may prove useful during hazard classification.

In addition, many substances presenting oxidizing solid hazards have already been classified. The Hazardous Materials Regulations table from the U.S. Department of Transportation can be used to assist in oxidizing solid classifications (see 49 CFR 172.101). The HCS criteria for oxidizing solids category 1, 2, or 3 corresponds to DOT's Class 5.1 Oxidizing Substances Packing Group I, II, or III, respectively. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use the test methods identified in Appendix B.14 to 29 CFR 1910.1200, and described below.

Classification Based on Test Methods in the *UN TDG Manual of Tests and Criteria*

The classification of oxidizing solids is based on tests described in Part III of the Fourth Revised Edition of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) - Manual of Tests and Criteria*. Test O.1, "Test for oxidizing solids," is performed in accordance with sub-section 34.4.1 of the manual. The test method measures the potential for a solid chemical to increase the burning rate or burning intensity of a combustible substance when the two are thoroughly mixed.

Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the methods, the apparatus used, and analysis of the test results.

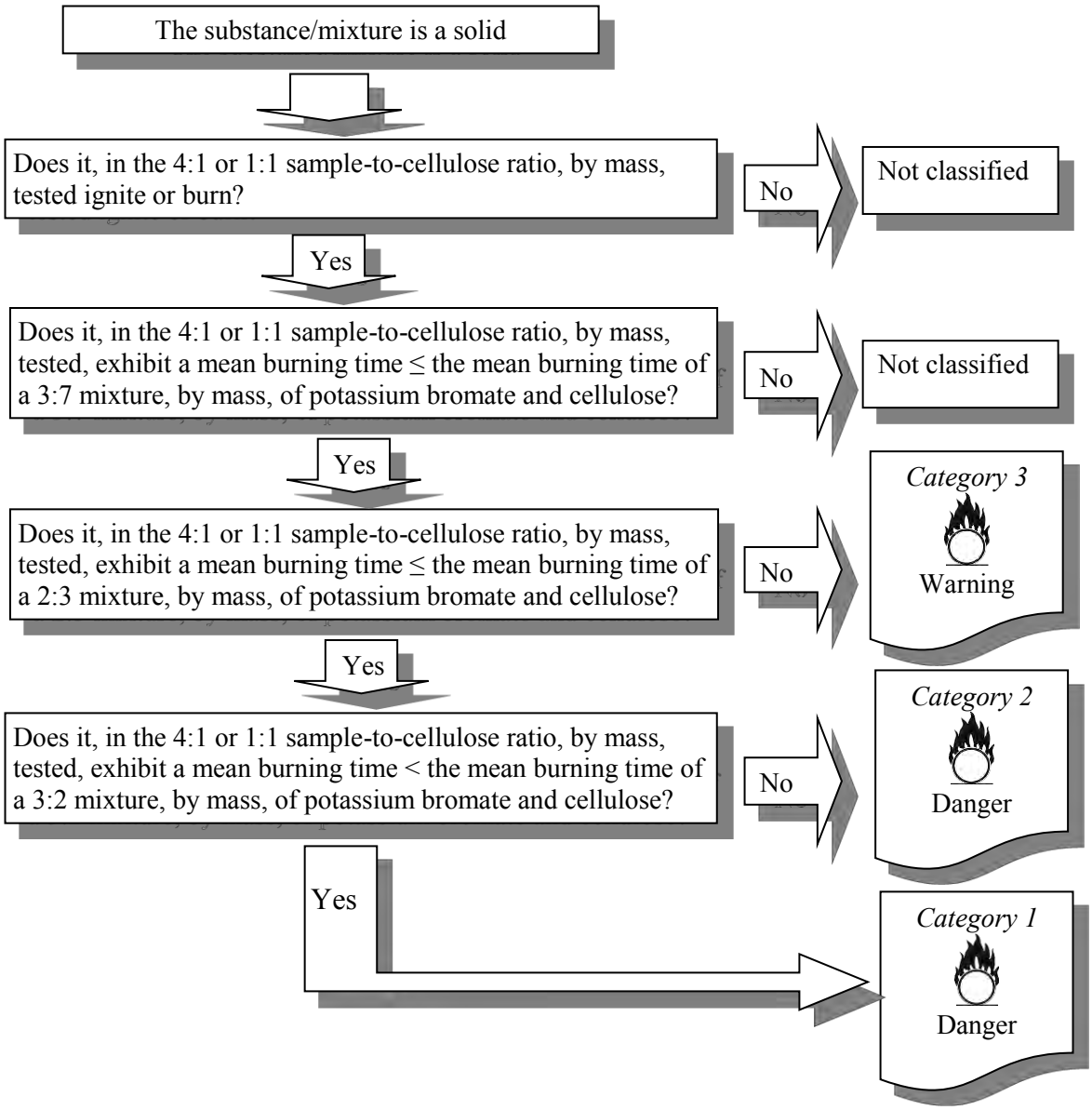
Classification Procedure

Classification of oxidizing solids is based on the results of Test O.1. You may also find that information provided by DOT-assigned transport packing groups to be helpful. The transport packing group assignments coincide with the hazard category assignments for oxidizing solids.

If the test results diverge from known experience in the handling and use of a chemical shown to be oxidizing, then professional judgment, based on known experience, takes precedence over the test results. When professional judgment is relied upon for classification, the classifier must be able to explain why professional judgment was used over the test results.

Figure VIII.12.2 presents the decision logic for classifying oxidizing solids based on available information or from the results of Test O.1.

Figure VIII.12.2. Decision logic for classifying oxidizing solids.



Oxidizing Liquid Classification Example

The following example illustrates the classification process and decision logic for oxidizing liquids when data are available for the given chemical.

Tests are performed using the *UN TDG, Manual of Tests and Criteria*, Part III, Sub-section 34.4.2, Test Method O.2: "Test for oxidizing liquids."

A liquid suspected of being an oxidizing liquid is tested to determine whether a mixture of the substance and cellulose spontaneously ignites. The mean time taken for the pressure to rise from 690 kPa to 2,070 kPa is compared with those of the reference substances. The reference substances are: 50% perchloric acid, 40% aqueous sodium chlorate solution and 65 % aqueous nitric acid. Five trials are performed with the mixture and each of the reference substances. The time taken for the pressure rise from 690 kPa to 2,070 kPa is noted. The mean time interval is used for classification.

Known data

A liquid substance is tested per *UN TDG Manual of Tests and Criteria*, Test Method O.2: "Test method for oxidizing liquids."

Test data/results

- 2.5 g of the liquid to be tested is mixed with 2.5 g of dried cellulose. The mixture did not spontaneously ignite.
- The mixture is heated, and the time taken for the pressure rise from 690 kPa to 2,070 kPa is measured. The mean pressure rise time for 5 trials is 4,210 seconds (s).
  - The test sample exhibited a pressure rise ≥ 2,070 kPa gauge.
  - The mean pressure rise time for the reference substance containing 65% aqueous nitric acid and cellulose is 4,767 s.
  - The mean pressure rise time for the reference substance containing 40% aqueous sodium chlorate and cellulose is 4,050 s.
  - The mean pressure rise time for the reference substance containing 50% perchloric acid and cellulose is 3,085 s.

Decision/Rationale

Using the test data, answer the questions posed in the oxidizing liquid decision logic, Figure VIII.12.1, above.

The substance is a liquid.

1. Does a 1:1 mixture, by mass, of substance and cellulose tested, exhibit a pressure rise ≥ 2,070 kPa gauge?
   ANSWER: Yes. The test sample exhibited a pressure rise of ≥ 2,070 kPa gauge.

2. Does a 1:1 mixture, by mass, of substance and cellulose tested, exhibit a mean pressure rise time less than or equal to the mean pressure rise time of a 1:1 mixture, by mass, of 65% aqueous nitric acid and cellulose?
   ANSWER: Yes. The mean pressure rise time for the liquid test substance is 4,210 s, which is less than 4,767 s for 65% aqueous nitric acid.

3. Does a 1:1 mixture, by mass, of substance and cellulose tested, exhibit a mean pressure rise time less than or equal to the mean pressure rise time of a 1:1 mixture, by mass, of 40% aqueous sodium chlorate and cellulose?
   ANSWER: No. The mean pressure rise time for the liquid test substance is 4,210 s, which is greater than 4,050 s for 40% aqueous sodium chlorate. The decision logic is exited and the substance is classified.

According to UN Test O.2, the classification criteria, and decision logic VIII.12.1, the liquid test substance fulfils the criteria for Oxidizing Liquids Category 3 and does not meet the criteria for Categories 1 and 2.

Resulting Classification

The chemical is classified as Oxidizing Liquids, Category 3.

Oxidizing Solid Classification Example

The following example illustrates the classification process and decision logic for oxidizing solids when data are available for the given chemical.

Tests are performed using the *UN TDG Manual of Tests and Criteri*a, Part III, Sub-section 34.4.1, Test Method O.1: "Test for oxidizing solids."

A chemical suspected of being an oxidizing solid is tested to determine whether a mixture of substance and cellulose ignites and burns, and to compare the mean burning time with those of reference mixtures.

Tests require that the substance in question be mixed with dry fibrous cellulose in ratios of 1:1 and 4:1, by mass, of sample to cellulose.

The burning characteristics of these mixtures are compared with the standard reference mixtures, 3:7, 3:2 and 2:3 ratios, by mass, of potassium bromate to cellulose. Five trials are performed on the test substance in each of the sample to cellulose ratios. Five trials are performed with each reference mixture.

Known data

The solid powder substance was tested using the *UN TDG, Manual of Tests and Criteri*a, Test Method O.1: "Test for oxidizing solids."

Test data/results

- The chemical in the particle size in which it will be transported and cellulose are prepared in ratios of 4:1 and 1:1, by mass.
- The reference substance (potassium bromate) and cellulose are prepared in the ratios 3:7, 2:3 and 3:2, by mass.
- The test is initiated. The solid substance samples are ignited and burned.
- The mean burning time is measured in five trials for the different sample ratios.
- The data for the 4:1 and 1:1 ratio of the test mixtures are
  - The mean burn time for the 4:1 ratio of the test mixture to cellulose is 105 s
  - The mean burn time for the 1:1 ratio of the test mixture to cellulose is 340 s
- The data for the standard reference mixtures, 3:7, 3:2 and 2:3 ratios of potassium bromate to cellulose are
  - The mean burn time for the 3.7 ratio of potassium bromate to cellulose is 100 s
  - The mean burn time for the 2.3 ratio of potassium bromate to cellulose is 54 s
  - The mean burn time for the 3.2 ratio of potassium bromate to cellulose is 4 s

Decision/Rationale

Using the test data, answer the questions posed in the oxidizing solid decision logic, Figure VIII.12.2, above.

The substance is a solid

1. Does a 4:1 or 1:1 sample-to-cellulose ratio, by mass, tested ignite or burn?
   ANSWER: Yes. The 4:1 and 1:1 solid substance samples ignited and burned.

2. Does a 4:1 or 1:1 sample-to-cellulose ratio, by mass, tested, exhibit a mean burning time less than or equal to the mean burning time of a 3:7 mixture, by mass, of potassium bromate and cellulose?
   ANSWER: No. The mean burn times for both the 4:1 and 1:1 solid substance sample-to-cellulose ratios (105 s, 340 s) are greater than the mean burning time of the 3:7 mixture, by mass, of potassium bromate and cellulose (100 s). The solid substance is not classified as an oxidizing solid. Exit the decision logic.

Resulting Classification

Since the solid substance does not fulfil the criteria for oxidizing solids, it is not classified as an oxidizing solid.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.13, Oxidizing Liquids.

29 CFR 1910.1200, Hazard Communication, Appendix B.14, Oxidizing Solids.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.13 Organic Peroxides

Introduction

The Organic Peroxides hazard class is the only hazard to which chemicals are assigned based on their chemical structure. The peroxide functional group (-O-O-) is relatively unstable and most organic peroxides will spontaneously decompose at a slow rate. Some organic peroxides, however, are capable of very violent reactions with detonation at normal temperatures, causing fires and explosions. Several organic peroxides are used in the plastics industry to initiate polymerization and serve as cross-linking agents. Recognizing an organic peroxide is quite simple because of the presence of the peroxide group (-O-O-) in its chemical structure. However, the characterization of the severity of the hazard is usually based upon fairly extensive laboratory testing. Examples of organic peroxides are benzoyl peroxide and allyl hydroperoxide.

Organic peroxides are liable to exothermic decomposition at normal or elevated temperatures. The decomposition can be initiated by heat, contact with impurities (e.g., acids, heavy-metal compounds, and amines), friction or impact. Decomposition may result in the evolution of harmful, or flammable, gases or vapors. The rate of decomposition increases with temperature and varies with the organic peroxide formulation. For certain organic peroxides, the temperature is controlled during transport. Some organic peroxides may decompose explosively, particularly if confined. This characteristic may be modified by the addition of diluents or by the use of appropriate packagings. Many organic peroxides also burn vigorously.

Contact of organic peroxides with the eyes should be avoided. Some organic peroxides will cause serious injury to the cornea, even after brief contact, or will be corrosive to the skin.

Definition

Organic peroxide means a liquid or solid organic chemical, which contains the bivalent -O-O- structure, and as such, is considered a derivative of hydrogen peroxide, where one or both of the hydrogen atoms have been replaced by organic radicals. The term organic peroxide includes mixtures containing at least one organic peroxide. Organic peroxides are thermally unstable chemicals, which may undergo exothermic self-accelerating decomposition. In addition, they may have one or more of the following properties:

(a) be liable to explosive decomposition;
(b) burn rapidly;
(c) be sensitive to impact or friction;
(d) react dangerously with other substances.

An organic peroxide is regarded as possessing explosive properties when in laboratory testing the formulation detonates, deflagrates rapidly, or shows a violent effect when heated under confinement.

Deflagration. *Propagation of a reaction zone at a velocity that is less than the speed of sound in the unreacted medium (Definition from NFPA 68).*

Detonation. *Propagation of a combustion zone at a velocity that is greater than the speed of sound in the unreacted medium (Definition from NFPA 68).*

Classification Criteria

Like self-reactive chemicals, organic peroxides are assigned to one of seven types, A to G, according to the degree of danger that they present. Table VIII.13.1 presents the classification criteria for organic peroxides.

Table VIII.13.1. Classification criteria for organic peroxides.

Organic Peroxide Type	Criteria
A	Any organic peroxide, which, as packaged, can detonate or deflagrate rapidly.
B	Any organic peroxide possessing explosive properties and which, as packaged, neither detonates nor deflagrates rapidly, but is liable to undergo a thermal explosion in that package.
C	Any organic peroxide possessing explosive properties when the chemical as packaged cannot detonate or deflagrate rapidly or undergo a thermal explosion.
D	Any organic peroxide which in laboratory testing meets the criteria in i, ii, or iii below: i. Detonates partially, does not deflagrate rapidly and shows no violent effect when heated under confinement; or ii. Does not detonate at all, deflagrates slowly and shows no violent effect when heated under confinement; or iii. Does not detonate or deflagrate at all and shows a medium effect when heated under confinement;
E	Any organic peroxide which, in laboratory testing, neither detonates nor deflagrates at all and shows low or no effect when heated under confinement.
F	Any organic peroxide which, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows only a low or no effect when heated under confinement as well as low or no explosive power.

Organic Peroxide Type	Criteria
G	Any organic peroxide which, in laboratory testing, neither detonates in the cavitated state nor deflagrates at all and shows no effect when heated under confinement nor any explosive power, provided that it is thermally stable (self-accelerating decomposition temperature is 60 °C (140 °F) or higher for a 50 kg (110 lb.) package), and, for liquid mixtures, a diluent having a boiling point of not less than 150 °C (302 °F) is used for desensitization. If the organic peroxide is not thermally stable or a diluent having a boiling point less than 150 °C (302 °F) is used for desensitization, it is defined as organic peroxide TYPE F.

Note: Type G has no hazard communication elements assigned but should be considered for properties belonging to other hazard classes.

Classification Procedure and Guidance

Organic peroxides are classified by definition based on their chemical structure and on the available oxygen and hydrogen peroxide contents of the mixture. In addition, data are needed on the ability of the chemical to detonate and deflagrate, and on the effects of heating under confinement.

Any organic peroxide is considered for classification in this class, unless it contains:

a) not more than 1.0% available oxygen from the organic peroxides when containing not more than 1.0% hydrogen peroxide; or
b) not more than 0.5% available oxygen from the organic peroxides when containing more than 1.0% but not more than 7.0% hydrogen peroxide.

The available oxygen content (in percent [%]) of an organic peroxide mixture is given by the formula:

$$16 \times \sum_{i}^{n} \left(\frac{n_i \times c_i}{m_i} \right)$$

where

n_i = number of peroxygen groups per molecule of organic peroxide i
c_i = concentration (mass %) of organic peroxide i
m_i = molecular mass of organic peroxide i

Available Literature

The classifier may use available scientific literature and other evidence to classify organic peroxides. The information needed to classify the chemicals may be found in available literature or through laboratory testing. Should data from laboratory testing be used, a chemical must be tested together with its package.

In addition, many substances presenting organic peroxide hazards have already been classified. The information in the U.S. Department of Transportation Hazardous Materials table can be used to assist in organic peroxide classification (See 49 CFR 172.101). Under DOT regulations, organic peroxides are considered Hazard Class 5 Division 5.2, organic peroxides. Organic peroxide chemicals, classified in accordance with the HCS, correspond to organic peroxide materials classified under DOT regulations. Therefore, the labeling requirements for organic peroxides in the HCS correspond to DOT's Hazard Class Division 5.2, organic peroxides. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Test Methods

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use the test methods identified in Appendix B.15 to 29 CFR 1910.1200, described below. The decision logic presented below should be used to determine the appropriate hazard classification category for organic peroxide chemicals if testing is performed to gather the necessary information.

The classification of organic peroxide chemicals is based on tests described in Part II of the Fourth Revised Edition of the *United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) – Manual of Tests and Criteria*, Sub-sections 20 to 28, Test Series A to H. The methods are designed for testing both organic peroxides and self-reactive chemicals.

Organic peroxide chemicals are classified into seven types. The tests are performed in two stages. The first stage uses preliminary small-scale tests to ascertain the stability and sensitivity of the chemicals and to ensure the safety of laboratory workers. During the second stage, classification tests are performed. A brief summary of the purpose of these tests is presented below. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

Preliminary procedure

Performing small-scale preliminary tests before attempting to handle larger quantities is essential to ensure the safety of laboratory workers. The preliminary tests determine the sensitivity of the chemical to mechanical stimuli (impact and friction), and to heat and flame. Four types of small-scale tests are used to make the preliminary assessment:

(e) A falling weight test to determine sensitivity to impact;
(f) A friction or impacted friction test to determine the sensitivity to friction;
(g) A test to assess thermal stability and the exothermic decomposition energy; and
(h) A test to assess the effect of ignition.

The details of these preliminary tests can be found in Part I of the Fourth Revised Edition of the *UN TDG Manual of Tests and Criteria*, Sub-section 13, Test Series 3. Appendix 6 of the *UN TDG Manual for Tests and Criteria* provides additional guidance on screening procedures.

Classification test

The classification of an organic peroxide chemical in one of the seven categories, Types A to G, is dependent on its detonation, explosive thermal explosion and deflagrating properties, its response to heating, the concentration and the type of diluent added to desensitize the substance. The classification of an organic peroxide chemical as Type A, B, or C is also dependent on the type of packaging in which the chemical is tested, as the package affects the degree of confinement to which the chemical is subjected.

Should testing be performed on the chemical, data from organic peroxide chemical test series A to H is needed. A brief description of the purpose of each of the tests described in the *UN TDG Manual for Tests and Criteria* is presented below.

Test Series A answers the question, "Does the chemical propagate a detonation?" Several tests are identified in the *UN TDG Manual for Tests and Criteria* and each measures the ability of a chemical to propagate a detonation by subjecting it to a detonating booster charge under confinement in a steel tube. The test methods include:

- BAM 50/60 steel tube test
- TNO 50/70 steel tube test
- UN gap test
- UN detonation test (the recommended test)

Test Series B answers the question "Can the chemical detonate as packaged for transport?" The tests measure the ability of a chemical to propagate a detonation when packaged for transport by subjecting it to the shock from a detonating booster charge. The test is required only for substances that propagate detonation.

Test Series C answers the question, "Does the chemical propagate a deflagration?" This series consists of two recommended tests – the time/pressure test, and the deflagration test. The time and pressure test measures the ability of a substance under confinement to propagate a deflagration. The deflagration test measures the ability of a chemical to propagate a deflagration.

Test Series D answers the question, "Does the chemical deflagrate rapidly in package?" The test measures the ability of a chemical to rapidly propagate a deflagration when packaged for transport. The test is required for substances that deflagrate rapidly in a Test Series C test.

Test Series E answers the question, "What is the effect of heating the chemical under defined confinement?" This test series consists of three test methods – the Koenen test, the Dutch pressure test, and the USA pressure test. For organic peroxide chemicals, the Dutch pressure test is recommended in combination with one of the other tests. The purpose of these three tests is described below.

The Koenen test determines the sensitivity of substances to the effect of intense heat under high confinement. The Dutch pressure vessel test and the USA pressure test determine the sensitivity of substances to the effect of intense heat under defined confinement.

Test Series F answers the question, "What is the chemical's explosive power?" Several tests are described in the *UN TDG Manual of Tests and Criteria* for use when testing for organic peroxides, including the Ballistic mortar Mk. IIId test, the Ballistic mortar test, the BAM Trauzl test, and the Modified Trauzl test. The Modified Trauzl test is the recommended test, measures the explosive power of a chemical, and is used for chemicals being considered for transport in intermediate bulk containers (IBCs) or tank-containers.

Test Series G answers the question, "Can the chemical explode as packaged for transport?" The test series uses two test methods – the thermal explosion test in package, and the accelerating decomposition test in package. The test is needed only for chemicals that show a violent effect in tests involving heating under defined confinement (Test Series E). The thermal explosion test in package is the recommended test and is used to determine the potential for thermal explosion in a package.

Temperature control

In addition to the classification tests, the thermal stability of the organic peroxide is needed to determine the Self-Accelerating Decomposition Temperature (SADT). The SADT is used to derive safe handling, storage and transport temperatures (control temperature), and alarm temperature (emergency temperature).

Self-accelerating decomposition temperature *(SADT) means the lowest temperature at which self-accelerating decomposition may occur with a substance as packaged. (Definition from GHS, Rev. 3)*

To protect those exposed to organic peroxides under normal conditions of use and foreseeable emergencies, including emergency responders, organic peroxides should be subjected to temperature control if their SADT is less than or equal to 55 °C (131 ºF), including the following organic peroxides:

a) organic peroxide types B and C with an SADT ≤ 50 °C (122 ºF);

b) organic peroxide type D showing a medium effect when heated under confinement with an SADT ≤ 50 °C (122 ºF), or showing a low or no effect when heated under confinement with an SADT ≤ 45 °C (113 ºF); and

c) organic peroxide types E and F with an SADT ≤ 45 °C (113 ºF).

The *UN TDG Manual of Tests and Criteria*, Part II, Sub-section 28, Test Series H, describes several test methods for determining the SADT, including the United States SADT test, the adiabatic storage test, the isothermal storage test, and the heat accumulation storage test. Since there are several test methods presented, the test selected and conducted should be representative of the package, both in size and material. Each test involves either storage at a fixed external temperature and observation of any reaction initiated or storage under near adiabatic conditions and measurement of the rate of heat generation versus temperature. The recommended tests are described below.

The United States SADT test determines the minimum constant temperature air environment at which auto-accelerative decomposition occurs for a substance in a specific package (up to 220 liters). The adiabatic storage test determines the rate of heat generation produced by a reacting substance as a function of temperature. The heat generation parameters obtained are used with the heat loss data relating to the package to determine the SADT of a substance in its packaging, including IBCs and tanks. The heat accumulation storage test determines the minimum constant air environment temperature at which thermally unstable substances undergo exothermic decomposition at conditions representative of the substance when packaged for transport. The test method can be used for the determination of the SADT of a substance in its packaging, including IBCs and small tanks (up to 2 m^3).

Classification Procedure

Organic peroxides are classified according to the classification principles given in the decision logic and the results of test series A to H. Classification also may be determined using information provided in available scientific literature. As the explanations above indicate, the tests are designed to provide the information necessary to answer the questions in the decision logic for organic peroxides, presented in Figure VIII.13.1.

- Test series A includes laboratory tests and criteria concerning propagation of detonation, as requested in box 1 of the flowchart.
- Test series B includes a test and criteria concerning the propagation of detonation of the chemical as packaged for transport, as requested in box 2 of the flowchart.
- Test series C includes laboratory tests and criteria concerning propagation of deflagration, as requested in boxes 3, 4, and 5 of the flowchart.
- Test series D includes a test and criteria concerning the propagation of a rapid deflagration of the substance as packaged for transport, as requested in box 6 of the flowchart.

- Test series E includes laboratory tests and criteria concerning the determination of the effect of heating under defined confinement, as requested in boxes 7, 8, 9, and 13 of the flowchart.
- Test series F includes laboratory tests and criteria concerning the explosive power of substances that are considered for transport in Intermediate Bulk Containers (IBCs) or tanks, or for exemption (see box 11 of the flowchart), as requested in box 12 of the flowchart.
- Test series G includes tests and criteria concerning the determination of the effect of a thermal explosion of the substance as packaged for transport, as requested in box 10 of the flowchart.
- Test series H includes tests and criteria concerning the determination of the SADT of organic peroxides.

Mixtures that include organic peroxides may be classified as the same type of organic peroxide as that of the most dangerous ingredient. However, since two stable ingredients can form a thermally less stable mixture, information on the SADT of the mixture is needed for classification.

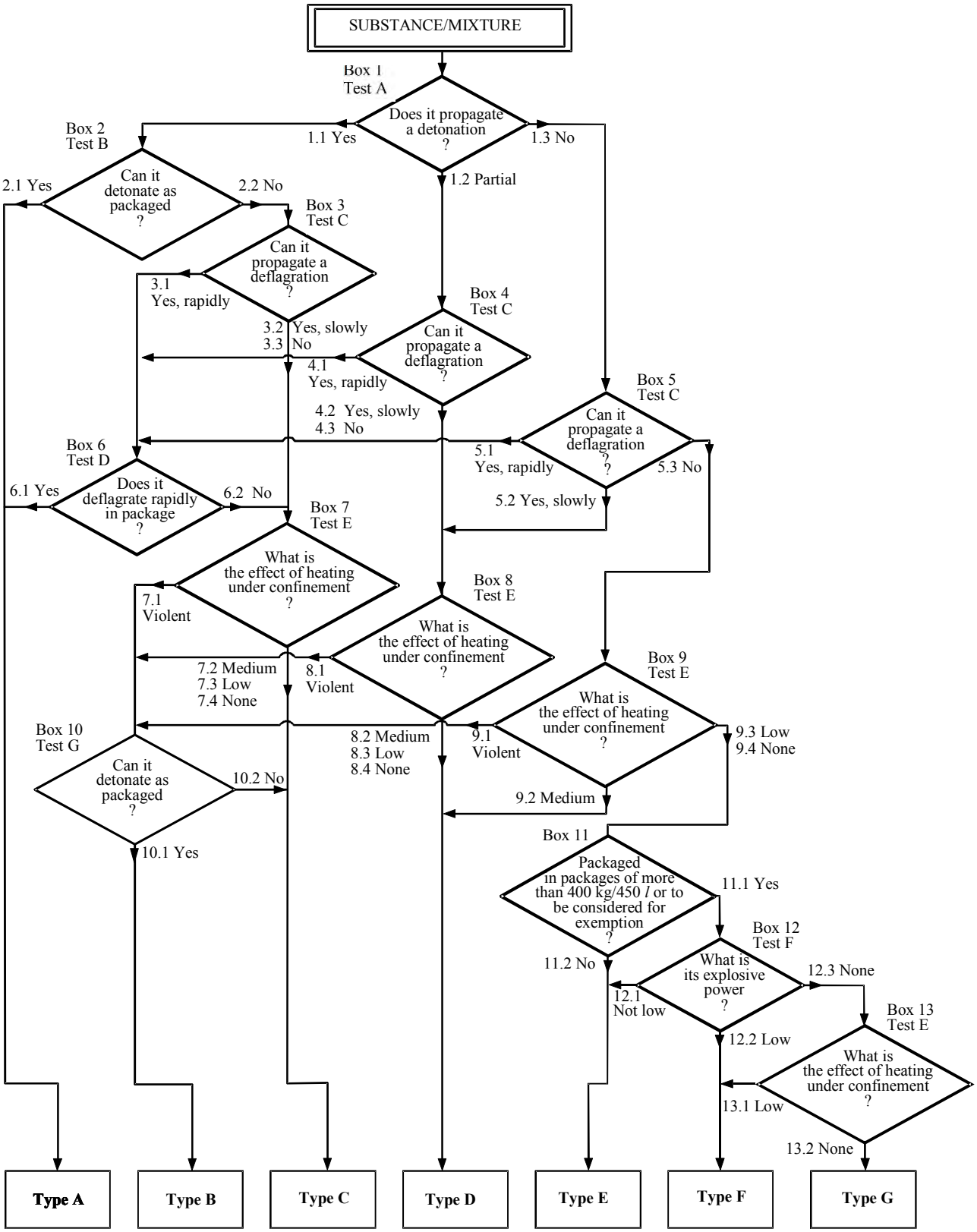
The decision logic for classifying organic peroxides is provided in Figure VIII.13.1. To answer the questions in the decision logic the following information is needed:

- propagation of detonation;
- propagation of deflagration;
- effect on heating in confinement; and
- thermal stability: SADT.

Data from additional tests may also be needed (for example, explosive power, or explosivity as packaged) depending on the circumstances and/or the results of the foregoing tests.

Classification follows the assessment of available data and, if applicable, the results of any testing performed. Once you have collected the data, compare it to the classification criteria for organic peroxide chemicals types A through G, presented in Table VIII.13.1. Follow the logic paths presented in the decision logic (or flowchart) in Figure VIII.13.1 to identify the appropriate classification for organic peroxide chemicals.

Figure VIII.13.1. Decision logic for classifying organic peroxides.



Organic Peroxide Classification Example

The following example illustrates the classification process and application of the decision logic for organic peroxides. The example was developed using information from the ECHA Guidance on the Application of Regulation (EC) No. 1272/2008.

A colorless liquid is suspected of being an organic peroxide and is tested according to the tests presented in the *UN TDG Manual of Tests and Criteria.* Organic peroxides, by definition, must contain the molecular structure -O-O-, and must contain a certain level of available oxygen and hydrogen peroxide content.

The *UN TDG Manual of Tests and Criteria* provides several cautionary notes and preliminary test procedures that must be followed before embarking on the classification test procedure. The tests are designed to provide the information necessary to answer the questions in the decision logic for organic peroxides and to apply the principles for classification. In the following example, the results of the tests are assessed in alphanumeric order; however, the tests are performed in the order given in section 20.4.5 of the *UN TDG Manual of Tests and Criteria.*

Known data

- Colorless liquid.
- Composition: technically pure (97%)
- Molecular formula: not available
- Apparent density: 900 kg/m^3
- Available oxygen content: 7.18%

Test results

Test Name	**Observation**	**Result**
Test series A - Detonation propagation [BAM 50/60 steel tube test]	Sample conditions: peroxide assay 97% Observations: fragmented part of the tube: 18 cm	Test result/criteria: No propagation of detonation (Exit 1.3 of Box 1/Test A 3 Decision Logic flowchart)
Test series B - Detonation as packaged	Not applicable	
Test series C - Deflagration propagation [Time/pressure test]	Test conducted on 5 g of sample three times; the time it took for the pressure to rise from 690 kPa to 2,070 kPA was noted. Shortest recorded time (4000 ms) is used for result.	Test result/criteria: Yes, slowly, because the time for pressure to rise from 690 kPa to 2,070 kPA is greater than or equal to 30 ms.

Test Name	Observation	Result
Test series C - Deflagration propagation [Deflagration test]	Test conducted two times on 265 cm^3 of sample at 25 °C, and the reaction rate noted for each. Shortest recorded rate (0.74 mm/s) is used for result.	Test result/criteria: Yes, slowly, because the deflagration rate is less than or equal to 5.0 mm/s and greater than or equal to 0.35 mm/s. Overall result: Yes, slowly (Exit 5.2 of Box 5/Test C Decision Logic flowchart)
Test series D - Deflagration as packaged	Not applicable	
Test series E - Effect of heating under confinement [Koenen test]	Tested 60 mm of sample. Limiting diameter: 2.0 mm fragmentation type "F," evaluated as "explosion."	Test result/criteria: Violent, because the limiting diameter is greater than or equal to 2.0 mm.
Test series E - Effect of heating under confinement [Dutch Pressure Vessel test]	Tested 10.0 g of sample. Limiting diameter: 6.0 mm (with 10 g)	Test result/criteria: Medium, because rupture of the disc with an orifice of 6.0 mm and a sample mass of 10.0 g. Overall result: Violent (Exit 8.1 of Box 8/Test E Decision Logic flowchart)
Test series F - Explosive Power	Not applicable	
Test series G - Detonation as packaged [Thermal explosion test in the package]	Tested 30-liter packaging. Observations: no fragmentation of the package (N.F.)	Test result/criteria: No fragmentation or a fragmentation into no more than three pieces shows that the Substance 23 does not explode in the package. Exit 10.2 of Box 10/Test G Decision Logic flowchart. Liquid is classified as an organic peroxide Type C.

Test Name	Observation	Result
Test series H - Thermal stability [Heat accumulation storage test; the recommended test for substances transported in packagings, IBCs, or small tanks.]	Tested 380 g of liquid. Half life time of cooling of Dewar vessel with 400 ml DMP: 10.0 hrs (representing substance in package) Observed: Self-accelerating decomposition at 35 °C (95 ºF), no self-accelerating decomposition at 30 °C (86 ºF). The self-accelerating decomposition temperature (SADT) is 35 °C (95 ºF).	Liquid has a SADT of 35 °C (95 ºF). Liquid is classified as an Organic Peroxide Type C because the substance does not detonate, but does exhibit violent effects when heated under confinement, and slowly deflagrates. In addition, the *UN Recommendations on the Transport of Dangerous Good, Model Regulations* and the *UN Manual of Tests and Criteria* recommend the use of temperature control for this substance since the self-accelerating decomposition temperature (SADT) is less than or equal to 50 °C (122 ºF).

Decision/Rationale

The liquid has 7.18% available oxygen. As required by Appendix B.15.2.1 of 29 CFR 1910.1200, the liquid is considered for classification as an organic peroxide since the available oxygen is greater than 1%.

To classify an organic peroxide, the classifier follows the decision logic for organic peroxides, answering the questions and following the flowchart:

Box 1, Test Series A

1. Does the chemical in question propagate a detonation?
   RESULT (Test series A): No, Exit 1.3

Box 5, Test C

2. Can the chemical in question propagate a deflagration?
   RESULT (Tests series C): Yes, slowly, Exit 5.2

Box 8, Test E

3. What is the effect of heating under confinement?
   RESULT (Tests series E): Violent, Exit 8.1

Box 10, Test G

4. Can it detonate as packaged?
   RESULT (Tests series G): No, Exit 10.2

By following the test logic, the classifier determines that Tests B, D, and F are not required for this chemical.

5. Test H is performed to determine whether the chemical in question requires temperature control measures.
   RESULT: Liquid has a SADT of 35 °C (95 ºF). Temperature control is required for this package.

Resulting Classification

The chemical is classified as an organic peroxide, Type C: Any organic peroxide possessing explosive properties when the substance or mixture as packaged cannot detonate or deflagrate rapidly or undergo a thermal explosion.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.15, Organic Peroxides.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.

NFPA 68, Standard on Explosion Protection by Deflagration Venting, 2013.

United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods (UN TDG) – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.14 Corrosive to Metals

Introduction

This *corrosive to metals* hazard class does not cover all chemicals that might corrode metals. Classification as *corrosive to metals* refers only to chemicals that corrode steel and/or aluminum and does not provide information about the corrosivity potential to other metals.

Two types of corrosion phenomena are considered when classifying chemicals as corrosive to metals: – the uniform corrosion attack and the localized corrosion (e.g., pitting corrosion, shallow pit corrosion).

Definition

A *chemical which is corrosive to metals* means a chemical which by chemical action will materially damage, or even destroy, metals.

Classification Criteria

A chemical which is corrosive to metals is classified in a single category when corrosion is observed in steel or aluminum surfaces (See Table VIII.14.1).

Table VIII.14.1. Classification criteria for corrosive to metals.

Category	Criteria
1	Corrosion rate on steel or aluminum surfaces exceeding 6.25 mm per year at a test temperature of 55 °C (131 °F) when tested on both materials.

Note: Where an initial test on either steel or aluminum indicates that the chemical being tested is corrosive, the follow-up test on the other metal is not necessary.

Classification Procedure and Guidance

To classify a chemical as corrosive to metal, data are necessary on its corrosion rate on steel and/or aluminum.

Available Literature

The classifier may use available scientific literature and other evidence to identify the corrosion rate on steel or aluminum for chemicals that are corrosive to metals. The required information may already exist and may be well-documented for many of these chemicals.

In addition, many substances presenting corrosive to metals hazards have already been classified. The information provided in the U.S. Department of Transportation Hazardous Material table can be used to assist in corrosive to metals classifications (See 49 CFR 172.101). Under DOT regulations, materials corrosive to metals are considered Class 8 hazardous materials. The HCS corrosive to metals category 1 corresponds to DOT Hazard Class 8, Packing Group III, corrosive

substances. Refer to the discussion on the interface between the HCS and DOT labeling in Chapter V of this document for more information.

Test Method

As mentioned throughout this guidance, the Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data. However, if you choose to test the substance or mixture, use the methods identified in Appendix B.16 to 29 CFR 1910.1200, described below. For mixtures, test data are required from the mixture as a whole.

The corrosion rate can be measured according to the test method of Part III, sub-section 37.4 of the *UN Recommendations on the Transport of Dangerous Goods (UN TDG), Manual of Tests and Criteria*, Test C.1, "Test for determining the corrosive properties of liquids and solids that may become liquid during transport."[25] This test method is designed to determine the corrosive capabilities of chemicals with metals; it is not applicable for determining corrosivity exposures to skin.

A brief summary of this test is presented below. Refer to the *UN TDG Manual of Tests and Criteria* for a complete description of the method, the apparatus used, and analysis of the test results.

Two types of metals are specified in the test method – carbon steel and aluminum, as follows:

a) For the purposes of testing steel:
Steel types S235JR+CR (1.0037 resp. St 37-2), S275J2G3+CR (1.0144 resp. St 44-3), ISO 3574, Unified Numbering System (UNS) G 10200, or SAE 1020;

b) For the purposes of testing aluminum:
Non-clad types 7075-T6 or AZ5GU-T6.

Test C.1 obtains two types of data:

- Uniform corrosion measured by mass loss in [percent], (*UN TDG Manual of Tests and Criteria* Table 37.4.1.4.1, reproduced in Table VIII.14.2 below) and
- Localized corrosion measured by intrusion depth in [micrometers] (*UN TDG Manual of Tests and Criteria* Table 37.4.1.4.2, reproduced in Table VIII.14.3 below).

[25] Note the method explains that chemicals that cannot be tested must be classified by comparing them with similar entries in the *United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations*.

Classification Procedure

Data from available information may be used to classify the chemical. However, if testing is performed, use the data from Test C.1 described above to determine the corrosion rates.

- For uniform corrosion, the measured loss of mass [in percent] within a given time extrapolated to one year, or
- For localized corrosion, the measured minimum intrusion depth [in µm] (depth of the deepest hole) within a given time.

In the case of uniform corrosion attack, the mass loss of the most corroded sample is used. The C.1 test is considered positive when, for any test specimen, the mass loss on the metal specimen is more than the amount stated in the following table (Table VIII.14.2). In Table VIII.14.2, the first column gives the exposure time in days and the second column gives the percent mass loss.

Table VIII.14.2. Minimum Mass Loss of Specimens after different Exposure Times.
[from *UN Manual of Tests and Criteria Table 37.4.1.4.1*]

Exposure Time	Mass Loss
7 days	13.5 %
14 days	26.5 %
21 days	39.2 %
28 days	51.5 %

The equation below is used to calculate rate of corrosion in mm/year using the minimum mass loss at the appropriate exposure time from the above table and the measured mass loss.

$$\frac{6.25\ mm/y}{\begin{array}{l}\text{min. mass loss (\%)}\\ \text{from table}\\ \text{at exposure time}\end{array}} \times \text{measured \% mass loss change} = \text{amount of corrosion in } mm/y$$

The mass loss of corrosion for the tested sample is determined as a percentage value as follows. Obtain the percent minimum mass loss at the appropriate exposure time from the **Minimum Mass Loss of Specimens after different Exposure Times** table (Table VIII.14.2). Use this value as shown in the above equation with the measured mass loss to calculate the corrosion rate for the tested sample in mm/year. If this value is greater than 6.25 mm/year, then the chemical is corrosive to metal.

When localized corrosion occurs besides or instead of uniform corrosion of the surface, the depth of the deepest hole is used to determine the intrusion. When the deepest intrusion exceeds the values shown in the following table (Table VIII.14.3), the C.1 test result is considered positive.

In Table VIII.14.3, the first column gives the exposure time in days and the second column gives the values for intrusion/depth of hole in micrometers (μm).

Table VIII.14.3. Minimum Intrusion Depths after Exposure Time.
[from *UN Manual of Tests and Criteria Table 37.4.1.4.2*]

Exposure Time	Min. Intrusion Depth
7 days	120 μm
14 days	240 μm
21 days	360 μm
28 days	480 μm

The equation below is used to calculate rate of corrosion in mm/year using the minimum intrusion depth at the appropriate exposure time from the above table and the measured intrusion depth.

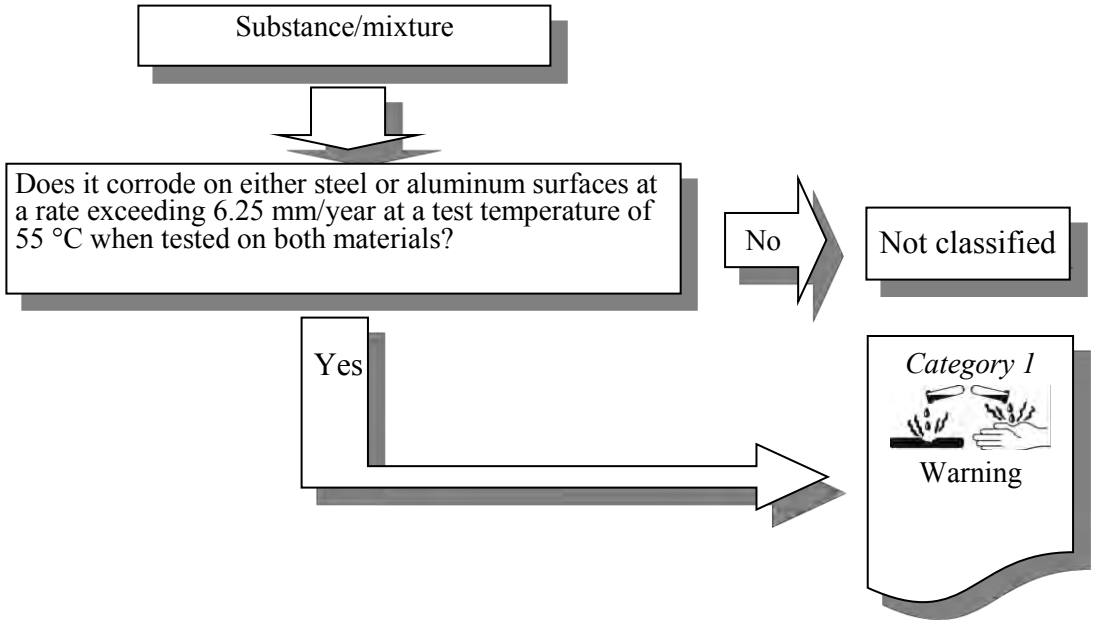
$$\frac{6.25\ mm/y}{\begin{array}{l}\text{min. intrusion}\\ \text{depth[μm]}\\ \text{from table}\\ \text{at exposure time}\end{array}} \times \text{measured intrusion depth} = \text{amount of corrosion in } mm/y$$

Obtain the minimum intrusion depth at the appropriate exposure time from the **Minimum Intrusion Depths after different Exposure Times table** (Table VIII.14.3). Use this value as shown in the above equation with the measured intrusion depth to calculate the corrosion rate for the tested sample in mm/year. If this value is greater than 6.25 mm/year, the chemical is corrosive to metal.

The values in the Tables VIII.14.2 and VIII.14.3 are calculated based upon a 6.25 mm/year corrosion rate.

Once you have collected the data and made the calculation(s) described above, compare it to the criteria for corrosive to metals category 1 presented in Table VIII.14.1. The chemical is classified as corrosive to metals if it corrodes either steel or aluminum surfaces at a rate exceeding 6.25 mm/year at a test temperature of 55 °C (131 °F). Follow the logic path presented in the decision logic (or flowchart) in Figure VIII.14.1 to identify the appropriate classification for corrosive to metals.

Figure VIII.14.1. Decision logic for classifying substances and mixtures corrosive to metals.



Corrosive to Metals Classification Example

The following example is provided to illustrate the corrosive to metals calculation and decision logic.

A liquid is suspected of being classified as corrosive to metals and is tested to determine if at 55 °C the liquid corrodes either steel or aluminum surfaces at a rate exceeding 6.25 mm/year.

Known data

- The substance is a liquid
- UN Test method C.1 test results showed after 21 days that the mass loss of corrosion to aluminum was 41.2 %.

Calculation

1. Calculate the corrosion rate in mm/year by referring to Table VIII.14.2. Use the below formula.

$$\frac{6.25\ mm/y}{\begin{array}{l}\text{min. mass loss (\%)}\\ \text{from table}\\ \text{at exposure time}\end{array}} \times \text{measured \% mass loss change} = \text{amount of corrosion in } mm/y$$

For this example

$$\frac{6.25\ mm/y}{39.2\ \%} = \frac{X\ mm/y}{41.2\ \%}$$

where 41.2 % is the measured mass loss after 21 days expressed as a percentage
where 39.2% is the minimum mass loss from Table 37.4.1.4.1 for 21 days
where 6.25 mm/year is the corrosion rate basis for 39.2% and the corrosion rate threshold for the corrosive to metals criteria

$$\frac{6.25\ mm/y}{39.2\ \%} \times 41.2\ \% = 6.569\ mm/y$$

The corrosion rate on aluminum is calculated to be 6.569 mm/year.

Decision/Rationale

Using the information from the test results and calculation, answer the question posed in the decision logic VIII.14.1, above.

1. Does the substance corrode either steel or aluminum surfaces at a rate exceeding 6.25 mm per year at a test temperature of 55 °C when tested on both materials?
   ANSWER: Yes. The corrosion rate on aluminum is calculated to be 6.569 mm/year.

Resulting Classification

The chemical is classified as a corrosive to metals, category 1, based on the outcome of UN Test Method C.1.

References

29 CFR 1910.1200, Hazard Communication, Appendix B.16, Corrosive to Metals.

49 CFR Parts 100-185, Other Regulations Relating to Transportation, Pipeline and Hazardous Materials Safety Administration, U.S. Department of Transportation.
United Nations Globally Harmonized System of Classification and Labelling of Chemicals, Third Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Model Regulations, Sixteenth Revised Edition, 2009.

United Nations Recommendations on the Transport of Dangerous Goods – Manual of Tests and Criteria, Fourth Revised Edition, 2003.

VIII.15 Combustible Dust

Introduction

Combustible dust hazards involve dusts or other small particles that present a fire or deflagration hazard when suspended at a sufficient concentration in air or some other oxidizing medium. Combustible dusts present an explosion hazard when they are contained in an enclosure (e.g., enclosed building, sand blasting chamber).

A small dust explosion can stir up dust that has settled on surfaces nearby, which in turn ignites, creating a secondary and often larger explosion. This secondary explosion can then force more dust in the air, creating a chain of explosions. This series of cascading explosions is generally more hazardous than the initial one.

Refer to OSHA's Hazard Communication Guidance on Combustible Dust for more information on combustible dusts, including a discussion on understanding and controlling the potential for dust explosions. This guidance is located on the combustible dust safety and health topics page, located at: www.osha.gov/dsg/combustibledust.

The ease of ignition and the severity of a combustible dust explosion are typically influenced by particle size. Other factors that influence the explosiveness of dusts include moisture content, ambient humidity, oxygen available for combustion, the shape of dust particles, and the concentration of dust in the air. Physical properties used to measure combustible dusts include:

- Minimum ignition energy (MIE), which predicts the ease and likelihood of ignition of a dispersed dust cloud.
- Minimum explosible concentration (MEC), which measures the minimum amount of dust dispersed in air required to spread an explosion. (The MEC is analogous to the Lower Flammable Limit (LFL) or Lower Explosive Limit (LEL) for gases and vapors in air.)
- Dust deflagration index (K_{st}), which measures the relative explosion severity compared to other dusts. The larger the value for K_{st}, the more severe the explosion (See Table VIII.15.1, below.) K_{st} provides the best "single number" estimate of the anticipated behavior of a dust deflagration.

Different dusts of the same chemical material can have different ignitability and explosibility characteristics, depending upon physical characteristics such as particle size, shape, and moisture content. These physical characteristics can change during manufacturing, use or while the material is being processed. Any combustible dust with a K_{st} value greater than zero can be subject to dust deflagration. Even weak explosions can cause significant damage, injury and death. For example, sugar has a relatively low K_{st}, but it fueled an explosion in 2008 that killed 14 workers at a refinery.

Not all materials present a combustible dust hazard, even when reduced to fine particles. For example, silicates, sulphates, nitrates, carbonates, phosphates, cement, salt, gypsum, sand, and limestone do not present fire or deflagration hazards. However, many materials do present dust explosion hazards. Many organic materials, plastics, and metals are explosible in dust form.

Definition

The HCS does not contain a definition of the term combustible dust. However, OSHA has provided a definition in the Agency's Combustible Dust National Emphasis Program (NEP). *Combustible dust* is defined in OSHA's Combustible Dust NEP as a solid combustible material, composed of distinct pieces or particles that presents "a fire or deflagration hazard when suspended in air or some other oxidizing medium over a range of concentrations, regardless of particle size or shape."

Classification Procedure and Guidance

The National Fire Protection Association (NFPA), FM-Global, and the American Society for Testing and Materials (ASTM) International suggest various tests, data, and criteria that may be used to determine whether a material presents a combustible dust hazard. The classifier must consider not only the hazards of the chemical in the form in which it is shipped, but also any hazards posed by the product in normal conditions of use and foreseeable emergencies. The classifier also must consider the full range of available information about those hazards.
For combustible dusts, often the best information is actual experience with the product. If the classifier knows that the product has been involved in a deflagration or dust explosion event, the classifier should classify the product as a combustible dust, unless the classifier can show that the conditions surrounding the event are not expected in normal conditions of use or foreseeable emergencies. In the absence of information on a deflagration or dust explosion event, classifiers may use one or more of the following approaches in determining whether such hazards exist, depending on the information that is available.

Laboratory Testing

If published test results are not available, then the use of test data is recommended. Voluntary consensus standards recognize that reliable test data for a material, based on scientifically validated tests, is strong evidence for determining whether a material presents a combustible dust hazard and should be used for classification if available. The Hazard Communication Standard does not require the testing of chemicals – only the collection and analysis of currently available data.

Reliable screening tests, such as that described in ASTM E1226, showing a positive normalized rate of pressure rise or dust deflagration index (Kst), and tests for Class II dusts may be used to determine whether a material presents a combustible dust hazard, and classification should be based on such data if it is available. Many voluntary standards recognize the ASTM E1226 (Standard Test Method for Explosibility of Dust Clouds) and ASTM E1515 (Standard Test Method for Minimum Explosible Concentration of Combustible Dusts) methods as reliable means to establish a combustible dust hazard.

OSHA's combustible dust NEP describes the Agency's own test method for determining the Kst, and the NEP treats a dust as presenting the hazard when the Kst is greater than zero. In addition, the NEP describes OSHA's method for determining whether a dust is a Class II dust for purposes of the electrical standard, which is also an indication that a dust presents a combustible dust hazard.

Published Test Results

Several NFPA standards publish lists of test results for various materials, including:

- NFPA 61 (Standard for the Prevention of Fires and Dust Explosions in Agricultural and Food Processing Facilities),
- NFPA 68 (Standard on Explosion Protection by Deflagration Venting),
- NFPA 484 (Standard for Combustible Metals), and
- NFPA 499 (Recommended Practice for the Classification of Combustible Dusts and of Hazardous (Classified) Locations for Electrical Installations in Chemical Process Areas)

Although the NFPA documents caution care in the use of these results because the extent of explosibility can vary even for different dusts of the same solid material, they nonetheless can "aid in the determination of the potential for a dust hazard to be present in [an] enclosure." (NFPA 61, A.6.2.1 (2013)).

As a part of a poster about combustible dust hazards, OSHA has published a list of combustible materials based on the information provided in the NFPA standards (www.osha.gov/Publications/combustibledustposter.pdf). In addition, there are public databases of dust explosibility characteristics that may be consulted, such as the "Gestis-Dust-EX" database maintained by the Institute for Occupational Safety and Health of the German Social Accident Insurance (www.dguv.de/ifa/GESTIS/GESTIS-STAUB-EX/index-2.jsp).

Dust Particle Size

For many years, NFPA 654 (Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids) defined combustible dust as a "finely divided solid material 420 microns or smaller in diameter (material passing a U.S. No. 40 Standard Sieve) that presents a fire or explosion hazard when dispersed and ignited in air."

OSHA used this definition in earlier combustible dust guidance, such as its 2005 Safety and Health Information Bulletin, and uses a similar criterion in defining "fugitive grain dust" in its Grain Handling Facilities standard (see 29 CFR 1910.272(c)). Some NFPA standards still use a size criterion in defining combustible dust, such as NFPA 61 (2013) and NFPA 704 (2012) (Standard System for the Identification of Hazardous Materials for Emergency Response).

Other NFPA standards, however, have changed their combustible dust definition to remove the size criterion, but discuss size in their explanatory notes. In general, the notes concerning particle size state that dusts of combustible material with a particle size of less than 420 microns

can be presumed to be combustible dusts. However, certain particles, such as fibers, flakes, and agglomerations of smaller particles, may not pass a No. 40 sieve but still have a surface-area-to-volume ratio sufficient to pose a deflagration hazard. In the most recent revisions, the explanatory notes in many of the NFPA standards have moved from a 420 to 500 micron size threshold. See NFPA 484 (2013), NFPA 654 (2013), NFPA 664 (2012) and FM Global Data Sheet 7-76 (2014).[26]

Where there are no test data, or if the testing is inconclusive, classification may be based on particle size, if particle size information is available. If the material will burn and contains a sufficient concentration of particles 420 microns or smaller to create a fire or deflagration hazard, then it should be classified as a combustible dust. A classifier may, if desired, instead use the 500 micron particle size (U.S. Sieve No. 35) threshold contained in more recent NFPA standards. Care must be used with this approach where the particles are fibers or flakes, or where agglomerations of smaller particles may be held together by static charges or by other means that would prevent the dust from passing through respective sieves No. 40 and 35, but would still present a fire or deflagration hazard.

[26] NFPA 664 is NFPA's Standard for the Prevention of Fires and Explosions in Wood Processing and Woodworking Facilities. FM Global Data Sheet 7-76 is a Property Loss Prevention Data Sheet on the Prevention and Mitigation of Combustible Dust Explosion and Fire.

References

29 CFR 1910.1200, Hazard Communication

29 CFR 1910.272, Grain Handling Facilities

Many informational materials are available on OSHA's Combustible Dust Safety and Health Topics Page (www.osha.gov/dsg/combustibledust), including:

Occupational Safety and Health Administration (2013). Classification of Combustible Dusts under the Revised Hazard Communication Standard. Washington, D.C. Retrieved from: www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=INTERPRETATIONS&p_id=28880#5

Occupational Safety and Health Administration (2009). *Hazard Communication Guidance for Combustible Dusts*, Washington DC. Retrieved from: www.osha.gov/Publications/3371combustible-dust.html

Combustible Dust National Emphasis Program Instruction, OSHA Directive CPL 03-00-008 (2008). www.osha.gov/OshDoc/Directive_pdf/CPL_03-00-008.pdf

OSHA Poster (2008), Combustible Dust. www.osha.gov/Publications/combustibledustposter.pdf

Consensus Standards related to combustible dust include:

ASTM E1226 (Standard Test Method for Explosibility of Dust Clouds)

ASTM E1515 (Standard Test Method for Minimum Explosible Concentration of Combustible Dusts)

NFPA 61, Standard for the Prevention of Fires and Dust Explosions in Agricultural and Food Processing Facilities

NFPA 68, Standard on Explosion Protection by Deflagration Venting

NFPA 484, Standard for Combustible Metals

NFPA 499, Recommended Practice for the Classification of Combustible Dusts and of Hazardous (Classified) Locations for Electrical Installations in Chemical Process Areas

NFPA 654, Standard for the Prevention of Fire and Dust Explosions from the Manufacturing, Processing, and Handling of Combustible Particulate Solids

NFPA 664, Standard for the Prevention of Fires and Explosions in Wood Processing and Woodworking Facilities

FM 7-76, "Prevention and Mitigation of Combustible Dust Explosions and Fires," Loss Prevention Data Sheet 7-76. FM Global, April 2014.

IX. HAZARDS NOT OTHERWISE CLASSIFIED

Introduction

Workers need to be informed of every health and physical hazard present in the workplace. Thus, the Hazard Communication Standard (HCS), like the GHS, includes a mechanism for informing workers of hazards other than the physical and health hazards specifically identified in the HCS classification criteria. These hazards are called "hazards not otherwise classified."

Definition

A *hazard not otherwise classified (HNOC)* means an adverse physical or health effect identified through evaluation of scientific evidence during the classification process that does not meet the specified criteria for the physical and health hazard classes addressed in this section. This does not extend coverage to adverse physical and health effects for which there is a hazard class addressed in the HCS, but the effect either falls below the cut-off value/concentration limit of the hazard class or is under a GHS hazard category that has not been adopted by OSHA (e.g., acute toxicity Category 5).

Classification Guidance[27]

During the classification of hazards not otherwise classified, consider the following:

a) An adverse physical or health effect is a material impairment of health or functional capacity, as that phrase is used in section 6(b)(5) of the OSH Act, 29 U.S.C. § 655(b)(5), resulting from workplace exposure to a chemical.

b) A health effect is determined in accordance with the weight-of-evidence criteria presented in Appendix A.0.3 of the HCS.

c) The term physical effect generally refers to a material impairment of health or functional capacity caused by the intrinsic hazard(s) of a particular chemical in normal conditions of use or foreseeable emergencies. Scalds caused by exposure to chemicals at high temperatures, and slips and falls caused by treading on a solid chemical shaped in a rounded form or spilled liquids are not covered physical effects under the HNOC definition. By way of example, water is not classified as an HNOC merely because an employee might be scalded by contact with boiling water or because an employee might contract hypothermia by being immersed in cold water for a long period of time. Similarly, water is not classified as an HNOC by virtue of the fact that an employee might be injured when slipping and falling on a wet surface or when sprayed by water at high pressure. The foregoing examples of adverse physical effects that are outside the scope of HNOC are designed to assist in better understanding the concept of HNOC. They are not intended to be exhaustive or limited to chemicals, such as water, which are not hazardous chemicals.

[27] Hazards not otherwise classified must be identified in Section 2 of the Safety Data Sheet. Although HNOCs are not required to be provided on the label, they may be included on the label as supplemental information.

APPENDIX A.
Glossary of Terms and Definitions

The following glossary presents brief explanations of acronyms and common terms used in this guidance.

Absorbed Dose. The amount of a substance that actually enters into the body, usually expressed as milligrams of substance per kilogram of body weight (mg/kg).

ACGIH. The American Conference of Governmental Industrial Hygienists is an organization of government and academic professionals engaged in occupational safety and health programs. ACGIH establishes recommended occupational exposure limits for chemical substances and physical agents known as Threshold Limit Values; see TLV.

Acid. A compound that undergoes dissociation in water with the formation of hydrogen ions. Acids have pH values below 7 and will neutralize bases or alkaline media. Acids will react with bases to form salts. Acids have a sour taste and with a pH in the 0 to 2 range cause severe skin and eye burns.

Acute Dose. The amount of a substance administered or received over a very short period of time (minutes or hours), usually within 24 hours.

Acute Toxicity. Those adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.

Aerosol. Any non-refillable receptacle containing a gas compressed, liquefied or dissolved under pressure, and fitted with a release device allowing the contents to be ejected as particles in suspension in a gas, or as a foam, paste, powder, liquid or gas.

Alkali. (Also referred to as a base). A compound that has the ability to neutralize an acid and form a salt. Alkali also forms a soluble soap with a fatty acid. Alkalis have pH values between 7 and 14. They are bitter in a water solution. Alkalis with pH values between 12 and 14 are considered to be corrosive (caustic) and will cause severe damage to the skin, eyes and mucous membranes. Common strong alkalis are the substance sodium and mixture potassium hydroxide.

Allergic Reaction. An abnormal immunologic response in a person who has become hypersensitive to a specific substance. Some forms of dermatitis and asthma may be caused by allergic reactions to chemicals.

ANSI. The American National Standards Institute is a privately funded, voluntary membership organization that identifies industrial and public needs for national consensus standards and coordinates development of such standards.

Aspiration. The entry of a liquid or solid chemical directly through the oral or nasal cavity, or indirectly from vomiting, into the trachea and lower respiratory system.

ASTM. The American Society for Testing and Materials develops voluntary consensus standards for materials, products, systems, and services. ASTM is a resource for sampling and testing methods, information on health and safety aspects of materials, safe performance guidelines, and effects of physical agents, biological agents, and chemicals.

Autoignition Temperature. The lowest temperature at which a flammable gas or vapor-air mixture will spontaneously ignite without spark or flame. Vapors and gases will spontaneously ignite at lower temperatures as the concentration of oxygen increases in the air. The autoignition temperature may also be influenced by the presence of catalytic substances. Materials should not be heated to greater than 80% of the autoignition temperature.

Benign. Not recurrent or not tending to progress; not cancerous.

Boiling Point (BP). The temperature at which a liquid changes to a vapor state, at a given pressure; usually expressed in degrees of Fahrenheit or Centigrade at sea level pressure (760 mm Hg or one atmosphere). Flammable materials with low boiling points generally present special fire hazards.

- *Initial boiling point* is the temperature of a liquid at which its vapor pressure is equal to the standard pressure (101.3 kPa[28]; 14.7 psi), i.e., the first gas bubble appears.

CAS Number. A number assigned to a specific chemical by the Chemical Abstracts Service, an organization operated by the American Chemical Society. CAS Numbers are used internationally to identify specific chemicals or mixtures.

Carcinogen. A substance or a mixture of substances which induce cancer or increase its incidence. Substances and mixtures which have induced benign and malignant tumors in well-performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans.

cc. Cubic centimeter is a volume measurement in the metric system that is equal in capacity to one milliliter (ml). One quart is approximately 946 cubic centimeters.

CFR. Code of Federal Regulations. A collection of the regulations that have been promulgated under United States law.

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[28] *Pascal [Pa]* is the SI Unit (International System of Units) for pressure.
1 Pa = 1 N/m^2 = 10^{-5} bar = 0.75 10^{-2} torr
The letter "k" stands for "kilo": 1 kPa = 1,000 Pa.

Chemical. The name assigned to any substance, or mixture of substances.

Chemical Name. The name given to a chemical in the nomenclature system developed by the International Union of Pure and Applied Chemistry (IUPAC) or the Chemical Abstracts Service (CAS) or a name that will clearly identify the chemical for hazard classification purposes.

Chemicals which, in contact with water, emit flammable gases. *S*olid or liquid chemicals which, by interaction with water, are liable to become spontaneously flammable or to give off flammable gases in dangerous quantities.

Chemical which is corrosive to metals. A chemical which by chemical action will materially damage, or even destroy, metals.

Chronic Toxicity. Adverse effects resulting from repeated doses or exposures to a substance over a relatively prolonged period of time.

Decomposition. Breakdown of a material or substance into simpler substances by heat, chemical reaction, electrolysis, decay, or other processes.

Dermal. Relating to the skin.

DNA. Deoxyribonucleic acid; the molecules in the nucleus of the cell that contain genetic information.

Dose. The amount of a substance received at one time. Dose is usually expressed as administered or absorbed dose (e.g., milligrams material/kilogram of body weight).

DOT. U.S. Department of Transportation; the federal agency that regulates transportation of chemicals and other hazardous and non-hazardous substances.

Epidemiology. The branch of science concerned with the study of human disease in specific populations, in order to develop information about the causes of disease and identify preventive measures.

Evaporation Rate. The ratio of the time required to evaporate a measured volume of a liquid to the time required to evaporate the same volume of a reference liquid (butyl acetate, ethyl ether) under ideal test conditions. The higher the ratio, the slower the evaporation rate. The evaporation rate can be useful in evaluating the health and fire hazards of a material.

Explosive Limits. The range of concentrations of a flammable gas or vapor (percent by volume in air) in which an explosion can occur if an ignition source is present. Also see Flammable Limits, LEL, and UEL.

Explosive chemical. A solid or liquid chemical which is in itself capable by chemical reaction of producing gas at such a temperature and pressure and at such a speed as to cause damage to the surroundings. Pyrotechnic chemicals are included even when they do not evolve gases.

- **Pyrotechnic chemical**. A chemical designed to produce an effect by heat, light, sound, gas or smoke or a combination of these as the result of non-detonative self-sustaining exothermic chemical reactions.
- **Explosive item**. An item containing one or more explosive chemicals.
- **Pyrotechnic item**. An item containing one or more pyrotechnic chemicals.
- **Unstable explosive**. An explosive which is thermally unstable and/or too sensitive for normal handling, transport, or use.
- **Intentional explosive**. A chemical or item which is manufactured with a view to produce a practical explosive or pyrotechnic effect.

Eye irritation. The production of changes in the eye following the application of a test substance to the anterior surface of the eye, which are fully reversible within 21 days of application.

Flammable. A material which is easily ignited and burns with extreme rapidity. The two primary measures of this physical hazard are the flashpoint and the autoignition temperature.

For specific information on the definition and test methods of flammable materials, refer to 29 CFR 1910.1200. Also see: Flammable Gas, Flammable Liquid, and Flammable Solid.

Flammable gas. A gas having a flammable range with air at 20°C (68°F) and a standard pressure of 101.3 kPa (14.7 psi).

Flammable liquid. A liquid having a flashpoint of not more than 93°C (199.4°F).

Flammable solid. A solid which is a readily combustible solid, or which may cause or contribute to fire through friction.

- **Readily combustible solids**. Powdered, granular, or pasty chemicals which are dangerous if they can be easily ignited by brief contact with an ignition source, such as a burning match, and if the flame spreads rapidly.

Flashback. Occurs when flame from a torch burns back into the tip, the torch, or the hose. It is often accompanied by a hissing or squealing sound with a smoky or sharp-pointed flame.

Flashpoint. The minimum temperature at which a liquid gives off vapor in sufficient concentration to form an ignitable mixture with air near the surface of the liquid, as determined by a method identified in Appendix B.6.3 of 29 CFR 1910.1200.

Gases under pressure. Gases which are contained in a receptacle at a pressure of 200 kPa (29 psi) (gauge) or more, or which are liquefied or liquefied and refrigerated. They comprise compressed gases, liquefied gases, dissolved gases and refrigerated liquefied gases.

Genetic. Pertaining to or carried by genes; hereditary.

Genotoxic and genotoxicity. These apply to agents or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Positive genotoxicity test results are usually taken as indicators for mutagenic effects.

Hazard. The inherent capacity of a substance to cause an adverse effect.

Hazard category. The division of criteria within each hazard class, e.g., oral acute toxicity and flammable liquids include four hazard categories. These categories compare hazard severity within a hazard class and should not be taken as a comparison of hazard categories more generally.

Hazard class. The nature of the physical or health hazards, e.g., flammable solid, carcinogen, acute toxicity.

Hazard not otherwise classified (HNOC). An adverse physical or health effect identified through evaluation of scientific evidence during the classification process that does not meet the specified criteria for the physical and health hazard classes addressed in this section. This does not extend coverage to adverse physical and health effects for which there is a hazard class addressed in this section, but the effect either falls below the cut-off value/concentration limit of the hazard class or is under a GHS hazard category that has not been adopted by OSHA (e.g., acute toxicity Category 5).

Hazardous chemical. Any chemical which is classified as a physical hazard or a health hazard, a simple asphyxiant, combustible dust, pyrophoric gas, or hazard not otherwise classified.

Health hazard. A chemical which is classified as posing one of the following hazardous effects: acute toxicity (any route of exposure); skin corrosion or irritation; serious eye damage or eye irritation; respiratory or skin sensitization; germ cell mutagenicity; carcinogenicity; reproductive toxicity; specific target organ toxicity (single or repeated exposure); or aspiration hazard. The criteria for determining whether a chemical is classified as a health hazard are detailed in Appendix A to 29 CFR 1910.1200 -- Health Hazard Criteria.

IARC. International Agency for Research on Cancer, a component of the World Health Organization, located in Lyon, France.

Ignitable. A solid, liquid or compressed gas which is capable of being set afire.

Inhalation. Breathing in of a substance in the form of a gas, vapor, fume, mist, or dust.

In Vitro. Outside a living organism (e.g., in a test tube).

Latency Period. The time that elapses between exposure and the first manifestations of disease or illness.

LC_{50} - Lethal Concentration 50, 50% Lethal Concentration. The concentration of a chemical in air or of a chemical in water which causes the death of 50% (one half) of a group of test animals. The LC_{50} can be expressed in several ways:

- as parts of material per million parts of air by volume (ppm) for gases and vapors,
- as micrograms of material per liter of air (mg/l), or
- as milligrams of material per cubic meter of air (mg/m^3) for dusts and mists, as well as for gases and vapors.

LD_{50} - Lethal Dose 50. The amount of a chemical, given all at once, which causes the death of 50% (one half) of a group of test animals. The LD_{50} dose is usually expressed as milligrams or grams of material per kilogram of animal body weight (mg/kg or g/kg).

LEL or LFL - Lower Explosive Limit or Lower Flammable Limit. Lowest concentration of a substance in air (usually expressed in percent by volume) that will produce a flash or fire when an ignition source (heat, electric arc, or flame) is present. At concentrations lower than the LEL, propagation of a flame will not occur in the presence of an ignition source. Also see UEL.

m^3. Cubic meter; a metric measure of volume, approximately 35.3 cubic feet or 1.3 cubic yards.

Malignant Tumor. A tumor that can invade surrounding tissues or metastasize to distant sites resulting in life-threatening consequences.

Melting Point. The temperature at which a solid substance changes to a liquid state.

Metabolism (biotransformation). The conversion of a chemical from one form to another within the body.

Metabolite. A chemical produced during metabolism.

mg/kg. Milligrams of substance per kilogram of body weight, commonly used as an expression of toxicological dose (e.g., 15 mg/kg).

mg/m^3. Milligrams per cubic meter; a unit for measuring concentrations of particulates or gases in the air (a weight per unit volume). For example, 20 mg/m^3.

milligram (mg). The most commonly used unit of measure in medicine and toxicity consisting of one thousandth of a gram ($1x10^{-3}$ g).

Mixture. a combination or a solution composed of two or more substances in which they do not react.

ml. Milliliter; a metric unit of volume. There are 1,000 milliliters in one liter. 1 teaspoon = 5 milliliters.

Mutation. A permanent change in the amount or structure of the genetic material in a cell. The term "*mutation*" applies both to heritable genetic changes that may be manifested at the phenotypic level and to the underlying DNA modifications when known (including, for example, specific base pair changes and chromosomal translocations). The terms "*mutagenic*" and "*mutagen"* are used for agents giving rise to an increased occurrence of mutations in populations of cells and/or organisms.

NFPA. The National Fire Protection Association is an international membership organization which promotes fire protection and prevention and establishes safeguards against loss of life and property by fire.

NIOSH. The National Institute for Occupational Safety and Health is a part of the Centers for Disease Control and Prevention, U.S. Public Health Service, U.S. Department of Health and Human Services.

NTP. The National Toxicology Program is a component of the U.S. Public Health Service. The NTP publishes the Annual Report on Carcinogens.

Odor Threshold. The lowest concentration of a substance in air that can be detected by smell.

Organic peroxide. A liquid or solid organic chemical which contains the bivalent -0-0- structure and as such is considered a derivative of hydrogen peroxide, where one or both of the hydrogen atoms have been replaced by organic radicals. The term organic peroxide includes mixtures containing at least one organic peroxide. Organic peroxides are thermally unstable chemicals, which may undergo exothermic self-accelerating decomposition. In addition, they may have one or more of the following properties:

a) Be liable to explosive decomposition;
b) Burn rapidly;
c) Be sensitive to impact or friction;
d) React dangerously with other substances.

Oxidation. A change in a chemical characterized by the loss of electrons. Oxidation is a reaction in which a substance combines with oxygen.

Oxidizing gas. Any gas which may, generally by providing oxygen, cause or contribute to the combustion of other material more than air does.

- "Gases which cause or contribute to the combustion of other material more than air does" means pure gases or gas mixtures with an oxidizing power greater than 23.5% (as determined by a method specified in ISO 10156 or 10156-2; see Appendix B.4 of 29 CFR 1910.1200).

Oxidizing liquid. A liquid which, while in itself not necessarily combustible, may, generally by yielding oxygen, cause, or contribute to, the combustion of other material.

Oxidizing solid. A solid which, while in itself is not necessarily combustible, may, generally by yielding oxygen, cause, or contribute to, the combustion of other material.

PEL - Permissible Exposure Limit. A legally enforceable occupational exposure limit established by OSHA, usually measured as an eight-hour time-weighted average, but also may be expressed as a ceiling concentration exposure limit.

Physical hazard. A chemical that is classified as posing one of the following hazardous effects: explosive; flammable (gases, aerosols, liquids, or solids); oxidizer (liquid, solid or gas); self-reactive; pyrophoric (liquid or solid); self-heating; organic peroxide; corrosive to metal; gas under pressure; or in contact with water emits flammable gas. The criteria for determining whether a chemical is classified as a physical hazard are detailed in Appendix B to 29 CFR 1910.1200 -- Physical Hazard Criteria.

ppm. Parts per million; the proportion (by volume) of a gas or vapor per million parts of air; also the concentration of a chemical in a liquid or solid form.

Pyrophoric gas. A chemical in a gaseous state that will ignite spontaneously in air at a temperature of 130°F (54.4°C) or below.

Pyrophoric liquid. A liquid which, even in small quantities, is liable to ignite within five minutes after coming into contact with air.

Pyrophoric solid. A solid which, even in small quantities, is liable to ignite within five minutes after coming into contact with air.

Reactivity. A substance's susceptibility to undergo a chemical reaction or change that may result in dangerous side effects, such as an explosion, burning, and corrosive or toxic emissions.

Reproductive toxicity. This hazard includes *adverse effects on sexual function and fertility* in adult males and females, as well as *adverse effects on development of the offspring*. Some reproductive toxic effects cannot be clearly assigned to either impairment of sexual function and fertility or to developmental toxicity. Nonetheless, chemicals with these effects shall be classified as reproductive toxicants.

For classification purposes, the known induction of genetically based inheritable effects in the offspring is addressed in ***Germ cell mutagenicity*** (See Appendix A.5 of 29 CFR 1910.1200).

- ***Adverse effects on sexual function and fertility*.** Any effect of chemicals that interferes with reproductive ability or sexual capacity. This includes, but is not limited to, alterations to the female and male reproductive system, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, parturition, pregnancy outcomes, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems.

- ***Adverse effects on development of the offspring.*** Any effect of chemicals which interferes with normal development of the conceptus either before or after birth, which is induced during pregnancy or results from parental exposure. These effects can be manifested at any point in the life span of the organism. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth and functional deficiency.

Respiratory sensitizer. A chemical that will lead to hypersensitivity of the airways following inhalation of the chemical.

Risk. The probability that an adverse effect will occur.

Self-accelerating decomposition temperature (SADT). The lowest temperature at which self-accelerating decomposition may occur with a substance as packaged.

Self-heating chemical. A solid or liquid chemical, other than a pyrophoric liquid or solid, which, by reaction with air and without energy supply, is liable to self-heat; this chemical differs from a pyrophoric liquid or solid in that it will ignite only when in large amounts (kilograms) and after long periods of time (hours or days).

- Self-heating of a substance or mixture is a process where the gradual reaction of that substance or mixture with oxygen (in air) generates heat. If the rate of heat production exceeds the rate of heat loss, then the temperature of the substance or mixture will rise which, after an induction time, may lead to self-ignition and combustion.

Self-reactive chemicals. Thermally unstable liquid or solid chemicals liable to undergo a strongly exothermic decomposition even without participation of oxygen (air). This definition excludes chemicals classified under 29 CFR 1910.1200 as explosives, organic peroxides, oxidizing liquids or oxidizing solids.

Serious eye damage. The production of tissue damage in the eye, or serious physical decay of vision, following application of a test substance to the anterior surface of the eye, which is not fully reversible within 21 days of application.

Simple asphyxiant. A substance or mixture that displaces oxygen in the ambient atmosphere, and can thus cause oxygen deprivation in those who are exposed, leading to unconsciousness and death.

Skin corrosion. The production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test substance for up to 4 hours. Corrosive reactions are typified by ulcers, bleeding, bloody scabs, and, by the end of observation at 14 days, by discoloration due to blanching of the skin, complete areas of alopecia (baldness), and scars. Histopathology should be considered to evaluate questionable lesions.

Skin irritation. The production of reversible damage to the skin following the application of a test substance for up to 4 hours.

Skin sensitizer. A chemical that will lead to an allergic response following skin contact.

Specific target organ toxicity - single exposure (STOT-SE). Specific, non-lethal target organ toxicity arising from a single exposure to a chemical. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in Appendices A.1 to A.7 and A.10 of 29 CFR 1910.1200 are included.

Specific target organ toxicity - repeated exposure (STOT-RE). Specific target organ toxicity arising from repeated exposure to a substance or mixture. All significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed and not specifically addressed in Appendices A.1 to A.7 and A.10 of 29 CFR 1910.1200 are included.

Solubility. The ability of a substance to be dissolved in a solvent. Solubility is expressed according to the solvent (e.g., solubility in water, solubility in acetone, etc.).

STEL. Short-Term Exposure Limit (ACGIH terminology); see TLV.

Substance. Chemical elements and their compounds in the natural state or obtained by any production process, including any additive necessary to preserve the stability of the product and any impurities deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition.

Synonym. Another name or names by which a material is known. Methyl alcohol, for example, is also known as methanol or wood alcohol.

Target Organ. An organ on which a substance exerts a toxic effect.

Teratogen. A substance that can cause malformations or alterations in the appearance or function of a developing embryo.

TLV - Threshold Limit Value. The occupational exposure limit published by the American Conference of Governmental Industrial Hygienists (ACGIH). ACGIH expresses Threshold Limit Values in four ways:

- **TLV-TWA: The allowable Time-Weighted Average -** A concentration for a normal 8-hour workday or 40-hour workweek.
- **TLV-STEL: Short-Term Exposure Limit -** A maximum concentration for a continuous 15-minute exposure period (maximum of four such periods per day, with at least 60 minutes between exposure periods, and provided the daily TLV-TWA is not exceeded).
- **TLV-C - Ceiling limit -** A concentration that should not be exceeded even instantaneously.
- **TLV-Skin -** The skin designation refers to the potential contribution to the overall exposure by the cutaneous route, including mucous membranes and the eye. Exposure can be either by airborne or direct contact with the substance. This designation indicates that appropriate measures should be taken to prevent skin absorption.

Toxic Substance. Any substance that can cause injury or illness, or which is suspected of being able to cause injury or illness under some conditions.

Toxicity. A relative property of a chemical agent that refers to a harmful effect on some biological mechanism and the conditions under which this effect occurs.

Toxicology. The study of the harmful interactions of chemicals on living organisms and biological systems.

Trade Name. The trademark name or commercial trade name for a material or product.

TWA. Time-Weighted Average; the concentration of a material to which a person is exposed, averaged over the total exposure time – generally the total workday (8 to 12 hours); also see TLV.

UEL or UFL. Upper explosive limit or upper flammable limit; the highest concentration of a vapor or gas (highest percentage of the substance in air) that will produce a flash of fire when an ignition source (e.g., heat, arc, or flame) is present. At higher concentrations, the mixture is too "rich" to burn. Also see LEL.

Unstable. Decomposing readily or another unwanted chemical change during normal handling or storage.

Vapor density. The weight of a vapor or gas compared to the weight of an equal volume of air is an expression of the density of the vapor or gas. Materials lighter than air (e.g., acetylene, methane, hydrogen) have vapor densities less than 1.0. Materials heavier than air (e.g., propane, hydrogen sulfide, and ethane) have vapor densities greater than 1.0. All vapors and gases will mix with air, but the lighter materials will tend to rise and dissipate (unless confined). Heavier vapors and gases are likely to concentrate in low places along or under floors, in sumps, sewers, manholes, trenches, and ditches, where they may create fire or health hazards.

Vapor pressure. Pressure exerted by a saturated vapor above its liquid in a closed container. Three facts are important to remember:

- Vapor pressure of a substance at 100° F will always be higher than the vapor pressure of the substance at 68° F (20° C),
- Vapor pressures reported on SDSs in millimeters of mercury (mmHg) are usually very low pressures; 760 mmHg is equivalent to 14.7 pounds per square inch (psi).
- The lower the boiling point of a substance, the higher its vapor pressure.

Volatility. The tendency or ability of a liquid or solid material to form a gas at ordinary temperatures. Liquids such as alcohol and gasoline, because of their tendency to evaporate rapidly, are called volatile liquids.

APPENDIX B.
Information Sources to Assist with Hazard Classification

This compilation is not intended to be a complete listing of the many literature sources and computerized databases that include information on the physical and health hazards of chemical substances. Researchers should conduct their own literature search and use the most recent editions of the literature, even though a date is provided in this list for some books and documents.

Documents and Books

I. Sources for Specific Chemical Data:

- **A Comprehensive Guide to the Hazardous Properties of Chemical Substances, 3rd Edition**. Pradyot Patnaik. Wiley & Sons, New York. 2007.
- **ATSDR's Toxicological Profiles.** U.S. Public Health Service, Atlanta, Georgia, USA. Available on CD-ROM and online at: www.atsdr.cdc.gov/toxprofiles/index.asp
- **Bretherick's Handbook of Reactive Chemicals Hazards: An Indexed Guide to Published Data, 7th Edition**. 2 volume set. L. Bretherick, P. L. Urben, and M. Pitt. Butterworth-Heinemann, Boston. 2006. Also on CD-ROM.
- **Chemical Reaction Hazards, 2nd Edition**. John Barton and Richard Rogers. Gulf Professional Publishing. 1997.
- **Chemical Safety Manual for Small Business**. 3rd Edition. American Chemical Society, Washington, D.C. 2007. Available online.
- **Chemically Induced Birth Defects, 3rd Edition**. James L. Schardein. Marcel Dekker, Inc., New York. 2000.
- **The Chemistry of Explosives**. Jacqueline Akhavan. Royal Society of Chemistry. 2011.
- **Chemistry of Hazardous Materials**. 6th Edition. Eugene Meyer. Prentice-Hall, Inc., Englewood Cliffs, NJ. 2013.
- **Clinical Toxicology of Commercial Products**. Gleason, Gosselin, and Hodge. The Williams and Wilkins Co., Baltimore. 1984.
- **The Comprehensive Handbook of Hazardous Materials: Regulations, Handling, Monitoring, and Safety**. H. L. A. Sacarello. Lewis Publishers, Inc., Boca Raton, Florida. 1994.
- **Cooper's Toxic Exposures Desk Reference with CD-ROM**. Andre R. Cooper, Sr., editor. CRC Press/Lewis Publishers, Inc., Boca Raton, Florida. 1996.
- **CRC Handbook of Chemistry and Physics, 94th Edition**. David R. Lide, editor. CRC Press, Boca Raton, Florida. 2013. Also on CD-ROM.
- **CRC Handbook of Toxicology**. Michael J. Derlanko and Mannfred A. Hollinger. CRC Press. 1995.
- **Dangerous Properties of Industrial and Consumer Chemicals**. Nicholas P. Cheremisinoff. Marcel Dekker, Inc., New York. 1994.

- **Dictionary of Chemical Names and Synonyms**. Philip H. Howard and Michael Neal. ACGIH Publication 9422. ACGIH, Cincinnati. 1992. Also available on CD-ROM. 1998.
- **Dictionary of Toxicology**. Robert A. Lewis, editor. Lewis Publishers, Inc., Boca Raton, Florida. 1998.
- **Emergency Responder Training Manual for the Hazardous Material Technician**. Wiley –Interscience, 2nd edition. Hoboken, NJ. 2004.
- **Emergency Response to Chemical Spills**. W. Brock Neely. Lewis Publishers, Inc., Boca Raton, Florida. 1992.
- **Emergency Response Guidebook**. A guidebook for first responders during the initial phase of a hazardous materials/dangerous goods incident. DOT, Washington, D.C. 2012. Available online.
- **Emergency Toxicology**. Peter Viccellio, editor. Lippincott-Raven. 1998.
- **Encyclopedia of Toxicology**. 3rd Edition. Philip Wexler, editor-in-chief. Elsevier Academic Press, San Diego. 2014.
- **Environmental and Occupational Medicine, 4th Edition**. William N. Rom, editor. Little, Brown and Co., Boston. 2006.
- **EPA's Integrated Risk Information System (IRIS).** United States Environmental Protection Agency. http://www.epa.gov/iris
- **Ethel Browning's Toxicity and Metabolism of Industrial Solvents**. Volume 3. 2nd edition. Elsevier Science Publishing Co., New York. 1992.
- **Explosives Identification Guide**. 2nd edition. Mike Pickett. Delmar Learning. 2004.
- **Fire Protection Guide to Hazardous Materials**. National Fire Protection Association (NFPA), Quincy, Massachusetts. 2010.
- **Fundamentals of Occupational Safety and Health.** Mark A. Friend and James P. Kohn. Bernan Press, London. 2014.
- **General and Applied Toxicology, 3rd edition**. Volume 1. Bryan Ballantyne, Timothy Marrs and Tore Syverson, editors. McMillan References, Ltd., London. 2009.
- **2013 Guide to Occupational Exposure Values**. ACGIH, Cincinnati. 2013.
- **Guidelines for Safe Storage and Handling of Reactive Materials**. Center for Chemical Process Safety (CCPS). American Institute of Chemical Engineering. 1995.
- **Guidelines for Chemical Reactivity Evaluation and Application to Process Design**. Center for Chemical Process Safety (CCPS), American Institute of Chemical Engineering. 1995.
- **Hamilton and Hardy's Industrial Toxicology, 5th Edition**. Raymond D. Harbison. Mosby, Inc., St. Louis. 1998.
- **Handbook of Chemical Health and Safety**. Robert Alaimo, editor. 2001.
- **Handbook of Hazardous Chemical Properties**. Nicholas P. Cheremisinoff. Butterworth-Heinemann. 1999.
- **Handbook of Hazardous Materials**. Morton Corn. Academic Press, San Diego. 1993.
- **Handbook of Highly Toxic Materials Handling and Management**. Stanley S. Grossel and Daniel A. Crowl, editors. Marcel Dekker, Inc., New York. 1994.

- **Handbook of Industrial Toxicology, 3rd Edition**. E.R. Plunkett, editor. Chemical Publishing Co., Inc., New York. 1987.
- **Handbook of Industrial Toxicology and Hazardous Materials**. Nicholas P. Cheremisinoff. CRC Press. 1999.
- **Handbook of Organic Solvent Properties**. Ian Smallwood. Butterworth-Heinemann. 1996.
- **Handbook of Physical Properties of Organic Chemicals**. Phillip H. Howard and William M. Meylan, editors. Lewis Publishers, Inc. 1996.
- **Handbook of Toxic and Hazardous Chemicals and Carcinogens, 6th Edition**. Marshall Sittig. Noyes Data Corp., Park Ridge, New Jersey. 2011.
- **Handbook of Toxicology, 3rd Edition**. Michael J. Derelanko and Mannfred A. Hollinger. CRC Press, Taylor and Francis Group, Florida. 2014.
- **Hawley's Condensed Chemical Dictionary, 15th Edition**. Richard J. Lewis, editor. Van Nostrand Reinhold, New York. 2007.
- **Hazardous and Toxic Materials: Safe Handling and Disposal, 2nd edition**. Howard Fawcett. 1988.
- **Hazardous Chemicals: Safety Management and Global Regulations.** T. S. S. Dikshith. CRC Press, Taylor and Francis Group, Florida. 2013.
- **Hazardous Chemicals Desk Reference, 6th Edition**. Richard J. Lewis, Jr., John Wiley & Sons/Van Nostrand Reinhold, New York. 2008.
- **Hazardous Chemicals Handbook, 2nd Edition**. P. Carson and C. J. Mumford. Butterworth-Heinemann. 2002.
- **Hazardous Industrial Chemicals - Material Safety Data Sheets - Preparation**. ANSI Standard Z400.1. American National Standards Institute, Washington, D.C. 2004.
- **Hazardous Materials Behavior and Emergency Response Operations**. Denis Zeimet and David Ballard. ASSE. 2000.
- **Hazardous Materials Chemistry, 2nd Edition**. A. Bevelacqua. 2005.
- **Hazardous Materials Chemistry for Emergency Responders: 3rd Edition**. Robert Burke. CRC Press. 2013.
- **Hazardous Materials Handbook**. Richard P. Pohanish and Stanley A. Greene. John Wiley & Sons. 1996.
- **Hazardous Materials Response Handbook, 3rd Edition**. National Fire Protection Association. Quincy, Massachusetts. 1997.
- **Hazardous Materials Toxicology: Clinical Principles of Environmental Health**. John B. Sullivan and Gary R. Krieger. William and Wilkins, Baltimore. 1992.
- **Hazardous Substances Resource Guide**. Richard P. Pohanish and Stanley A. Green, editors. Gale Research, Inc., Detroit. 1993.
- **Health Protection from Chemicals in the Workplace**. P. Lewis. Prentice Hall, Englewood Cliffs, New Jersey. 1992.
- **IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans**. International Agency for Research on Cancer, WHO, Lyon, France and available online.

- **Improving Reactive Hazard Management**. U.S. Chemical Safety and Hazard Investigation Board, Report No. 2001-01-H. 2002.
- **Industrial Organic Chemicals, 3rd edition**. Harold A. Wittcoff, Bryan Reuben, and Jeffery Plotkin. 2012.
- **Kirk Othmer Encyclopedia of Chemical Technology, Fifth edition**. 15 volumes. Wiley-Interscience. 2004.
- **The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 15th Edition**. Maryadele J. O'Neil, Ann Smith, Patricia, E. Heckelman, John R. Obenchain, Jo Ann R. Gallipeau , and Mary Ann D'Arecca, editors. Merck Co. 2013.
- **MERCK Index**. Full text of the printed edition. Gives concise information on over 10,000 chemicals and available online at: https://www.rsc.org/merck-index.
- **NIOSH Pocket Guide to Chemical Hazards**. National Institute for Occupational Safety and Health, U.S. Public Health Service. NIOSH Pub. 2005-151. U.S. Government Printing Office, Washington, D.C. 2005. Available online.
- **NTP's Annual Report on Carcinogens**. National Toxicology Program. Research Triangle Park, NC. Available online.
- **Occupational Health and Safety, 3rd Edition**. Marci Balge and Gary Krieger, editors. National Safety Council, Chicago, Illinois. 2000.
- **Occupational Health Guidelines for Chemical Hazards**. NIOSH/OSHA. NIOSH Pub. No. 81-123. 1981. Available online.
- **Occupational Health Risk Assessment and Management**. Blackwell Science, Ltd., Oxford, England. 1999.
- **Occupational Medicine, 3rd Edition**. Carl Zenz, O. Bruce Dickerson and Edward P. Horvath, Jr., Mosby - Year Book, Inc., St. Louis. 1994.
- **Occupational Toxicology, 2nd edition**. Neill H. Stacey and Chris Winder, editors. Taylor & Francis, Inc., Bristol, Pennsylvania. 2002.
- **OSHA Technical Manual, 5th edition**. OSHA. 1999.
- **Patty's Hygiene and Toxicology, 6th Edition**, 13 Volume Set. Eula Bingham, Barbara Cohrssen, and Charles H. Powell. John Wiley & Sons, New York. 2010.
- **Patty's Industrial Hygiene and Toxicology, 5th edition**. Robert Harris. John Wiley & Sons, New York. 2000.
- **Patty's Toxicology Mini Set Volume Two and Three - Metals**. Eula Bingham and Barbara Cohrssen, editors. John Wiley & Sons, New York. 2001.
- **Patty's Toxicology, 6th edition (6 volume set)**. Eula Bingham, Barbara Cohrssen, and Charles H. Powell. 2012.
- **Proctor and Hughes' Chemical Hazards of the Workplace, 5th Edition**. Gloria J. Hathaway and Nick H. Proctor. Van Nostrand Reinhold, New York. 2004.
- **Product Safety Management and Engineering, 2nd Edition**. Willie Hammer. ASSE. 1993.
- **Rapid Guide to Chemical Incompatibilities**. Richard Pohanish and Stanley Greene. 1997.

- **Rapid Guide to Hazardous Chemicals in the Workplace, 4th Edition**. Richard J. Lewis, Sr., Van Nostrand Reinhold. 2000.
- **Recognition of Health Hazards in Industry, 2nd Edition**. William A. Burgess. John Wiley and Sons, New York. 1995.
- **Reproductively Active Chemicals; A Reference Guide**. Richard J. Lewis. Van Nostrand Reinhold, New York. 1991.
- **Sax's Dangerous Properties of Industrial Materials, 12th edition**. 5 volume set. Richard J. Lewis. Wiley-Interscience. 2004.
- **Sittig's Handbook of Toxic and Hazardous Chemicals and Carcinogens, 4th edition**. Two Volume Set. Richard P. Pohanish, editor. Noyes Publications. 2012.
- **Storage and Handling of Petroleum Liquids, 3rd edition**. Hughes, John R., Center for Chemical Process Safety (CCPS), American Institute of Chemical Engineering. John Wiley & Sons. 1988.
- **Threshold Limit Values and Biological Exposure Indices**. ACGIH, Cincinnati. 2013. Available online.
- **Toxicology Desk Reference. The Toxic Exposure and Medical Monitoring Index, 5th edition**. Robert P. Ryan and Claude E. Terry, editors. Taylor & Francis. 1999.
- **Toxicology of Industrial Compounds**. Hemut Thomas, Robert Hess and Felix Waechter. Taylor & Francis, London. 1995.
- **Wiley Guide to Chemical Incompatibilities, 3rd Edition**. Richard P. Pohanish and Stanley A. Greene. John Wiley & Sons. 2009.

II. Useful References on Principles and Procedures:

- **A Textbook of Modern Toxicology, 4th Edition**. Ernest Hodgson and Patricia E. Levi. McGraw-Hill Professional. 2010.
- **Basic Concepts of Industrial Hygiene**. Ronald M. Scott. 1997.
- **Basic Environmental Toxicology**. Lorris G. Cockerham and Barbara S. Shane. CRC Press, Boca Raton, Florida. 1993.
- **Basic Toxicology: Fundamentals, Target Organs, and Risk Assessment, 5th Edition**. Frank C. Lu. Taylor and Francis, Washington, D.C. 2009.
- **Casarett and Doull's Toxicology: The Basic Science of Poisons, 8th Edition**. Louis J. Casarett, Curtis D. Klaasen, and John Doull, editors. McGraw-Hill Professional, New York. 2013.
- **Chemical Hazard Communication Guidebook, 2nd Edition**. Andrew B. Waldo and Richard deC. Hinds. McGraw Hill Book Company, Highstown, New Jersey. 1995.
- **Comprehensive Review in Toxicology, 3rd Edition**. Peter D. Bryson. Aspen Publishers, Rockville, Maryland. 1996.
- **Comprehensive Toxicology**. 2nd Edition. I. Glenn Sipes, A. Jay Gaddolfi, and Charlene A. McQueen, Elsevier Science. 2010.
- **Dictionary of Toxicology, 2nd edition**. Ernest Hodgson, Richard Mailman, and Robert Dow. McMillan References, Ltd. London. 1998.

- **Essentials of Environmental Toxicology**. W. William Hughes. Taylor and Francis, Washington, D.C. 1996.
- **Fundamentals of Industrial Hygiene**. 6th Edition. Barbara A. Plog and Patricia J. Quinlan, National Safety Council. 2012.
- **Industrial Toxicology: Safety and Health Applications in the Workplace**. Phillip L. Williams and James L. Burson. Van Nostrand Reinhold, New York. 1989.
- **Information Resources in Toxicology, 4th edition**. P. J. Hakkinen, Gerald Kennedy, Frederick Stoss, and Philip Wexler, editors. Academic Press. 2009.
- **International Directory of Testing Laboratories**, ASTM, West Conshohocken, Pennsylvania. Available online.
- **Loomis's Essentials of Toxicology, 4th Edition**. Ted A. Loomis. Academic Press, San Diego, California. 1996.
- **The Occupational Environment: Its Evaluation and Control**. Second Edition. Salvatore R. Dinardi, editor. AIHA. 2003.
- **Principles and Methods of Toxicology, 5th Edition**. A. Wallace Hayes, editor. Raven Press, New York. 2007.
- **Principles of Toxicology: Environmental and Industrial Applications, 2nd Edition**. Phillip L. Williams, Robert C. James and Stephen M. Roberts, editors. 2000.
- **Toxicology: A Primer on Toxicology Principles and Applications**. Michael A. Kamrin. Lewis Publishers, Inc., Boca Raton, Florida. 1988.

Comprehensive Bibliographic and Factual Databases:

- **Chemical Hazard Response Information System (CHRIS).** This database, developed by the U.S. Coast Guard, contains physical and chemical properties and health hazards for over 1,000 chemical substances. U.S. Coast Guard. Department of Transportation. Available online. The link is to the Manual.
- **Chemical Information Systems (CIS)**. CIS is a collection of 33 databases from various sources like EPA, NIOSH, and NLM that contains references to literature including: toxicological and/or carcinogenic research data; information on handling hazardous materials; chemical/physical property information; regulations; safety and health effects information; and pharmaceutical data. It is operated by the **National Information Services Corporation (NISC USA)**, Baltimore, Maryland.
- **CHEMTREC Hazard Information Transmission**. Chemical profiles represent a synthesis of information from reference materials and MSDSs submitted by industry. The database is for use of groups which respond to chemical emergencies.
- **eChem Portal**. Developed by the Organisation for Economic Co-operation and Development (OECD), this is a global portal to information on chemical substances, designed to improve the availability of hazard data on chemicals.
- **Immediately Dangerous to Life or Health (IDLHs)**. The "immediately dangerous to life or health" air concentration values (IDLHs) are used by NIOSH as respirator selection criteria. They were first developed in the mid-1970s, and reviewed and revised in 1994.

- **International Chemical Safety Cards (ICSCs)**. ICSC cards summarize essential health and safety information on chemicals for their use at the "shop floor" level by employees and employers in factories, agriculture, construction and other workplaces. The ICSC project is an undertaking of the International Programme on Chemical Safety (IPCS). The U.S. version of the ICSCs has been modified by the National Institute for Occupational Safety and Health (NIOSH) to include the following: Occupational Safety and Health Administration Permissible Exposure Limits (OSHA PELs); National Institute for Occupational Safety and Health Recommended Exposure Limits (NIOSH RELs); IDLHs, and links to the NIOSH Pocket Guide to Chemical Hazards.
- **NIOSH Pocket Guide to Chemical Hazards (NPG)**. The NPG is intended as a source of general industrial hygiene information on several hundred chemicals/classes for employees, employers, and occupational health professionals.
- **Occupational Safety and Health Guidelines for Chemical Hazards**. Summarizes information on permissible exposure limits, chemical and physical properties, and health hazards. It provides recommendations for medical surveillance, respiratory protection, and personal protection and sanitation practices for specific chemicals subject to federal occupational safety and health regulations.
- **Registry of Toxic Effects of Chemical Substances (RTECS®)**. This is an extensive chemical database originally developed and published by NIOSH that serves as an important reference for the identification of health hazards literature. It is now maintained and marketed by MDL Information Systems.
- **Toxic Substances Control Act Test Submissions (TSCATS)**. An index of unpublished health and safety studies and test data for over 2,700 chemicals submitted to EPA under the *Toxic Substances Control Act* (TSCA).
- **NLM Databases**: This service contains a links to a number of databases, including those listed below.
  - **CCRIS**. Chemical Carcinogenesis Research Information System – carcinogenicity, mutagenicity, tumor promotion, and tumor inhibition data provided by the National Cancer Institute (NCI). Contains coverage of literature on cancer research and testing from 1963 to the present.
  - **ChemIDplus**. This is an online data file that contains names, synonyms, CAS registry numbers, and a locator for other databases that contain information for thousands of chemicals.
  - **CHEMID/SUPERLIST**. This file serves as a locator for NLM databases containing information for over 180,000 compounds. It also lists chemicals regulated by other government agencies.
  - **DART**. A bibliographic database covering teratology and other aspects of developmental and reproductive toxicology. Serves as a continuation of ETIC, below.
  - **DERMAL**. Contains toxic effects, absorption, distribution, metabolism, and excretion data related to dermal absorption of 650+ chemicals.
  - **DIRLINE**. A database containing information about information resource centers, primarily health and biomedical organizations.

- **EMIC**. A bibliographic database on chemical agents that have been tested for mutagenic activity.
- **ETIC**. A bibliographic database on chemical agents that have been tested for mutagenic activity.
- **GENETOX**. Peer-reviewed mutagenicity test data from the Environmental Protection Agency (EPA).
- **Haz-Map**. Haz-Map is an occupational health database designed for health and safety professionals and for consumers seeking information about the health effects of exposure to chemicals and biologicals at work.
- **Household Products**. This database links over 5,000 consumer brands to health effects from Material Safety Data Sheets (MSDS) provided by the manufacturers and allows scientists and consumers to research products based on chemical ingredients.
- **HSDB. Hazardous Substances Data Bank**. This is a peer-reviewed database which contains chemical and physical properties for over 4,200 chemicals.
- **IRIS**. Integrated Risk Information System - data from the Environmental Protection Agency (EPA) in support of human health risk assessment, focusing on hazard identification and dose-response assessment.
- **ITER**. Integrated search of any or all of the following databases: Hazardous Substances Data Bank (HSDB), Integrated Risk Information System (IRIS), International Toxicity Estimates for Risk (ITER), Chemical Carcinogenesis Research Information (CCRIS), and Genetic Toxicology (GENE-TOX).
- **PubMed/MEDLINE**. Indexes articles from 3,200+ biomedical journals published in the U.S. and abroad. It is a major source of biomedical literature with coverage from 1966 to the present. Produced by the NLM.
- **TERIS**. Produced by the University of Washington and deals with the risks of prenatal exposure to hazardous substances.
- **Toxicology Tutorials**. Three college-level tutorials covering principles of toxicology, toxicokinetics, and cellular toxicology.
- **TOXLINE**. Contains comprehensive bibliographic coverage of toxicology information in published literature.
- **TRI**. Toxics Release Inventory, an annual report of the EPA that estimates releases of toxic chemicals to the environment.

Internet Addresses for Information or Publications Related to Chemical Hazards and Hazard Communication:

- American Conference of Governmental Industrial Hygienists (ACGIH)
- American Industrial Hygiene Association (AIHA)
- American Society of Safety Engineers (ASSE)
- Canadian Centre for Occupational Safety and Health
- Health Canada
- Center for Chemical Process Safety
- Department of Transportation, Pipeline and Hazardous Materials Administration

- Environmental Protection Agency (EPA)
- European Chemicals Agency (ECHA)
- MSDSOnline.com
- MSDS.com
- National Institute for Occupational Safety and Health (NIOSH)
- National Library of Medicine (NLM) Data Bases
- Occupational Safety and Health Administration (OSHA)
- United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS)
- United Nations Transport of Dangerous Goods (TDG)

APPENDIX C.
List of Substances Deemed Toxic or Hazardous by an Authoritative Process

The following sources were consulted to develop this list:

- 29 CFR 1910, Subpart Z - Toxic and Hazardous Substances
- American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs)
- International Agency for Research on Cancer (IARC) "Monographs on the Evaluation of Carcinogenic Risks to Humans"
- National Toxicology Program (NTP) "Report on Carcinogens"

Note: These sources may be periodically updated, so the most current list should be consulted.

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2,4,5-T
2,4-D (Dichlorophenoxyacetic acid)
Acetaldehyde
Acetic acid
Acetic anhydride
Acetone
Acetonitrile
Acetylene tetrabromide
Acrolein
Acrylamide
Acrylic acid
Aldrin
Allyl alcohol
Allyl chloride
Allyl glycidyl ether
Allyl propyl disulfide
alpha-Alumina
Aluminum metal
Aluminum, soluble salts
Aluminum, welding fumes
2-Aminopyridine
Amitrole
Ammonia
Ammonium sulfamate

sec-Amyl acetate
n-Amyl acetate
Aniline and homologs
Anisidine (o-, p- isomers)
Antimony
Antimony compounds
ANTU (alpha-Naphthyl thiourea)
Arsenic
Arsine
Atrazine
Azinphos-methyl
Barium
Barium sulfate
Barium, soluble compounds
Benomyl
Benzene
Benzoyl peroxide
Benzyl chloride
Beryllium
Beryllium compounds, n.o.s.
Bismuth telluride (Sedoped)
Bismuth telluride, undoped
Borates, tetra, sodium salts, anhydrous
Borates, tetra, sodium salts, decahydrate
Borates, tetra, sodium salts, pentahydrate
Boron oxide
Boron tribromide
Boron trifluoride
Bromine
Bromine pentafluoride
Bromoform
Butadiene (1,3-Butadiene)
2-Butanone (Methyl ethyl ketone)
2-Butoxyethanol
n-Butyl acetate
tert-Butyl acetate
sec-Butyl acetate
Butyl acrylate
tert-Butyl alcohol
sec-Butyl alcohol
n-Butyl alcohol
tert-Butyl chromate

n-Butyl glycidyl ether (BGE)
n-Butyl lactate
Butyl mercaptan
Butylamine (n-)
p-tert-Butyltoluene
Cadmium
Cadmium fume
Calcium carbonate
Calcium cyanamide
Calcium hydroxide
Calcium oxide
Calcium silicate
Calcium sulfate
Camphor, synthetic
Caprolactam
Captafol (Difolatan)
Captan
Carbaryl (Sevin)
Carbon black
Carbon dioxide
Carbon disulfide
Carbon monoxide
Carbon tetrachloride
Catechol (pyrocatechol)
Cellulose
Chlordane
Chlorinated camphene
Chlorinated diphenyl oxide
Chlorine
Chlorine dioxide
Chlorine trifluoride
1-Chloro-1-nitropropane
2-Chloro-6-(trichloromethyl)pyridine
Chloroacetaldehyde
alpha-Chloroacetophenone (Phenacyl chloride)
Chlorobenzene
o-Chlorobenzylidene malonitrile
Chlorobromomethane
Chlorodifluoromethane
Chlorodiphenyl (42% chlorine) (PCB)
Chlorodiphenyl (54% chlorine) (PCB)
Chloroform (Trichloromethane)

Chloropicrin
Chloropicrin/methyl chloride
beta-Chloroprene
Chromates
Chromic acid
Chromium
Chromium (III) compounds, soluble
Chromium insoluble salts
Clopidol
Coal dust (greater than or equal to 5% SiO_2), respirable quartz fraction
Coal tar pitch volatiles
Cobalt carbonyl
Cobalt hydrocarbonyl
Cobalt metal, dust and fume
Copper
Copper dusts and mists
Cotton dust (raw)
Crag herbicide (Sesone)
Cresol, all isomers
Crotonaldehyde
Crotonaldehyde, (E)-
Cumene
Cyanides (as CN)
Cyanogen
Cyclohexane
Cyclohexanol
Cyclohexanone
Cyclohexene
Cyclopentadiene
Cyclopentane
Cyhexatin
Decaborane
Demeton (Systox)
Di-sec octyl phthalate (Di-2-ethylhexyl-phthalate)
Diacetone alcohol (4-Hydroxy-4-methyl-2-pentanone)
Diazomethane
Diborane
Dibutyl phosphate
Dibutyl phthalate
Dichloro diphenyl trichloroethane (DDT)
1,1-Dichloro-1-nitroethane
1,3-Dichloro-5,5-dimethyl hydantoin

Dichloroacetylene
o-Dichlorobenzene
p-Dichlorobenzene
Dichlorodifluoromethane
1,1-Dichloroethane
Dichloroethyl ether
1,2-Dichloroethylene
Dichlorofluoromethane
1,3-Dichloropropene
1,2-Dichlorotetrafluoroethane
Dichlorvos (DDVP)
Dicyclopentadienyl iron
Dieldrin
Diethanolamine
Diethylamine
2-Diethylaminoethanol
Difluorodibromomethane
Diglycidyl ether (DGE)
Diisobutylketone
Diisopropylamine
Dimethyl 1,2-dibromo-2,2-dichloroethyl phosphate
Dimethyl acetamide
Dimethyl aniline (N,N-dimethylaniline)
1,1-Dimethyl hydrazine
Dimethyl phthalate
Dimethyl sulfate
Dimethylamine
Dimethylformamide
Dinitro-o-cresol
Dinitrobenzene (alpha-)
Dinitrobenzene (meta-)
Dinitrobenzene (para-)
Dinitrobenzene, all isomers
Dinitrotoluene
Dioxane (Diethylene dioxide)
Diphenyl (Biphenyl)
Diphenylamine
Dipropylene glycol, methyl ether
Disulfiram
Emery
Endosulfan
Endrin

Epichlorohydrin
EPN
Ethanolamine
2-Ethoxyethanol
2-Ethoxyethyl acetate (Cellosolve acetate)
Ethyl acrylate
Ethyl alcohol (Ethanol)
Ethyl amyl ketone (5-Methyl-3-heptanone)
Ethyl benzene
Ethyl bromide
Ethyl butyl ketone (3-Heptanone)
Ethyl chloride
Ethyl ether
Ethyl formate
Ethyl mercaptan
Ethyl silicate
Ethylacetate
Ethylamine
Ethylene chlorohydrin
Ethylene diamine
Ethylene dibromide (1,2-Dibromoethane)
Ethylene dichloride
Ethylene glycol
Ethylene glycol, dinitrate
N-Ethylmorpholine
Fenaminphos
Ferbam
Ferrovanadium dust
Fluorides
Fluorine
Fluorotrichloromethane (Trichlorofluoromethane)
Formaldehyde
Formamide
Formic acid
Furfural
Furfuryl alcohol
Gasoline
Glycerin mist
Glycidol
Grain dust (oat, wheat, barley)
Graphite, natural
Graphite, synthetic

Gypsum
Hafnium
Heptachlor
Heptane (n-Heptane)
Hexachlorobutadiene
Hexachloroethane
Hexachloronaphthalene
Hexafluoroacetone
n-Hexane
2-Hexanone (Methyl n-butyl ketone)
Hexone (Methyl isobutyl ketone)
sec-Hexyl acetate
Hydrazine
Hydrogen bromide
Hydrogen chloride
Hydrogen cyanide
Hydrogen fluoride
Hydrogen peroxide
Hydrogen selenide
Hydrogen sulfide
Hydroquinone
Indium
Indium compounds, n.o.s.
Iodine
Iodoform
Iron oxide fume
Isoamyl acetate
Isoamyl alcohol (primary and secondary)
Isobutyl acetate
Isobutyl alcohol
Isooctyl alcohol
Isophorone
Isopropyl acetate
Isopropyl alcohol
Isopropyl ether
Isopropyl glycidyl ether (IGE)
Isopropylamine
N-Isopropylaniline
Kaolin
Ketene
L.P.G. (liquified petroleum gas)

Lead
Lindane
Lithium hydride
Magnesite
Magnesium oxide fume
Malathion
Maleic anhydride
Manganese compounds (as Mn)
Manganese fume (as Mn)
Mercury
Mercury (organo) alkyl compounds
Mesityl oxide

Methanol
Methoxychlor
Methyl acetate
Methyl acetylene (Propyne)
Methyl acetylene - Propadiene mixture (MAPP)
Methyl acrylate
Methyl alcohol
Methyl bromide (Bromomethane)
Methyl cellosolve (2-methoxyethanol)
Methyl cellosolve acetate (2-Methoxyethyl acetate)
Methyl chloride
Methyl chloroform (1,1,1-Trichloroethane)
Methyl formate
Methyl hydrazine (Monomethyl hydrazine)
Methyl iodide
Methyl isoamyl ketone

Methyl isobutyl ketone
Methyl isocyanate
Methyl methacrylate
Methyl n-amyl ketone
Methyl parathion
alpha-Methyl styrene
Methylal (Dimethoxymethane)
Methylamine
Methylcyclohexane
Methylcyclohexanol
o-Methylcyclohexanone
Methylene bisphenol isocyanate (MDI)
Methylene chloride

4,4'-Methylenebis (2-chloroaniline) (MBOCA)
Methylisobutyl carbinol
Methylmercaptan
Mica
Molybdenum
Molybdenum insoluble compounds
Molybdenum soluble compounds
Monomethylaniline
Morpholine
Naphtha (coal tar)
Naphthalene
Nickel
Nickel carbonyl
Nickel insoluble compounds
Nickel soluble compounds
Nicotine
Nitric acid
Nitric oxide
p-Nitroaniline
Nitrobenzene
p-Nitrochlorobenzene
Nitroethane
Nitrogen dioxide
Nitrogen trifluoride
Nitroglycerin
Nitromethane
2-Nitropropane
1-Nitropropane
o-Nitrotoluene
m-Nitrotoluene
p-Nitrotoluene
Octachloronaphthalene
Octane
Oil mist, mineral

Organo (alkyl) mercury
Osmium tetroxide
Oxalic acid
Oxygen difluoride
Ozone
Paraquat
Paraquat methosulfate

Parathion
Particulates not otherwise regulated

Phenol
Pentaborane
Pentachloronaphthalene
Pentachlorophenol
Pentaerythritol
Pentane
2-Pentanone (Methyl propyl ketone)
Perchloroethylene (Tetrachloroethylene)
Perchloryl fluoride
Petroleum distillates (naphtha) (rubber solvent)
Phenol
Phenyl ether
Phenyl ether-Biphenyl mixture vapor
Phenyl glycidyl ether (PGE)
Phenyl mercaptan
p-Phenylene diamine
Phenylhydrazine
Phosdrin (Mevinphos)
Phosgene (Carbonyl chloride)
Phosphine
Phosphoric acid
Phosphorus (yellow)
Phosphorus pentachloride
Phosphorus pentasulfide
Phosphorus trichloride
Phthalic anhydride
m-Phthalodinitrile
Picloram
Picric acid
Pindone (2-pivalyl-1,3-indandione)
Plaster of paris
Platinum
Platinum soluble salts
Portland cement
Propane
n-Propyl acetate
n-Propyl alcohol
n-Propyl nitrate
Propylene dichloride

Propylene imine
Propylene oxide
Pyrethrum
Pyridine
Quinone
Resorcinol
Rhodium
Rhodium soluble compounds
Rhodium, insoluble compounds
Ronnel
Rosin core solder pyrolysis products, as formaldehydeRotenone
Rouge
Selenium
Selenium compounds
Selenium hexafluoride
Silica, amorphous, diatomaceous earth, containing less than1% crystalline silica
Silica, amorphous, precipitated and gel
Silica, crystalline, tridymite
Silica, fused
Silica-crystalline, cristobalite
Silica-crystalline, quartz
Silica-crystalline, tripoli
Silicon
Silicon carbide
Silicon tetrahydride
Silver soluble compounds
Silver, metal
Soapstone
Sodium fluoroacetate
Sodium hydroxide
Starch
Stibine
Stoddard solvent
Strychnine
Styrene
Subtilisins (proteolytic enzymes)
Sucrose
Sulfur dioxide
Sulfur hexafluoride
Sulfur monochloride
Sulfur pentafluoride
Sulfuric acid

Sulfuryl fluoride
Sulprofos
Talc (containing no asbestos)
Tantalum metal
Tantalum, oxide dusts
TEDP (Sulfotep)
Tellurium
Tellurium compounds, n.o.s.
Tellurium hexafluoride
Temephos
TEPP
Terphenyls
1,1,2,2-Tetrachloro-1,2-difluoroethane
1,1,1,2-Tetrachloro-2,2-difluoroethane
1,1,2,2-Tetrachloroethane

Tetrachloroethylene
Tetrachloronaphthalene
Tetraethyllead
Tetrahydrofuran
Tetramethyl lead
Tetramethyl succinonitrile
Tetranitromethane
Tetryl (2,4,6-Trinitro-phenylmethylnitramine)
Thallium soluble compounds
Thallium soluble compounds
4,4'-Thiobis (6-tert-butyl-m-cresol)
Thioglycolic acid
Thiram
Tin
Tin inorganic compounds
Tin organic compounds
Titanium dioxide
Toluene
Toluene 2,4-diisocyanate (TDI)
o-Toluidine
Tributyl phosphate
1,1,2-Trichloro-1,2,2-trifluoroethane
Trichloroacetic acid
1,2,4-Trichlorobenzene
1,1,2-Trichloroethane
Trichloroethylene

Trichloronaphthalene
1,2,3-Trichloropropane
Triethylamine
Trifluorobromomethane
Trimethyl benzene
2,4,6-Trinitrotoluene (TNT)
Triorthocresyl phosphate
Triphenyl phosphate
Tungsten
Tungsten, insoluble compounds
Tungsten, soluble compounds
Turpentine
Uranium
Uranium insoluble compounds
Uranium soluble compounds
Vanadium

Vanadium pentoxide
Vegetable oil mist
Vinyl acetate
Vinyl bromide
Vinyl toluene
Vinylidene chloride (1,1-Dichloroethylene)
Warfarin
Welding fumes (total particulate)
Wood dust, all soft and hard woods, except western red cedar
Wood dust, western red cedar
m-Xylene-alpha, alpha'-diamine
Xylenes (o-, m-, p- isomers)
Xylidine
Yttrium
Zinc chloride fume
Zinc oxide
Zinc stearate
Zirconium
Zirconium compounds, n.o.s.

APPENDIX D.
OSHA-Designated Carcinogens

29 CFR 1910, Subpart Z - Toxic and Hazardous Substances. Occupational Safety and Health Administration.

Chemical Name
1,2-Dibromo-3-chloropropane
1,3–Butadiene
2-Acetylaminofluorene
3,3'-Dichlorobenzidine (and its salts)
4-Aminodiphenyl
4-Dimethylaminoazobenzene
4-Nitrobiphenyl
Acrylonitrile
alpha-Naphthylamine
Asbestos
Benzene
Benzidine
beta-Naphthylamine
beta-Propiolactone
bis-Chloromethyl ether
Cadmium
Chromium (VI) compounds
Coke oven emissions
Ethylene oxide
Ethyleneimine
Formaldehyde
Inorganic arsenic

Lead
Methyl chloromethyl ether
Methylene chloride
Methylenedianiline
N-Nitrosodimethylamine
Vinyl chloride

Workers' Rights

Workers have the right to:

- Working conditions that do not pose a risk of serious harm.
- Receive information and training (in a language and vocabulary the worker understands) about workplace hazards, methods to prevent them, and the OSHA standards that apply to their workplace.
- Review records of work-related injuries and illnesses.
- File a complaint asking OSHA to inspect their workplace if they believe there is a serious hazard or that their employer is not following OSHA's rules. OSHA will keep all identities confidential.
- Exercise their rights under the law without retaliation, including reporting an injury or raising health and safety concerns with their employer or OSHA. If a worker has been retaliated against for using their rights, they must file a complaint with OSHA as soon as possible, but no later than 30 days.

For more information, see OSHA's Workers page.

OSHA Assistance, Services and Programs

OSHA has a great deal of information to assist employers in complying with their responsibilities under OSHA law. Several OSHA programs and services can help employers identify and correct job hazards, as well as improve their injury and illness prevention program.

Establishing an Injury and Illness Prevention Program

The key to a safe and healthful work environment is a comprehensive injury and illness prevention program.

Injury and illness prevention programs are systems that can substantially reduce the number and severity of workplace injuries and illnesses, while reducing costs to employers. Thousands of employers across the United States already manage safety using injury and illness prevention programs, and OSHA believes that all employers can and should do the same. Thirty-four states have requirements or voluntary guidelines for workplace injury and illness prevention programs. Most successful injury and illness prevention programs are based on a common set of key elements. These include management leadership, worker participation, hazard identification, hazard prevention and control, education and training, and program evaluation and improvement. Visit OSHA's Injury and Illness Prevention Programs web page at www.osha.gov/dsg/topics/safetyhealth for more information.

Compliance Assistance Specialists

OSHA has compliance assistance specialists throughout the nation located in most OSHA offices. Compliance assistance specialists can provide information to employers and workers about OSHA standards, short educational programs on specific hazards or OSHA rights and responsibilities, and information on additional compliance assistance resources. For more details, visit www.osha.gov/dcsp/compliance_assistance/cas.html or call 1-800-321-OSHA (6742) to contact your local OSHA office.

Free On-site Safety and Health Consultation Services for Small Business

OSHA's On-site Consultation Program offers free and confidential advice to small and medium-sized businesses in all states across the country, with priority given to high-hazard worksites. Each year, responding to requests from small employers looking to create or improve their safety and health management programs, OSHA's On-site Consultation Program conducts over 29,000 visits to small business worksites covering over 1.5 million workers across the nation.

On-site consultation services are separate from enforcement and do not result in penalties or citations. Consultants from state agencies or universities work with employers to identify workplace hazards, provide advice on compliance with OSHA standards, and assist in establishing safety and health management programs.

For more information, to find the local On-site Consultation office in your state, or to request a brochure on Consultation Services, visit www.osha.gov/consultation, or call 1-800-321-OSHA (6742).

Under the consultation program, certain exemplary employers may request participation in OSHA's **Safety and Health Achievement Recognition Program (SHARP)**. Eligibility for participation includes, but is not limited to, receiving a full-service, comprehensive consultation visit, correcting all identified hazards and developing an effective safety and health management program. Worksites that receive SHARP recognition are exempt from programmed inspections during the period that the SHARP certification is valid.

Cooperative Programs

OSHA offers cooperative programs under which businesses, labor groups and other organizations can work cooperatively with OSHA. To find out more about any of the following programs, visit www.osha.gov/cooperativeprograms.

Strategic Partnerships and Alliances

The OSHA Strategic Partnerships (OSP) provide the opportunity for OSHA to partner with employers, workers, professional or trade associations, labor organizations, and/or other interested stakeholders. OSHA Partnerships are formalized through unique agreements designed to encourage, assist, and recognize partner efforts to eliminate serious hazards and achieve model workplace safety and health practices. Through the Alliance Program, OSHA works with groups

committed to worker safety and health to prevent workplace fatalities, injuries and illnesses by developing compliance assistance tools and resources to share with workers and employers, and educate workers and employers about their rights and responsibilities.

Voluntary Protection Programs (VPP)

The VPP recognize employers and workers in private industry and federal agencies who have implemented effective safety and health management programs and maintain injury and illness rates below the national average for their respective industries. In VPP, management, labor, and OSHA work cooperatively and proactively to prevent fatalities, injuries, and illnesses through a system focused on: hazard prevention and control, worksite analysis, training, and management commitment and worker involvement.

Occupational Safety and Health Training

The OSHA Training Institute partners with 27 OSHA Training Institute Education Centers at 42 locations throughout the United States to deliver courses on OSHA standards and occupational safety and health topics to thousands of students a year. For more information on training courses, visit www.osha.gov/otiec.

OSHA Educational Materials

OSHA has many types of educational materials in English, Spanish, Vietnamese and other languages available in print or online. These include:

- Brochures/booklets;
- Fact Sheets;
- Guidance documents that provide detailed examinations of specific safety and health issues;
- Online Safety and Health Topics pages;
- Posters;
- Small, laminated QuickCards™ that provide brief safety and health information; and
- *QuickTakes*, OSHA's free, twice-monthly online newsletter with the latest news about OSHA initiatives and products to assist employers and workers in finding and preventing workplace hazards. To sign up for *QuickTakes* visit www.osha.gov/quicktakes.

To view materials available online or for a listing of free publications, visit www.osha.gov/publications. You can also call 1-800-321-OSHA (6742) to order publications.

Select OSHA publications are available in e-Book format. OSHA e-Books are designed to increase readability on smartphones, tablets and other mobile devices. For access, go to www.osha.gov/ebooks.

OSHA's web site also has information on job hazards and injury and illness prevention for employers and workers. To learn more about OSHA's safety and health resources online, visit www.osha.gov or www.osha.gov/html/a-z-index.html.

NIOSH Health Hazard Evaluation Program

Getting Help with Health Hazards

The National Institute for Occupational Safety and Health (NIOSH) is a federal agency that conducts scientific and medical research on workers' safety and health. At no cost to employers or workers, NIOSH can help identify health hazards and recommend ways to reduce or eliminate those hazards in the workplace through its Health Hazard Evaluation (HHE) Program.

Workers, union representatives and employers can request a NIOSH HHE. An HHE is often requested when there is a higher than expected rate of a disease or injury in a group of workers. These situations may be the result of an unknown cause, a new hazard, or a mixture of sources. To request a NIOSH Health Hazard Evaluation go to www.cdc.gov/niosh/hhe/request.html. To find out more, in English or Spanish, about the Health Hazard Evaluation Program:

E-mail HHERequestHelp@cdc.gov or call 800-CDC-INFO (800-232-4636).

OSHA Regional Offices

Region I
Boston Regional Office
(CT*, ME*, MA, NH, RI, VT*)
JFK Federal Building, Room E340
Boston, MA 02203
(617) 565-9860 (617) 565-9827 Fax

Region II
New York Regional Office
(NJ*, NY*, PR*, VI*)
201 Varick Street, Room 670
New York, NY 10014
(212) 337-2378 (212) 337-2371 Fax

Region III
Philadelphia Regional Office
(DE, DC, MD*, PA, VA*, WV)
The Curtis Center
170 S. Independence Mall West
Suite 740 West
Philadelphia, PA 19106-3309
(215) 861-4900 (215) 861-4904 Fax

Region IV
Atlanta Regional Office
(AL, FL, GA, KY*, MS, NC*, SC*, TN*)
61 Forsyth Street, SW, Room 6T50
Atlanta, GA 30303
(678) 237-0400 (678) 237-0447 Fax

Region V
Chicago Regional Office
(IL*, IN*, MI*, MN*, OH, WI)
230 South Dearborn Street
Room 3244
Chicago, IL 60604
(312) 353-2220 (312) 353-7774 Fax

Region VI
Dallas Regional Office
(AR, LA, NM*, OK, TX)
525 Griffin Street, Room 602
Dallas, TX 75202
(972) 850-4145 (972) 850-4149 Fax
(972) 850-4150 FSO Fax

Region VII
Kansas City Regional Office
(IA*, KS, MO, NE)
Two Pershing Square Building
2300 Main Street, Suite 1010
Kansas City, MO 64108-2416
(816) 283-8745 (816) 283-0547 Fax

Region VIII
Denver Regional Office
(CO, MT, ND, SD, UT*, WY*)
Cesar Chavez Memorial Building
1244 Speer Boulevard, Suite 551
Denver, CO 80204
(720) 264-6550 (720) 264-6585 Fax

Region IX
San Francisco Regional Office
(AZ*, CA*, HI*, NV*, and
American Samoa,
Guam and the Northern Mariana Islands)
90 7th Street, Suite 18100
San Francisco, CA 94103
(415) 625-2547 (415) 625-2534 Fax

Region X
Seattle Regional Office
(AK*, ID, OR*, WA*)
300 Fifth Avenue, Suite 1280
Seattle, WA 98104
(206) 757-6700 (206) 757-6705 Fax

*These states and territories operate their own OSHA-approved job safety and health plans and cover state and local government employees as well as private sector employees. The Connecticut, Illinois, Maine, New Jersey, New York and Virgin Islands programs cover public employees only. (Private sector workers in these states are covered by Federal OSHA). States with approved programs must have standards that are identical to, or at least as effective as, the Federal OSHA standards.

Note: To get contact information for OSHA area offices, OSHA-approved state plans and OSHA consultation projects, please visit us online at www.osha.gov or call us at 1-800-321-OSHA (6742).

How to Contact OSHA

For questions or to get information or advice, to report an emergency, fatality, inpatient hospitalization, amputation, or loss of an eye, or to file a confidential complaint, contact your nearest OSHA office, visit www.osha.gov or call OSHA at 1-800-321-OSHA (6742), TTY 1-877-889-5627.

For assistance, contact us.
We are OSHA. We can help.


OSHA®
www.osha.gov

U.S. Department of Labor

For more information:

OSHA® Occupational Safety and Health Administration

www.osha.gov (800) 321-OSHA (6742)