

ENSURING LABORATORY SAFETY: KEY ELEMENTS OF HAZARD ASSESSMENT, RISK EVALUATION, AND EXPERIMENT PLANNING

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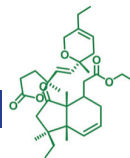
ABSTRACT

A key element of planning an experiment is assessing the hazards and potential risks associated with the chemicals and laboratory operations to be used. The primary responsibility for proper hazard evaluations and risk assessments lies with the person performing the experiment. Ensuring laboratory safety requires thorough risk assessment, with evaluations often conducted by trained personnel and authorized by supervisors. Collaboration fosters a safety culture, ensuring hazard comprehension among all involved. Chemical hygiene plans and material safety data sheets (MSDSs) are crucial references, mandated by federal regulations, providing comprehensive hazard information. However, limitations exist, urging reliance on specific laboratory operating procedures. The Globally Harmonized System (GHS) offers standardized hazard communication. Local Chemical Safety Summaries (LCSSs), precautionary labels, and additional resources further aid risk assessment. A curated list of references, including international safety cards, NIOSH guides, and industry handbooks, complements traditional sources for comprehensive laboratory risk assessment. Laboratory safety hinges on meticulous risk assessment, often led by trained personnel and endorsed by supervisors. Collaborative efforts cultivate a safety ethos, ensuring universal understanding of hazards. Chemical hygiene plans and material safety data sheets (MSDSs), mandated by federal regulations, serve as vital references for hazard information. Yet, limitations prompt reliance on specific laboratory procedures. The Globally Harmonized System (GHS) standardizes hazard communication. Local Chemical Safety Summaries (LCSSs), precautionary labels, and additional resources enhance risk assessment. A curated list of references, featuring international safety cards, NIOSH guides, and industry handbooks, augments conventional sources for a comprehensive laboratory risk assessment.

Key words: Hazard, Toxicity, Safety, Peroxides

INTRODUCTION

An essential aspect of experiment planning involves evaluating the potential hazards and risks associated with the chemicals and laboratory procedures intended for use. The responsibility for conducting thorough hazard assessments and risk evaluations primarily rests on the individual conducting the experiment. While trained laboratory personnel may carry out the



actual assessments, these should be reviewed and approved by the supervisor. The supervisor is also accountable for ensuring that everyone involved in or around the experiment comprehends the evaluations and assessments. Some organizations have environmental health and safety offices equipped with industrial hygiene specialists to guide trained personnel and their supervisors in risk assessment. Fostering a safety-oriented culture, the supervisor and scholars in the laboratory must collaborate to establish a secure environment and ensure that hazards are identified and assessed appropriately before commencing work.

All laboratory staff should be acquainted with and easily access their institution's chemical hygiene plan. In certain laboratories, chemical hygiene plans encompass standard operating procedures for working with specific chemicals, and these plans may suffice as the primary source for risk assessment and experiment planning. However, since most chemical hygiene plans only provide general procedures for handling chemicals, it is advisable for laboratory personnel to consult additional resources for information on the properties of substances expected in the proposed experiment. Many laboratories mandate the documentation of specific hazards and controls for a proposed experiment.

MATERIAL SAFETY DATA SHEETS (MSDSS)

Federal regulations, specifically the OSHA Hazard Communication Standard 1910.1200, mandate that manufacturers and distributors of hazardous chemicals must furnish users with material safety data sheets (MSDSs). These sheets are designed to offer the necessary information for safeguarding users against any potential hazards associated with the product, following the guidelines of the Globally Harmonized System for Hazard Communication. MSDSs have emerged as the primary means through which the potential dangers of materials acquired from commercial sources are communicated to trained laboratory personnel. It is a legal requirement, as per the OSHA Hazard Communication Standard, for institutions to retain and readily provide the MSDSs supplied by chemical suppliers.

OSHA recommends adhering to the general 16-part format established by the American National Standards Institute (ANSI Z400.1) for creating MSDSs. The information typically contained in an MSDS includes:

1. Information regarding the supplier, including address and phone number, along with the date the MSDS was prepared or revised.
2. Details about the chemical.
3. Properties related to both physical and chemical aspects.
4. Hazards associated with flammability, reactivity, and explosion.
5. Data on toxicity.



6. Acute and chronic health hazards, along with the signs and symptoms of exposure.
7. Procedures for storage and handling.
8. Guidelines for emergency response and first aid.
9. Considerations for disposal.
10. Information regarding transportation.

Material Safety Data Sheets (MSDSs) continue to be the most reliable sole reference for evaluating hazards and appraising risks associated with chemical substances. Nevertheless, it is crucial for laboratory personnel to acknowledge the constraints of MSDSs when applied to operations conducted at the laboratory scale. In instances where MSDSs prove insufficient, there should be accessible, specific laboratory operating procedures tailored to the particular manipulations intended for use in the laboratory.

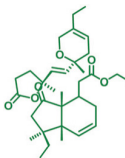
1. The quality of MSDSs produced by different chemical suppliers varies widely.
2. Unique morphology of solid hazardous chemicals may not be addressed in MSDSs; for example, an MSDS for nano-size titanium dioxide may not present the unique toxicity considerations for these ultra-fine particulates.
3. MSDSs must describe control measures and precautions for work on a variety of scales.
4. Many MSDSs comprehensively list all conceivable health hazards associated with a substance without differentiating which are most significant and which are most likely to actually be encountered. As a result, trained laboratory personnel may not distinguish highly hazardous materials from moderately hazardous and relatively harmless ones.

GLOBALLY HARMONIZED SYSTEM (GHS) FOR HAZARD COMMUNICATION

The Globally Harmonized System (GHS) for the Classification and Labeling of Chemicals stands as a globally acknowledged framework for hazard classification and communication, accessible at <http://www.unece.org>. Developed with collaboration from the International Labour Organization (ILO), the Organisation for Economic Co-operation and Development, and the United Nations Sub-Committee of Experts on the Transport of Dangerous Goods, the GHS aims to standardize hazard communication, enhancing the safety of international trade and commerce.

The GHS identifies 16 categories of physical hazards, 10 categories of health hazards, and an environmental hazard.

- flammable liquids;
- oxidizing gases;



- self-reactive substances;
- self-heating substances;
- organic peroxides; and
- corrosive to metals.
- explosives;
- oxidizing gases;
- flammable gases;
- flammable aerosols;
- oxidizing liquids;
- flammable solids;
- gases under pressure;
- substances which, in contact with water, emit flammable gases;

Health hazards include

- carcinogenicity,
- reproductive toxicology,
- target organ systemic toxicity—single exposure,
- target organ systemic toxicity—repeated exposure, and
- aspiration hazard.
- acute toxicity,
- skin corrosion or irritation,
- serious eye damage or eye irritation,
- respiratory or skin sensitization,
- germ cell mutagenicity,

Environmental hazard includes

- Hazardous to the aquatic environment: acute aquatic toxicity or chronic aquatic toxicity with bioaccumulation potential rapid degradability.

LABORATORY CHEMICAL SAFETY SUMMARIES (LCSSS)

While Material Safety Data Sheets (MSDSs) are valuable references, they have limitations when applied to risk assessment within the specific laboratory setting. Laboratory Chemical



Safety Summaries (LCSSs) offer information on chemicals in the context of laboratory usage. These documents are summaries and are not meant to be exhaustive or meet the needs of all potential users of a chemical. LCSSs provide essential information necessary for evaluating the risks associated with the use of a specific chemical in the laboratory. They also feature a succinct critical discussion, presented in a style easily understandable to trained laboratory personnel, covering the toxicity, flammability, reactivity, and explosivity of the chemical. Additionally, LCSSs provide recommendations for handling, storage, and disposal of the substance, along with first-aid and emergency response procedures.

LABELS

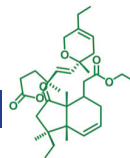
According to the OSHA Hazard Communication Standard, it is mandatory for commercial suppliers to furnish their chemicals in containers featuring precautionary labels. These labels typically offer brief and non-technical overviews of the main hazards linked to the contents. It is important to emphasize that precautionary labels do not serve as substitutes for MSDSs and LCSSs, which remain the primary sources of information for laboratory risk assessment. Nevertheless, labels play a significant role as helpful reminders of the essential hazards associated with the substance.

ALTERNATIVE INFORMATION SOURCES

The above mentioned resources establish the groundwork for assessing chemical risks in the laboratory. While MSDSs and LCSSs cover details about toxic effects, there are instances where laboratory personnel should seek more comprehensive information. This is especially crucial when dealing with chemicals with high acute or chronic toxicity, or when planning to work extensively and frequently with a specific toxic substance over an extended period.

The following annotated list provides references on the hazardous properties of chemicals and which are useful for assessing risks in the laboratory.

1. Fire Protection Guide to Hazardous Materials, 13th edition (NFPA, 2001). This resource contains hazard data on hundreds of chemicals and guidance on handling and storage of, and emergency procedures for those chemicals.
2. Fire Protection for Laboratories Using Chemicals (NFPA, 2004). This is the national fire safety code pertaining to laboratory use of chemicals. It describes the basic requirements for fire protection of life and property in the laboratory
3. Hazardous Chemicals Handbook, 2nd edition (Carson and Mumford, 2002). This book is geared toward an industrial audience. It provides basic information about chemical hazards and synthesizes technical guidance from a number of authorities in chemical safety. The chapters are organized by hazard (e.g., “Toxic Chemicals,” “Reactive Chemicals,” and “Cryogenics”).



4. A Comprehensive Guide to the Hazardous Properties of Chemical Substances, 3rd edition (Patnaik, 2007). This particularly valuable guide is written at a level appropriate for typical laboratory personnel. It covers more than 1,500 substances; sections in each entry include uses and exposure risk, physical properties, health hazards, exposure limits, fire and explosion hazards, and disposal or destruction. Entries are organized into chapters according to functional group classes, and each chapter begins with a general discussion of the properties and hazards of the class. 2009 TLVs and BEIs: Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. A booklet listing ACGIH threshold limit values (TLVs) and short-term exposure limits (STELs). These values are under continuous review, and this booklet is updated annually. The multivolume publication Documentation of the Threshold Limit Values and Biological Exposure Indices reviews the data that were used to establish the TLVs.
5. International Chemical Safety Cards from the International Programme on Chemical Safety (IPCS, 2009). The IPCS is a joint activity of the ILO, the United Nations Environment Programme, and the World Health Organization. The cards contain hazard and exposure information from recognized sources and undergo international peer review. They are available in 18 languages and can be found online through the NIOSH Web site, www.cdc.gov/niosh, or through the ILO Web site, www.ilo.org.
6. NIOSH Pocket Guide to Chemical Hazards (HHS/ CDC/NIOSH, 2007). This volume is updated regularly and is found on the NIOSH Web site (<http://www.cdc.gov/niosh>). These charts are quick guides to chemical properties, reactivities, exposure routes and limits, and first-aid measures.
7. A number of Web-based resources also exist. Some of these are NIOSH Databases and Information Resources (www.cdc.gov/niosh) and TOXNET through the National Library of Medicine (NLM; www.nlm.nih.gov).

THE NATIONAL LIBRARY OF MEDICINE DATABASES

The databases provided by the National Library of Medicine (NLM) are user-friendly and can be accessed free of charge on the internet. TOXNET stands out as an online compilation of toxicological and environmental health databases. One example is TOXLINE, an online database that taps into journals and other resources to provide current toxicological information on drugs and chemicals, spanning from 1900 to the present.

Databases accessible through TOXNET encompass the Hazardous Substance Data Base (HSDB), Carcinogenic Potency Database (CPDB), Developmental and Reproductive Toxicology Database (DART), Genetic Toxicology Data Bank (GENE-TOX), Integrated Risk



Information System (IRIS), Chemical Carcinogenesis Research Information System (CCRIS), and International Toxicity Estimates for Risk (ITER). Other NLM-supplied databases providing access to toxicological information include PubMed (with access to MEDLINE), PubChem, and ChemIDPlus. Most databases allow for free text searching.

Another source for toxicity data is the Chemical Abstracts Service (CAS). Various services, including DIALOG, ORBIT, STN, and SciFinder, provide access to CAS. The search procedures for CAS may vary among these services. Additional details can be found on the CAS website at www.cas.org. It is recommended to search any of the mentioned databases using the CAS registry number for the specific chemical.

TRAINING

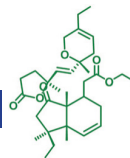
Training sessions are a crucial information source for laboratory personnel, and their pivotal role in establishing a safe environment should not be underestimated. The value of facts lies in the ability to interpret and apply them to specific problems, and training offers the necessary context for their utilization. Ideal training involves hands-on, scenario-based exercises, allowing participants to practice activities and behaviors safely. This type of training is particularly beneficial for mastering emergency response procedures.

Case studies are another effective tool, especially in raising awareness of specific safety concerns. Before initiating any laboratory activity, it is essential to ensure that personnel have received sufficient training to perform required tasks safely. If there are new equipment, materials, or techniques to be used, conducting a risk assessment is crucial, and any knowledge gaps should be addressed before commencing work.

ADVERSE EFFECTS OF LABORATORY CHEMICALS

The chemicals encountered in laboratory settings exhibit diverse physical, chemical, and toxicological properties, as well as varied physiological effects. Prior to incorporating these chemicals into an experiment, it is crucial to comprehensively understand the associated risks. The risk of toxic effects is contingent on both the extent of exposure and the inherent toxicity of a given chemical. The following discussion delves into the factors that determine the extent of exposure, including dose, duration and frequency of exposure, and the route of exposure.

Exposure to chemicals with minimal inherent toxicity, such as phosphate buffer, even in substantial doses, presents a low risk. Conversely, even small quantities of chemicals with high inherent toxicity or corrosiveness may result in significant adverse effects. The duration and frequency of exposure play critical roles in determining whether a chemical will induce harmful effects. While a single exposure may be adequate for certain chemicals to cause adverse health effects, others necessitate repeated exposure for toxic effects to manifest.



For most substances, the route of exposure—whether through the skin, eyes, gastrointestinal tract, or respiratory tract—is a crucial consideration in risk assessment. In the case of systemic toxicants, the internal dose to the target organ becomes a pivotal factor. Acute toxicants often have well-defined toxicity parameters derived from animal studies and accidental human exposures. However, obtaining analogous quantitative data for decisions regarding the neurotoxicity and immunogenicity of various chemicals is frequently challenging.

When planning experiments and assessing potential toxicity hazards, it is important to recognize that the combined toxic effects of two substances may surpass the individual toxic effects of each substance. Given that chemical reactions often yield unassessed mixtures of substances, it is prudent to assume that mixtures, particularly those resulting from chemical reactions, may exhibit greater toxicity than their most toxic component. Additionally, reactions involving multiple substances may produce reaction products that are considerably more toxic than the initial reactants. Trained laboratory personnel may not anticipate the formation of toxic reaction products in cases where reactants are unintentionally mixed. For instance, the inadvertent mixing of formaldehyde (a common tissue fixative) and hydrogen chloride results in the generation of bis(chloromethyl)ether, a potent human carcinogen.

All laboratory personnel should possess a foundational understanding of basic toxicology principles and be able to identify major classes of toxic and corrosive chemicals. The subsequent sections of this chapter provide a summary of the essential concepts involved in evaluating the risks associated with the use of toxic chemicals in the laboratory.

DOSE-RESPONSE RELATIONSHIPS

Toxicology is the scientific study of the harmful effects of chemicals on living organisms. Fundamental principles in toxicology emphasize that no substance is entirely devoid of risk, and exposure to any chemical can lead to toxic effects if the dose is sufficiently high. For instance, water, an essential element for life, can be fatal if ingested in a significantly large amount, while sodium cyanide, a highly lethal chemical, may cause no permanent effects at sufficiently low doses.

The critical determinant of whether a substance poses harm or safety to an individual lies in the relationship between the amount and concentration of the chemical reaching the target organ and the resulting toxic effects. In toxicology, this relationship is termed the dose-response relationship, wherein the dose represents the amount of the chemical, and the response denotes the effect it induces. While this relationship is unique for each chemical, similar types of chemicals often share comparable dose-response patterns.

Among the vast array of laboratory chemicals, a wide spectrum of doses exists that can produce toxic effects, ranging from mild to severe, and even fatal outcomes. Many chemicals



have an established threshold dose, below which they are generally considered non-harmful to most individuals, as determined by established rules or consensus.

Certain chemicals, such as dioxin, exhibit extreme toxicity, causing death in laboratory animals exposed to microgram doses. Conversely, other substances may show no harmful effects even at doses exceeding several grams. The acute toxicity of laboratory chemicals, occurring after a single exposure, is often assessed through the lethal dose 50 (LD50) or lethal concentration 50 (LC50) values. The LD50 is the amount of a chemical that, under controlled laboratory conditions, causes the death of half (50%) of the test animals when ingested, injected, or applied to the skin. For volatile chemicals, the LC50, representing the concentration in air that kills 50% of exposed test animals, is frequently reported. The larger the LD50 or LC50, the more substantial the amount of the chemical required to cause lethality, indicating lower toxicity. While lethal dose values may vary across species, chemicals highly toxic to animals generally pose a high risk of toxicity to humans as well.

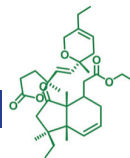
EVALUATING THE RISKS OF EXPOSURE TO HAZARDOUS LABORATORY CHEMICALS

Exposure to a hazardous chemical can lead to either local toxic effects, systemic toxic effects, or a combination of both. Local effects manifest as injury at the site of initial contact, with typical locations being the eyes, skin, nose and lungs, and the digestive tract. Examples of local effects encompass inhalation of hazardous materials causing toxicity in the nose and lungs, contact with harmful substances on the skin or eyes resulting in effects ranging from mild irritation to severe tissue damage, and ingestion of caustic substances causing burns and ulcers in the mouth, esophagus, stomach, and intestines.

In contrast, systemic effects occur after the toxicant has been absorbed into the bloodstream and distributed throughout the body. While some chemicals produce adverse effects on all tissues, others selectively target specific organs without affecting others. The affected organ, such as the liver, lungs, kidneys, or central nervous system, is termed the target organ of toxicity, regardless of whether it hosts the highest concentration of the chemical.

Numerous systemic toxic effects from chemicals are known, stemming from single (acute) exposures or repeated and prolonged (chronic) exposures that may become apparent only after a prolonged latency period.

Laboratory chemicals are categorized into various classes of toxic substances, with many displaying multiple types of toxicity. The initial step in assessing risks for a planned laboratory experiment involves identifying potentially hazardous substances among the chemicals to be



used. The term “health hazard” encompasses chemicals classified as carcinogens, toxic or highly toxic agents, reproductive toxins, irritants, corrosives, sensitizers, hepatotoxins, nephrotoxins, neurotoxins, agents affecting the hematopoietic systems, and substances damaging the lungs, skin, eyes, or mucous membranes. The OSHA Laboratory Standard additionally designates certain chemicals as particularly hazardous substances (PHSs), requiring special handling procedures. PHSs include select carcinogens (strongly implicated as potential causes of cancer in humans), reproductive toxins, and compounds with high acute toxicity. When working with these substances for the first time, consulting with a safety professional before starting work is advisable. This ensures a thorough review of safety protocols and compliance with special emergency response requirements in case of personnel exposure or accidental release.

The subsequent section outlines the most common classes of toxic substances encountered in laboratories.

ACUTE TOXICANTS

Acute toxicity refers to a chemical’s capacity to induce harmful effects following a singular exposure. Substances with acute toxicity can lead to local and systemictoxic effects. This category encompasses corrosive chemicals, irritants, and sensitizers (allergens). Evaluating the risks associated with acute toxicants involves categorizing a substance based on its acute toxicity hazard level, as illustrated in the table below.

Toxicity Rating	Hazard Level	Inhalation LC ₅₀ (rats, mg/m ³ for 1 h)	Skin Contact LD ₅₀ (rabbits, per kg)	Inhalation LC ₅₀ (rats, ppm for 1 h)	Oral LD ₅₀ (rats, per kg)
Highly toxic	High	<2,000	<200 mg	<200	<50 mg
Moderately toxic	Medium	2,000 to 20,000	200 mg to 1 g	200 to 2,000	50 to 500 mg
Slightly toxic	Low	20,000 to 200,000	1 to 5 g	2,000 to 20,000	500 mg to 5 g

Special attention is given to any substance classified according to the above criteria as having a high level of acute toxicity hazard. Chemicals with a high level of acute toxicity make up one of the categories of PHSs defined by the OSHA Laboratory Standard. The following table lists some of the most common chemicals with a high level of acute toxicity that are encountered in the laboratory



COMPOUNDS DEMONSTRATING ELEVATED ACUTE TOXICITY

Hydrogen fluoride	Sodium cyanide (and other cyanide salts)
Arsine	Nickel carbonyl
Diazomethane	Osmium tetroxide
Hydrogen cyanide	Sodium azide
Diborane (gas)	Ozone
Chlorine	Nitrogen dioxide
Dimethyl mercury	Phosgene
Acrolein	Methyl fluorosulfonate

Compounds showing acute toxicity

TYPES OF TOXINS

Allergens, Sensitizers Irritants and Corrosive Substances

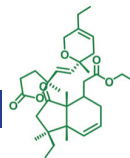
Quantitative toxicological parameters like the lethal dose offer limited guidance in assessing risks associated with corrosives, irritants, allergens, and sensitizers, as these substances primarily exert their harmful effects locally. It would be beneficial for the chemical research community to develop a quantitative measure specifically tailored for such localized effects.

When planning experiments involving corrosive substances, it is essential to review basic prudent handling practices. This ensures adequate protection of the skin, face, and eyes through the appropriate selection of corrosion-resistant gloves, protective clothing, and eyewear, including face shields in some cases.

Similarly, LD50 and LC50 data do not serve as indicators for the irritant effects of chemicals. Hence, special attention should be given to identifying irritant chemicals by consulting Laboratory Chemical Safety Summaries (LCSSs), Material Safety Data Sheets (MSDSs), and other informational sources. Allergens and sensitizers, as another class of acute toxicants, exhibit effects not captured by LD50 or LC50 data.

CARCINOGENS

A carcinogen is a substance capable of causing cancer. Cancer, in the simplest sense, is the uncontrolled growth of cells and can occur in any organ. The mechanism by which cancer develops is not well understood, but the current thinking is that some chemicals interact directly with DNA, the genetic material in all cells, to result in permanent alterations. Other chemical carcinogens modify DNA indirectly by changing the way cells grow. Carcinogens are chronically toxic substances; that is, they cause damage after repeated or long-duration



exposure, and their effects may become evident only after a long latency period. Carcinogens are particularly insidious toxins because they may have no immediate apparent harmful effects.

NEUROTOXINS

Neurotoxic chemicals induce an adverse effect on the structure or function of the central or peripheral nervous system, which can be permanent or reversible. The detection of neurotoxic effects may require specialized laboratory techniques, but often they are inferred from behavior such as slurred speech and staggered gait. Many neurotoxins are chronically toxic substances with adverse effects that are not immediately apparent. Some chemical neurotoxins that may be found in the laboratory are mercury (inorganic and organic), organophosphate pesticides, carbon disulfide, xylene, trichloroethylene, and n-hexane.

ASPHYXIANTS

Asphyxiants are substances that interfere with the transport of an adequate supply of oxygen to vital organs of the body. The brain is the organ most easily affected by oxygen starvation, and exposure to asphyxiants leads to rapid collapse and death. Simple asphyxiants are substances that displace oxygen from the air being breathed to such an extent that adverse effects result. Acetylene, carbon dioxide, argon, helium, ethane, nitrogen, and methane are common asphyxiants. Certain other chemicals have the ability to combine with hemoglobin, thus reducing the capacity of the blood to transport oxygen. Carbon monoxide, hydrogen cyanide, and certain organic and inorganic cyanides are examples of such substances.

REPRODUCTIVE AND DEVELOPMENTAL TOXINS

Reproductive toxins are defined by the OSHA Laboratory Standard as substances that cause chromosomal damage (mutagens) and substances with lethal or teratogenic (malformation) effects on fetuses. These substances have adverse effects on various aspects of reproduction, including fertility, gestation, lactation, and general reproductive performance, and can affect both men and women. Various reproductive hazards have been noted following exposure to halogenated hydrocarbons, nitro aromatics, arylamines, ethylene glycol derivatives, mercury, bromine, carbon disulfide, and other chemical reagents.

The following outline provides a summary of the steps that laboratory personnel should use to assess the risks of managing physical hazards in the laboratory.

1. Identify chemicals to be used and circumstances of use.
2. Consult sources of information. Consult an up-to-date laboratory chemical safety summary, material safety data sheet, or NIOSH Pocket Guide to Chemical Hazards (HHS/CDC/NIOSH, 2007).



3. Evaluate type of physical, flammable, explosive, or reactive hazard(s) posed by the chemicals.
4. Evaluate the hazards posed by chemical changes over the course of the experiment.
5. Evaluate type of physical hazard(s) posed by the equipment required.
6. Select appropriate procedures to minimize risk.
7. Prepare for contingencies. Be aware of institutional procedures in the event of emergencies and accidents.

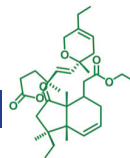
FLAMMABLE HAZARDS

Substances prone to catching fire and burning easily in the presence of air, known as flammable materials, can exist in solid, liquid, or gaseous states. In laboratory settings, the predominant fire risk often stems from flammable liquids or vapors generated by these liquids. Another potential hazard is the rapid ignition of compounds, leading to explosive reactions. Safe handling of substances with fire-causing properties necessitates understanding their tendencies to vaporize, ignite, or combust under various laboratory conditions.

FLAMMABILITY CHARACTERISTICS

The flash point is the temperature at which a liquid has sufficient vapor pressure to create an ignitable mixture with air near its surface. It's noteworthy that several commonly used organic liquids have flash points below room temperature. For instance, acetone has a flash point of $-18\text{ }^{\circ}\text{C}$, benzene at $-11.1\text{ }^{\circ}\text{C}$, diethyl ether at $-45\text{ }^{\circ}\text{C}$, and methyl alcohol at $11.1\text{ }^{\circ}\text{C}$. The level of hazard associated with a flammable liquid is also influenced by additional properties like ignition and boiling points. Taking acetone as an example, at ambient pressure and temperature, a spill can generate a concentration of up to 23.7% acetone in the air. Despite being relatively non-toxic, the extreme fire hazard posed by an acetone spill is evident due to its low flash point of $-18\text{ }^{\circ}\text{C}$ and upper and lower flammable limits of 2.6% and 12.8% acetone in the air, respectively.

	NFPA Flammability Ratinga	Flash Point ($^{\circ}\text{C}$)	Boiling Point ($^{\circ}\text{C}$)	Ignition Temperature ($^{\circ}\text{C}$)	Flammable Limits (% by volume)	
					Lower	Upper
Acetaldehyde	4	-39	21	175	4	60
Acetic acid (glacial)	2	39	118	463	4	19.9



Acetone	3	-20	56	465	2.5	12.8
Acetonitrile	3	6	82	524	3	16
Carbon disulfide	4	-30	46	90	1.3	50
Cyclohexane	3	-20	82	245	1.3	8
Diethylamine	3	-23	57	312	1.8	10.1
Diethyl ether	4	-45	35	180	1.9	36
Dimethyl sulfoxide	2	95	189	215	2.6	42
Ethyl alcohol	3	13	78	363	3.3	19
Heptane	3	-4	98	204	1.05	6.7
Hexane	3	-22	69	225	1.1	7.5
Hydrogen	4		-252	500	4	75
Isopropyl alcohol	3	12	83	399	2	12.7 @ 200 (93)
Isopropyl alcohol	3	12	83	399	2	12.7 @ 200 (93)
Methyl alcohol	3	11	64	464	6	36
Methyl ethyl ketone	3	-9	80	404	1.4 @ 200 (93)	11.4 @ 200 (93)
Pentane	4	<-40	36	260	1.5	7.8
Styrene	3	31	146	490	0.9	6.8
Tetrahydrofuran	3	-14	66	321	2	11.8
Toluene	3	4	111	480	1.1	7.1
p-Xylene	3	25	138	528	1.1	7

NFPA Fire Hazard Ratings, Flash Points (FP), Boiling Points (bp), Ignition Temperatures, and Flammable Limits of Some Common Laboratory Chemicals



a 0, will not burn under typical fire conditions; 1, must be preheated to burn, liquids with FP ≥ 93.4 °C (200 °F); 2, ignitable when moderately heated, liquids with FP between 37.8 °C (100 °F) and 93.4 °C (200 °F); 3, ignitable at ambient temperature, liquids with FP < 22.8 °C (73 °F), bp ≥ 37.8 °C (100 °F) or FP between 22.8 °C and 37.8 °C (100 °F); 4, extremely flammable, readily dispersed in air, and burns readily, liquids with FP < 22.8 °C (73 °F), bp < 37.8 °C (100 °F).

SOURCE: Adapted with permission from Fire Guide to Hazardous Materials (13th Edition), Copyright © 2001, National Fire Protection Association.

IGNITION TEMPERATURE

The ignition temperature, also known as the autoignition temperature, of a substance -be it solid, liquid, or gaseous -is the minimum temperature necessary to initiate self-sustained combustion without relying on an external heat source. A lower ignition temperature implies a higher susceptibility to fires initiated by standard laboratory equipment.

As an illustration, carbon disulfide, with an ignition temperature of 90 °C, can be triggered by a steam line or a glowing light bulb. Similarly, diethyl ether, possessing an ignition temperature of 160 °C, can be ignited by a hot plate.

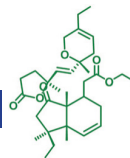
REACTIVE HAZARDS

WATER REACTIVES

Water-reactive substances are those that undergo violent reactions upon contact with water. Examples include alkali metals such as lithium, sodium, and potassium, many organometallic compounds, and certain hydrides. When exposed to water, these materials generate heat and produce flammable hydrogen gas, which can ignite or explosively combine with atmospheric oxygen. Additionally, some anhydrous metal halides (e.g., aluminum bromide), oxides (e.g., calcium oxide), nonmetal oxides (e.g., sulfur trioxide), and halides (e.g., phosphorus pentachloride) react exothermically with water, leading to a potentially explosive reaction if there is insufficient coolant water to dissipate the generated heat.

PYROPHORICS

Pyrophoric materials undergo rapid oxidation upon exposure to oxygen or moisture in the air, leading to spontaneous ignition. Finely divided metals often exhibit pyrophoric properties, and the extent of their reactivity is influenced by factors such as particle size, the presence of moisture, and the thermodynamics associated with the formation of metal oxides or metal nitrides. Additionally, other reducing agents, including metal hydrides, alloys of reactive metals, low-valent metal salts, and iron sulfides, can also be classified as pyrophoric.



EXPLOSIVE HAZARDS

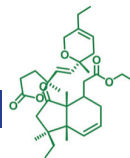
An explosive refers to any chemical compound or mechanical mixture that, when exposed to heat, impact, friction, detonation, or other suitable initiation, undergoes rapid chemical transformation, producing large volumes of gases that exert pressure on the surrounding medium. Notably, hydrogen and chlorine exhibit explosive reactions in the presence of light. Substances such as acids, bases, and others act as catalysts for the explosive polymerization of acrolein, while various metal ions catalyze the violent decomposition of hydrogen peroxide. Materials sensitive to shock encompass acetylides, azides, nitrogen triiodide, organic nitrates, nitro compounds, perchlorate salts (especially those of heavy metals like ruthenium and osmium), numerous organic peroxides, and compounds containing diazo, halamine, nitroso, and ozonide functional groups.

The table below enumerates several explosive compounds. Some can be triggered by the action of a metal spatula on the solid, while others are so sensitive that their own crystal formation can set them off. For instance, diazomethane (CH_2N_2) and organic azides may explosively decompose when exposed to a ground glass joint or other sharp surfaces.

Structural Feature	Compound
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—O—N=O}$	Acyl or alkyl nitrites
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—O—NO}_2$	Acyl or alkyl nitrates
$\text{— C} \equiv \text{C —}$	Acetylenic compounds
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N=N—O—C—}$	Arenediazoates
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N=N—S—C—}$	Arenediazo aryl sulfides
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N=N—C—}$	Azo compounds



$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{O-O-H}$	Alkylhydroperoxides
$\text{N} \rightarrow \text{Cr-O}_2$	Aminechromiumperoxocomplexes
---N_3	Azides (acyl, halogen, nonmetal, organic)
---O-X	Alkyl perchlorates, chlorite salts, halogen oxides, hypohalites, perchloric acid, perchloryl compounds
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{N=N-O-N=N} \begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array}$	Bis-arenediazo oxides
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{N=N-S-N=N} \begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array}$	Bis-arenediazo sulfides
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{N}_2^+ \text{S}^-$	Diazoniumsulfides and derivatives, "xanthates"
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{N}_2^+ \text{Z}$	Diazonium carboxylates or salts
$\begin{array}{c} \diagup \\ \text{CN}_2 \\ \diagdown \end{array}$	Diazo compounds
$\begin{array}{c} \text{N=N} \\ \\ \text{C} \\ \diagup \quad \diagdown \end{array}$	Diazirines

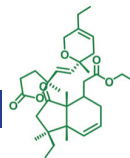


Structural Feature	Compound
	Diazirines
	Fluorodinitromethyl compounds
$\text{— C} \equiv \text{C — X}$	Haloacetylene derivatives
	High-nitrogen compounds, tetrazoles
$\text{— N}^+ \text{— OH Z}^-$	Hydroxylammonium salts
$\text{N}^+ \text{— HZ}^-$	Hydrazinium salts, oxosalts of nitrogenous bases
$\text{— C} \equiv \text{C — Metal}$	Metal acetylides
	Metal fulminates or aci-nitro salts
	N-Nitro compounds
	N-Metal derivatives



Structural Feature	Compound
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—O—O—H}$	Alkylhydroperoxides
$\text{N} \rightarrow \text{Cr—O}_2$	Aminechromiumperoxocomplexes
—N_3	Azides (acyl, halogen, nonmetal, organic)
—O—X	Alkyl perchlorates, chlorite salts, halogen oxides, hypohalites, perchloric acid, perchloryl compounds
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N=N—O—N=N—C} \begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array}$	Bis-arenediazo oxides
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N=N—S—N=N—C} \begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array}$	Bis-arenediazo sulfides
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N}_2^+\text{S}^-$	Diazoniumsulfides and derivatives, “xanthates”
$\begin{array}{c} \diagup \\ \text{C} \\ \diagdown \end{array} \text{—N}_2^+\text{Z}^-$	Diazonium carboxylates or salts
$\begin{array}{c} \diagup \\ \text{CN}_2 \\ \diagdown \end{array}$	Diazo compounds
$\begin{array}{c} \text{N=N} \\ \diagdown \quad \diagup \\ \text{C} \\ \diagup \quad \diagdown \end{array}$	Diazirines

Functional Groups in Some Explosive Compounds



SOURCE: Carson and Mumford (2002). Reprinted from Hazardous Chemicals Handbook (Second Edition), Carson, P. and Mumford, C. "Reactive Chemicals", p. 228, Copyright 2002, with permission from Elsevier

AZOS, PEROXIDES, AND PEROXIDIZABLES

Organic azo compounds and peroxides rank among the most perilous substances manipulated in chemical laboratories, yet they are frequently employed as reagents, serving as sources of free radicals and oxidants. These substances generally fall into the category of low-power explosives, displaying sensitivity to shock, sparks, or inadvertent ignition, surpassing the shock sensitivity of most primary explosives like TNT. To manage the risks associated with these chemicals, inventories should be restricted and subject to regular inspections.

It is crucial not to cool liquids or solutions of these compounds to the point of freezing or crystallization, as this significantly heightens the risk of explosion. Storage units, such as refrigerators and freezers housing such compounds, should be equipped with backup power supplies in case of electricity loss. Users must possess a comprehensive understanding of the hazards associated with these materials and undergo proper training for their safe handling.

Certain commonly used laboratory chemicals have the potential to form peroxides when exposed to oxygen in the air (refer to the table below). Some chemicals progressively accumulate peroxides to potentially hazardous levels over time, while others maintain a relatively low equilibrium concentration of peroxide, becoming perilous only when concentrated through processes like evaporation or distillation.

Class A: Chemicals prone to spontaneously forming explosive levels of peroxides without requiring concentration	
Butadiene	Potassium metal
Chlorobutadiene (chloroprene)	Sodium amide (sodamide)
Divinyl acetylene	Tetrafluoroethylene
Isopropyl ether	Vinylidene chloride
Potassium amide	
Class B: These chemicals are a peroxide hazard on concentration (distillation/evaporation). A test for peroxide should be performed if concentration is intended or suspected.	
Acetal	Dioxane (p-dioxane)
Cumene	Ethylene glycol dimethyl
Cyclohexene	ether (glyme)
Cyclooctene	Furan



Cyclopentene	Methyl acetylene
Diacetylene	Methyl cyclopentane
Dicyclopentadiene	Methyl-isobutyl ketone
Diethylene glycol dimethyl ether (diglyme)	Tetrahydrofuran
Diethyl ether	Tetrahydronaphthalene
	Vinyl ethers
Class C: Unsaturated monomers that may autopolymerize as a result of peroxide accumulation if inhibitors have been removed or are depleted	
Acrylic acid	Styrene
Butadiene	Vinyl acetate
Chlorotrifluoroethylene	Vinyl chloride
Ethyl acrylate	Vinyl pyridine
Methyl methacrylate	

Classes of chemicals that can form peroxides

* These lists are illustrative, not comprehensive. SOURCES: Jackson et al. (1970) and Kelly (1996)

Essentially all compounds containing C—H bonds pose the risk of peroxide formation if contaminated with various radical initiators, photosensitizers, or catalysts. For instance, secondary alcohols such as isopropanol form peroxides when exposed to normal fluorescent lighting and contaminated with photosensitizers, such as benzophenone. Acetaldehyde, under normal conditions, autoxidizes to form acetic acid.

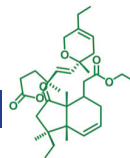
PHYSICAL HAZARDS

COMPRESSED GASES

Compressed gases can expose the trained laboratory personnel to both mechanical and chemical hazards, depending on the gas. Hazards can result from the flammability, reactivity, or toxicity of the gas; from the possibility of asphyxiation; and from the gas compression itself, which could lead to a rupture of the tank or valve.

NONFLAMMABLE CRYOGENS

Nonflammable cryogens, particularly liquid nitrogen, can cause severe tissue damage due to extreme cold upon contact with either the liquid or boil-off gases. In poorly ventilated areas, the inhalation of gas resulting from boil-off or spills can lead to asphyxiation. Another



potential hazard involves the risk of explosion arising from the condensation of liquid oxygen in vacuum traps or the formation of ice plugs, as well as the absence of functioning vent valves in storage Dewars. The warming of a cryogenic liquid in a sealed container is significant because 1 volume of liquid nitrogen at atmospheric pressure vaporizes to 694 volumes of nitrogen gas at 20 °C. This process generates enormous pressure, posing the risk of vessel rupture.

HIGH-PRESSURE REACTIONS

Experiments conducted at elevated pressures, especially those exceeding 1 atm, carry the risk of explosion due to potential equipment failures. Hydrogenation reactions, commonly performed under heightened pressures, pose a particular hazard with the potential formation of explosive O₂/H₂ mixtures and the reactivity/pyrophoricity of the catalyst. Additionally, the utilization of supercritical fluids is another scenario where high pressures may be encountered, introducing an additional element of risk.

VACUUM WORK

Precautions for working with vacuum lines and other glassware utilized at subambient pressure primarily focus on the substantial risk of injury in the event of glass breakage. The level of hazard is not significantly influenced by the vacuum magnitude, as the external pressure leading to implosion always equals 1 atmosphere. Consequently, evacuated systems employing aspirators should be treated with the same level of caution as high-vacuum systems. Injury caused by shattered glass is not the sole peril in vacuum work. Additional dangers may arise from the potential toxicity of chemicals within the vacuum system, as well as the risk of fire following the breakage of a flask (e.g., one containing a solvent stored over sodium or potassium).

ULTRAVIOLET, VISIBLE, AND NEAR-INFRARED RADIATION

Radiation emitted from lamps and lasers in the laboratory, including ultraviolet, visible, and infrared radiation, can pose various hazards. For instance, medium-pressure Hanovia 450 Hg lamps are commonly employed for ultraviolet irradiation in photochemical experiments. Ultraviolet lights utilized in biosafety cabinets, decontamination devices, or light boxes for DNA visualization can lead to severe skin and corneal burns. Powerful arc lamps have the potential to cause eye damage and even blindness within a matter of seconds. Incorrect use of lasers can present risks to the eyes of operators and others in the vicinity, as well as pose a potential fire hazard.

The associated hazards with lasers depend on their type and can include mutagenic, carcinogenic, or otherwise toxic laser dyes and solvents; flammable solvents; ultraviolet or



visible radiation emitted from pump lamps; and electric shock from lamp power supplies.

ELECTRICAL HAZARDS

The risk of electrocution from electrically powered instruments, tools, and equipment is largely mitigated by taking reasonable precautions, making the presence of such equipment in the laboratory generally safe. However, it is crucial not to undermine these safety features through thoughtless or uninformed modifications. Malfunctions in equipment can potentially lead to electrical fires, presenting a unique set of concerns in laboratory settings.

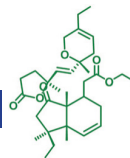
The insulation on wires may be compromised by corrosive chemicals, organic solvent vapors, or ozone (emitted by ultraviolet lights, copying machines, etc.). In locations prone to moisture, such as cold rooms or cooling baths, promptly addressing eroded insulation on electrical equipment is imperative. Furthermore, sparks generated by electrical equipment can act as ignition sources in the presence of flammable vapor. Certain equipment, like electrophoresis equipment, may involve high voltages and stored electrical energy, necessitating careful operation.

MAGNETIC FIELDS

Increasingly, instruments that generate large static magnetic fields (e.g., NMR spectrometers) are present in research laboratories. Such magnets typically have fields of 14,000 to 235,000 G (1.4 to 23.5 T), far above that of Earth's magnetic field, which is approximately 0.5 G. The magnitude of these large static magnetic fields falls off rapidly with distance. Many instruments now have internal shielding, which reduces the strength of the magnetic field outside of the instrument. Strong attraction occurs when the magnetic field is greater than 50 to 100 G and increases by the seventh power as the separation is reduced. However, this highly nonlinear falloff of magnetic field with distance results in an insidious hazard.

HAZARDS RELATED TO ERGONOMICS IN THE LABORATORY

General workplace hazards also apply in the laboratory. For example, laboratory personnel are often involved in actions such as pipetting and computer work that can result in repetitive-motion injuries. Working at a bench or at a microscope without considering posture can result in back strain, and some instruments require additional in-room ventilation that may raise the background noise level to uncomfortable or hazardous levels. With these and other issues such as high or low room temperatures and exposure to vibrations, it is important to be aware of and to control such issues to reduce occupational injuries. For example, microscope users may find that using a camera to view images on a screen, rather than direct viewing through the eyepiece, reduces back and eye strain. The Centers for Disease Control and Prevention (CDC) and the National Institutes of Health have information on their Web sites (www.cdc.



gov and www.nih.gov, respectively) describing specific ergonomic concerns for laboratories and proposed solutions. The CDC provides a downloadable self-assessment form to aid in evaluating these hazards. NIOSH (www.cdc.gov/niosh) and OSHA (www.osha.gov) provide information about vibration, noise levels, and other workplace hazards.

BIOLOGICAL HAZARD

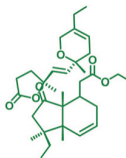
Concerns regarding biohazards arise in laboratories that handle microorganisms or materials contaminated with them. Individuals who are likely to encounter blood or potentially infectious materials at work fall under the coverage of OSHA's Bloodborne Pathogen Standard. While these hazards are commonly found in clinical and infectious disease research laboratories, they can also be present in any laboratory dealing with bodily fluids, tissues, or primary or immortalized cell lines of human or animal origin. Furthermore, biohazards are a consideration in labs utilizing microorganisms, including replication-deficient viral vectors, for protein expression or other *in vitro* applications. The risk assessment for biological toxins mirrors that of chemical agents, relying on factors such as the potency of the toxin, the quantity used, and the procedures involved in its usage.

CONCLUSION

Adherence to federal regulations, such as the OSHA Hazard Communication Standard 1910.1200, is crucial for ensuring the safe handling of hazardous chemicals in laboratories. Material Safety Data Sheets (MSDSs) are indispensable tools for communicating essential information about chemical hazards to trained personnel. However, limitations exist, including variations in MSDS quality, insufficient coverage of unique morphologies, and the challenge of distinguishing significant hazards in comprehensive lists. The Globally Harmonized System (GHS) for Hazard Communication, designed to standardize hazard communication internationally, further enhances chemical risk assessment. GHS classifies physical, health, and environmental hazards, providing a comprehensive framework for understanding and addressing risks associated with various chemicals. Laboratory Chemical Safety Summaries (LCSSs) offer valuable context-specific information for assessing risks associated with laboratory use. Labels on chemical containers serve as essential reminders of principal hazards, complementing MSDSs and LCSSs. Additional sources, such as International Chemical Safety Cards, NIOSH Pocket Guide, and databases like TOXNET, provide comprehensive data for risk assessment. Training plays a pivotal role in creating a safe laboratory environment. Scenario-based, hands-on training, coupled with case studies, helps personnel interpret and apply safety information effectively. Recognizing the diverse toxicological properties of laboratory chemicals is crucial, considering factors such as dose-response relationships, local and systemic toxic effects, and inherent toxicity. In conclusion,



the assessment of chemical hazards in the laboratory involves a comprehensive understanding of acute toxicity, physical hazards, and reactivity. Acute toxicity is categorized based on hazard levels, with special attention given to highly toxic substances. Toxins such as irritants, corrosive substances, allergens, and sensitizers pose local effects not reflected in traditional toxicological parameters. Asphyxiants, neurotoxins, reproductive toxins, and carcinogens require specialized attention due to their specific health impacts. Beyond toxicity, the evaluation of flammable, reactive, and explosive hazards is crucial in risk assessment. The laboratory personnel's risk assessment process involves identifying chemicals, consulting reliable sources, and evaluating physical hazards associated with substances and experimental conditions. Adequate precautions, including proper protective equipment, are essential when handling corrosive substances. For flammable hazards, understanding flash points, boiling points, and ignition temperatures is crucial. Reactive hazards, including water reactivity and pyrophoric properties, necessitate careful handling to avoid violent reactions. The presence of explosive compounds requires strict control, as highlighted in the table of explosive functional groups.



SUGGESTED READINGS

OSHA Hazard Communication Standard 1910.1200

Dedicated website: <http://www.unece.org>

International Chemical Safety Cards from the International Programme on Chemical Safety (IPCS, 2009)

Dedicated website: www.cdc.gov/niosh

Dedicated website: www.ilo.org

NIOSH Pocket Guide to Chemical Hazards (HHS/ CDC/NIOSH, 2007)

Dedicated website: <http://www.cdc.gov/niosh>

A Comprehensive Guide to the Hazardous Properties of Chemical Substances, 3rd edition (Patnaik, 2007).

Hazardous Chemicals Handbook, 2nd edition (Carson and Mumford, 2002)

NIOSH Databases and Information Resources (www.cdc.gov/niosh)

TOXNET through the National Library of Medicine (NLM; Dedicated website: www.nlm.nih.gov)

Dedicated website: www.cas.org

NIOSH Pocket Guide to Chemical Hazards (HHS/CDC/NIOSH, 2007)

Dedicated website: www.cdc.gov

Dedicated website: www.nih.gov

Dedicated website: www.cdc.gov/niosh

