SAFE USE OF CHEMICALS

A Practical Guide

T. S. S. Dikshith

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To my parents,

Gowramma and Turuvekere Subrahmanya Dikshith

and to

my wife, Saroja Dikshith

A hundred times every day I remind myself, that my inner and outer life depended on the labors of other men, living and dead, and that I must exert myself in order to give in the same measure as I have received and am still receiving.

Albert Einstein

Preface

Let noble thoughts come to us from every side.

Rigveda (I–89–I)

Chemical substances have become an essential part of human activities. Proper use of chemical substances help human society protect itself from hunger, thirst, famine, disease, and infection with good grains, fruits, and vegetables. Synthesis, formulations, and proper use of newer drugs and pharmaceuticals have offered the benefits of improved health care to society. In short, proper and judicious application of a variety of chemical substances has improved the quality of life. In contrast, improper use or misuse of chemical substances has resulted in health disorders and fatalities. Furthermore, improper use has caused chemical disasters both at the workplace and in the environment.

Societal development requires use of chemical substances with pragmatism, as well as proper and good management. The users of chemical substances must be well aware of the implications of improper use of a chemical substance by itself or in combination with another chemical. In fact, all chemical substances are toxic and there is no absolute safety. It is the manner of use of a chemical substance that brings either good or danger to the user, to the immediate workplace, and to the society at large.

Improper use and waste disposal of chemical substances endangers human health and causes environmental pollution and chemical disasters. The adverse health effects of chemical substances depend on many factors, including the toxicity of the candidate chemical, the duration or period of exposure, and the exposed individual's age and health status, among others. To contain the adverse health effects of chemical substances, the user must be aware of the properties and mechanisms of action. The term "toxic industrial chemical" refers to a variety of chemical substances used in industry and in various processes. Any chemical substance can be toxic or harmful to human health in some dose. Toxic industrial chemicals are known to pose risks when they are stored in large quantities in one location. An act of sabotage or an accident can result in large-scale release of toxic chemicals or their degraded products; when those living nearby breathe this air they may develop health disorders. The environment also may become polluted. Examples include a chemical explosion at Seveso, Italy, that released chlorine gas from a large tank into the surrounding air; the Love Canal disaster in Niagara Falls in the late 1970s; and the Bhopal, India, tragedy in 1984. Chemical industries along rivers and lakes or in densely populated or environmentally sensitive areas have created critical situations.

Societal progress and development depend on the knowledge and proper use of chemical substances using a pragmatic approach—certainly not by misuse or reckless imposition of bans on chemical substances. There are no safe chemical substances. Huge amounts of time, money, and human effort have been spent to identify

newer molecules for human use. These chemical molecules have been identified, synthesized, and formulated for human use in the form of drugs, pesticides, preservatives, and many other useful products. Misuse or negligence during the use and management of chemical substances will not achieve human safety. Today, imparting proper education, suitable guidance, and good training to students, workers, and society at large is very necessary to assuring human safety. The global requirement of the day is to achieve economic progress for the developing as well as the developed parts of the world.

The purpose of this book is to provide and promote basic and elementary knowledge about chemical substances, irrespective of workplace, laboratory, factory, field, or home. Timely availability of knowledge protects the health of workers by reducing the possibilities of chemical disasters. This book offers a comprehensive, integrated, speedy, and easy tool for the management of a number of chemical substances commonly used, handled, stored, and transported by a large population. The list of chemical substances includes but is not limited to industrial solvents, pesticides, metals, air pollutants, toxic gases, and drugs. The book also offers guidance to students, basic scientists, toxicologists, industrial workers, professionals, risk assessors, and regulatory agencies. Because chemical substances are ubiquitous and their application universal, these individuals often require a single standardized, comprehensive book of data for reference. The author has made every effort to collect and collate information from different published sources about a large number of chemical substances. Essentially, this book provides ready information to users at times of need.

The information on each chemical substance is concise and easy to understand. It includes the chemical name with CAS (Chemical Abstracts Service) number, the International Union of Pure and Applied Chemistry (IUPAC) name, molecular formula, synonyms and trade names, use and exposure, toxicity and health effects, whether it is carcinogenic, exposure limits, and methods of proper storage and disposal, with relevant references. Tables and appendices provide additional information. In certain chapters of this book, chemical substances are listed in alphabetical order to facilitate speedy and easy access for the reader; the classifications of chemical substances are included separately.

It is important to state here that this compilation does not discourage the use of chemical substances. Chemical substances are essential and, when they are used properly, societal development and improvement of the quality of life are possible. This book educates students, semiskilled workers in different occupations, householders, and other users about the basic realities of chemical substances, the responsibilities associated with using them, and the immediate short- and long-term consequences of improper use and negligence during handling.

The author is fully aware of the fact that, in spite of his efforts to present an up-to-date and comprehensive compilation in one place, many gaps must have occurred. The book seeks to provide an integrated, yet simple description of chemical substances commonly used, handled, stored, and transported by workers and householders. The salient features of the book include:

information on general fundamentals as well as about specific hazards and effects of chemical substances;
information about the basics of exposure and response to chemical substances in the work environment;
evaluation of toxic responses in different body systems; and
general perspectives on the problem of chemical exposure and its possible health effects.

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1 Introduction

Today, almost everyone works or lives with chemicals and chemical products. Over the centuries man has lived in a chemical age, but especially so during the past several decades. Many of the chemical substances can have deleterious effects on animals, humans, and the environment. These substances are capable of causing physical hazards (e.g., fire or explosion) or health hazards (such as systemic toxicity and chemical burns). Improper use of chemical substances causes a wide range of health hazards. It is the responsibility of the user to evaluate each chemical substance and know its potential to cause adverse health effects and pose physical hazards, such as flammability in the workplace. The manufacturers, importers, and distributors of different chemical substances must be sure that containers of hazardous chemicals leaving the workplace are properly labeled with the identity of the chemical and appropriate hazard warnings. In the workplace, each container must be marked with the identity of hazardous chemicals contained in it and must show hazard warnings appropriate for employee protection.

There are several ways to use chemicals wisely. One can reduce both the probability and consequences of accidents to negligible levels. Use of chemical substances is always associated with risks. However, these risks can be minimized with knowledge, proper use, and good practices. In other words, safety from chemical substances depends on knowledge, judicious use, safe practices, appropriate methods of engineering controls, proper use of personal protective equipment, use of minimum quantities of materials, and substitution of a less hazardous chemical substance when possible.

Chemical substances that make up the world around us include more than 100 fundamental elements, such as iron, lead, mercury, carbon, oxygen, and nitrogen. They also include combinations of different elements, acids, and salts. A process of chemical reaction is triggered, making one substance chemically convert into another. Man-made chemical compounds have changed lives. In fact, the twentieth century could well be called the "age of chemistry." Industries, factories, homes, laboratories, fields, farm yards, gardens, and city roads are flooded with aerosols, artificial sweeteners, cosmetics, detergents, dyes, paints, pesticides, pharmaceuticals, plastics, refrigerants, and synthetic fabrics, as well as many other substances. The list of chemical substances is endless. To satisfy the ever growing global demand for these products, the annual production of chemical substances, according to estimates of the World Health Organization (WHO), amounts to about $1.5 trillion. Further, reports of WHO state that approximately 100,000 chemical substances are now on the market and each year more than 1000–2000 others are added to the list.

This flood of chemical substances, however, invites questions regarding human health and environmental safety. Clearly, society is sailing into uncharted waters.

The public is a part of an experimental generation, and the full effects will not be known for decades to come. The most often affected by chemical substances and pollutants are poor, illiterate, semiskilled workers and people with little or no access to basic information about chemical substances. Many people are not fully aware of the short- and long-term possible health hazards posed by chemical substances to which they are directly or indirectly exposed daily. This increased trend and the manner of exposure to a plethora of chemical substances in workplaces or other environments cannot be ignored.

A Green History of the World points to the need for basic knowledge about chemical substances and proper management of their use. The book states that 20% of California's water wells have pollution levels, including pesticides, above official safety limits. The book states:

> In Florida, 1,000 wells have been closed because of contamination. In Hungary 773 towns and villages have water that is unfit for human consumption and in Britain ten per cent of aquifers are polluted above the safety limits set by the WHO, and in parts of both Britain and the United States tap water cannot be given to newborn babies because of high nitrate levels.[1]

Mercury is another useful but potentially toxic chemical. It finds its way into the environment through sources ranging from industrial smokestacks to billions of fluorescent lights. Similarly, lead can be found in many products, from fuel to paint and products of paint. Lead is toxic, especially to children, and prolonged periods of exposure to fumes and emissions of processes using lead can affect a child's IQ.[2] According to the United Nations Environment Program (UNEP), each year approximately 100 tons of mercury, 3800 tons of lead, 3600 tons of phosphates, and 60,000 tons of detergents enter the Mediterranean Sea as a result of human activities. Understandably, the sea is in crisis, but it is not alone. In fact, the United Nations declared 1998 "the International Year of the Ocean." Worldwide, all oceans are in trouble, particularly because of pollution. While chemical technology has provided us many products and improved the global economy, improper use and waste disposal methods have disturbed human health and caused disasters to the environment. As one newspaper columnist recently said, "Have we made ourselves hostages to progress?"[3]

1.1 CHEMICAL SUBSTANCES AND POISONING OF HUMANS

Human exposure to a variety of chemical substances and the subsequent poisonings and fatalities have caused significant global concern. In fact, recent reports indicate that as many as 350,000 people died worldwide from unintentional poisoning and more than 94% of fatal poisonings occurred in countries with low- and middle-income populations. While accurate global figures are not available, approximately a million people died as a result of suicide, and possibly as many as a quarter of these deaths resulted from ingestion of chemical substances. Pesticide-related suicides and fatalities have affected a significant percent of the global population. In fact, over

60% of successful suicides in China are the result of pesticide poisoning and over 71% in Sri Lanka.[4]

Overdoses account for a quarter of all suicides in England. Further, the number of people who survive the immediate effects of their overdose long enough to reach medical attention but subsequently die in hospital is unknown. In England, during 1997 and 1999, there were 233,756 hospital admissions for overdose, and 1149 (0.5%) of these ended in death of the patient. Of these deaths, 29% accounted for overdose suicides—7% of total suicides.[5] Around a quarter of all overdose suicide deaths occur subsequent to hospital admission. Detailed research is required to discover if better preadmission and in-hospital medical management of those taking serious overdoses may prevent some of these deaths. Proper management of chemicals can control the misuse of these chemicals.

In the light of these human health developments, there is an urgent need to educate industrial workers as well as the general public about chemical substances. Also, regulatory systems need to be updated for the collection of compatible data on human poisonings. The Intergovernmental Forum for Chemical Safety (IFCS Forum III) has already discussed these important aspects under Program Area D7 in October 2000 in Salvador da Bahia, Brazil. Collection of compatible data and categorization of chemical substances, types of poisonings, and identity (chemical structure), use, or function of different chemical substances, as well as many other aspects, need to occur to achieve safe use of chemical substances by all.

1.2 GENERAL SAFETY GUIDELINES

Before using a chemical substance, one should ask, "What would happen if…?" The answer to this question requires an understanding of the hazards associated with the candidate chemical substance, equipment, and procedures involved. The hazardous properties of the chemical substance and the intended use dictate the precautions to be observed by the user. Another important distinction is the difference between hazard and risk. The two terms are sometimes used as synonyms; however, "hazard" is a much more complex concept because it includes conditions of use. The hazard presented by a chemical substance has two components: (1) the inherent capacity to do harm by virtue of its toxicity, flammability, explosiveness, corrosiveness, and many other properties; and (2) the ease with which a chemical substance can come into contact with a person or other object of concern. These two components together determine the risk (the likelihood or probability that a chemical substance will cause harm). Thus, an extremely toxic chemical such as strychnine cannot cause poisoning if it is in a sealed container and does not have direct contact with the user. In contrast, a chemical substance that is not highly toxic becomes fatal if a large amount is ingested, so users should never underestimate the risks of chemical substances. Chemical substances such as buffers, sugars, starches, agar, and naturally occurring amino chemicals are considered nonhazardous.

Chemical safety is inherently linked to other safety issues, including laboratory procedures, personal protective equipment, electrical safety, fire safety, and hazardous waste disposal. Specific chemical substances, uses, and possible health effects are discussed in different chapters of this book. The responsibility of workers as well

as management for the safe use of chemical substances in the workplace involves (1) manner of use, (2) quantity of use, (3) purpose of use, and (4) method of waste disposal after use. In conclusion, users must be responsible and always vigilant to achieve proper management of chemical substances.

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2 Chemical Substances and Categorization

2.1 INTRODUCTION

Chemical substances include different classes and categories of materials. A very broad categorization includes industrial solvents, metals and metal compounds, pesticides, organic and inorganic dusts, fumigants, toxic gases, corrosive chemical substances, asphyxiates, irritants, oxidizing agents, neurotoxicants, nephrotoxicants, carcinogens, mutagens, and teratogens. More information on candidate chemical substances of each group is provided in other pages of the book. The following pages list, in brief, some of the chemical substances for easy identification and proper and judicious use by workers.

2.2 CHEMICALS AND CATEGORIZATION

Chemical substances are many and the classifications are several and elaborate. For purposes of easy and ready identification by common users, chemical substances are categorized as (1) industrial solvents; (2) metals and metal compounds; (3) pesticides; (4) toxic dust, fumes, gases, vapors; (5) fumes and dust of metals; (6) asphyxiates; (7) corrosive substances; (8) eye, skin, lung, and respiratory irritants; (9) neurotoxic chemicals; (10) oxidizing agents; and (11) carcinogens, mutagens, and teratogens. Chemical substances are also well classified as petrochemicals, drugs and pharmaceuticals, food additives, colors and dyes, plastics, rubber, and many others. The details of classifications and grouping of chemical substances are available in the literature.

2.2.1 Industrial Solvents

Industrial solvents are chemical substances, usually liquid, that are commonly used to dissolve unwanted substances or material. Solvents are liquids used for purposes of mixing and to dissolve other substances, such as paints, greases, wax, and oils. Solvents are found in fuels, adhesives, glues, cleaning fluids, epoxy resins, hardeners, lacquers, paints, paint thinners, primers, and even nail polish removers. Prolonged periods of exposure to some solvents (such as acetone, alcohols, benzene, gasoline, mineral spirits, methylene chloride, toluene, turpentine, and xylene) cause acute and chronic health effects. Solvents are among the most frequently used industrial chemicals because of their ability to clean grime and grease. Application of different solvents in industries and homes is very common and has become a global trend. Industrialization and, more particularly, polymers, paints, and coating industries use solvents in very large quantities around the globe. Human exposure to different solvents in workplace air and the general atmosphere is very common. The

uses, manner of exposure, health effects, and environmental impact of different solvents are discussed in other chapters of this book. More information is available in the literature.[1–6]

2.2.2 Metals and Metal Compounds

Different metals and metal compounds have been in use since the beginning of human civilization. Metals include aluminum, antimony, cobalt, copper, chromium, iron, nickel, manganese, molybdenum, selenium, tin, vanadium, and zinc. The list of toxic metals includes but is not limited to arsenic, beryllium, cadmium, hexavalent chromium, lead, and mercury. Contamination of food, water, and the air by metals, particularly lead and cadmium, has caused global concern. Several studies have shown elevated levels of lead, nickel, chromium, and manganese in children's hair.

Occupational exposure to metals (metal fume fever [MFF]) causes acute and chronic health disorders such as fever, headache, fatigue, cough, and a metallic taste. Metal fumes in workplaces have close linkages with zinc oxide, magnesium, cobalt, and copper oxide fumes. Prolonged periods of exposure to copper have also caused its accumulation in liver, brain, kidney, and cornea, leading to the classic impairment and stigmata of Wilson's disease and Indian childhood cirrhosis. In fact, chronic exposure to many of the heavy metals has been associated with human cancer. Many toxic heavy metals (e.g., lead, manganese, and cadmium), combined with prenatal or neonatal developmental insults and stress, have been reported to cause brain damage and disturb the normal functioning of essential neurotransmitters. Details on metals and health hazards are discussed in other pages of this book and in the literature.[6–13]

2.2.3 Pesticides

Pesticide is used to control pests of different kinds, such as target insects, vegetation, and fungi. Pesticides are known poisons used specifically for the control of crop pests and rodents. Some are very poisonous, or toxic, and may seriously injure or even kill humans. Others are relatively nontoxic. Pesticides can irritate the skin, eyes, nose, or mouth. The health effects of pesticides depend on the type of pesticide. The organophosphate and carbamate pesticides affect the nervous system. Others cause irritation to the skin, eyes, and mucous membranes. Several pesticides are carcinogens and some others cause disturbances to the hormone or endocrine system in the body.

Prolonged periods of exposure to high concentrations of pesticides cause (1) reproductive effects, (2) teratogenic effects, (3) carcinogenic effects, (4) mutagenic effects, (5) neurotoxicity, and (6) immunosuppression. The array of chemical substances called pesticides is grouped under different classes: for instance, organophosphate pesticides (OPPs), organochlorine pesticides (OCPs), carbamates, synthetic pyrethroids, biopesticides, and microbial pesticides. The OPPs affect the nervous system by disrupting the enzyme that regulates acetylcholine, a neurotransmitter. Many of the OCPs are known for heavy persistence in the environment and are banned or restricted from further use. The carbamate pesticides, like OPPs, also affect the nervous system by disupting an enzyme that regulates acetylcholine. However, the

enzyme activity usually is reversible. The synthetic pyrethroids form the synthetic version of the naturally occurring pesticide pyrethrin (found in chrysanthemums). Some of the synthetic pyrethroids cause adverse effects to the nervous system.

More information on pesticides and health effects is available in the literature.[6–6c] It is alarming to note that, according to reports of the National Academy of Sciences (NAS), in 1984 more than 67% of the then existing pesticides had not been properly evaluated. The NAS observed that on the basis of data, the potential risks posed by cancer-causing pesticides in our food are over one million additional cancer cases in the U.S. population alone over the next 70 years.[13,14]

2.2.4 Toxic Dust, Fumes, Gases, and Vapors

The public and, more particularly, industrial workers in workplaces, are exposed to different kinds and forms of toxic chemical substances—for instance, solids, liquids, gases, vapors, dusts, fumes, fibers, and mists. How a chemical substance gets into the body and its effect on health depend on the form or the physical properties of the candidate chemical substance. Welding fumes are a complex mixture of metallic oxides, silicates, and fluorides. Many kinds of occupations, such as welding, cutting, and allied processes, produce fumes and gases, leading to serious health effects on workers.

Fumes are solid particles that originate from welding consumables, the base metal, and any coatings present on the base metal. Exposure to toxic fumes causes irritation of eyes, skin, and the respiratory system and severe complications. Metal fumes cause toxicity with symptoms such as nausea, headaches, dizziness, and MFF. After chronic exposure to manganese fumes, industrial workers suffer deleterious health effects such as impaired speech and gait. During welding on plated, galvanized, or painted metals, fumes get generated with cadmium, zinc oxide, or lead, which are known toxicants. Toxic gases generated during material welding include carbon monoxide, nitrogen dioxides, and ozone.

2.2.4.1 Fumes and Dust of Metals

Breathing the fumes generated from the heating of heavy metals may result in MFF, which is characterized by irritation of the lungs, dry throat, chills, fever, and pain in the limbs. Cadmium fumes may cause emphysema. Exposure to hydrocarbons, chromium, beryllium, and arsenic fumes may cause lung cancer. The metal alloys as sold in solid form are generally not considered hazardous. However, with different processes, such as grinding, melting, cutting, and other activities, dust or fumes and particulates are released to the work environment. The hazards caused by these manufacturing activities become very serious, leading to metal poisoning and other health effects. Inhalation of cobalt metal fume and dust may cause interstitial fibrosis, interstitial pneumonitis, myocardial and thyroid disorders, and sensitization of the respiratory tract and skin.

Inhalation of toxic substances represents the most common means by which injurious substances enter the body. Air contaminants in the workplace present both acute and chronic dangers to health. Inhalation of toxic substances can cause serious local damage to the mucous membranes of the mouth, throat, and lungs or pass through the lungs into the circulatory system, producing systemic poisoning at sites remote

from the point of entry. Several thousand deaths per year are attributed to exposure to dust, fumes, gases, vapors, and mist in the workplace. Exposure to organic dusts such as coal dust can cause asthma, chronic bronchitis, and emphysema. Mineral dusts such as asbestos can cause asbestosis, characterized by coughing and breathlessness, or mesothelioma, a cancer of the lung lining. Exposure to toxic chemical dusts may result in irritation, bronchitis, and cancer, depending on the nature of the chemical. The poisoning effect may be rapid or slow, depending upon the amount of the substance inhaled and its toxicity, as well as the duration of exposure.

Exposure to acid and alkaline gases such as hydrochloric acid and ammonia will cause extreme local irritation to the lungs. Some gases such as carbon monoxide may pass into the blood stream and cause systemic injuries. Vapors are the gaseous state of liquids. Inorganic vapors are generally harmless. Exposure to organic vapors, however, may cause nose and throat irritation, pulmonary edema, or cancer. Mists are fine suspensions of liquid in air and can cause chemical burns of the lungs, lung disease, and cancer. Common mists include sulfuric acid and sodium hydroxide from oven cleaners. The presence of environmental pollutants in the Arctic is particularly troubling because the Arctic ecosystem is fragile and slow to recover from impacts. Toxic chemicals accumulating in the Arctic include persistent organic pollutants (POPs), such as DDT (dichloro-diphenyl-trichloroethane) and PCBs (polychlorinated biphenyls), and heavy metals, including mercury, cadmium, and lead. While some heavy metals provide essential micronutrients, others are naturally toxic. All metals have serious negative effects at high concentrations. For more information refer to the literature.[6,15]

2.2.5 Asphyxiates

Asphyxiates paralyze the respiratory center and weaken the body. They disturb the maintenance of an adequate oxygen supply to different systems in the body. The most common asphyxiates are carbon dioxide, carbon monoxide, cyanides, helium, nitrogen, and nitrous oxide.

2.2.6 Corrosive Substances

Corrosive chemical substances are those that cause visible destruction or permanent changes in human skin tissue at the site of contact or are highly corrosive to steel. These chemical substances on contact with living tissue or on leakage cause severe damage. On contact with human tissue, most corrosive substances produce chemical burns, while certain substances, such as chromic acid, produce deep ulceration. Many corrosive substances have a defatting action on the skin and may cause dermatitis. Corrosive substances cause material damage during transport. Inhalation of corrosive mists (or dusts) causes irritation and burns to the inner lining of the windpipe and lungs. The majority of these are common basic chemicals used extensively in all fields of industry.

In the first instance, all corrosive chemical substances must be clearly labeled with the correct chemical name. Corrosive chemical substances include strong acids, bases and alkalis, dehydrating agents, halogens, organic halides, esters, and many

other substances. The concentrations of acids and bases and alkalis could be listed as follows: acetic acid > 25% concentration, hydrochloric acid > 25% concentration, nitric acid > 20% concentration, chromic acid, hydrofluoric acid, perchloric acid > 10% concentration, sulfuric acid > 15% concentration, fuming sulfuric acid, ammonium hydroxide > 35% by weight of gas, potassium hydroxide (caustic potash), sodium hydroxide > 5% concentration, aluminum chloride, bromine, phosphorous trichloride, potassium bifluoride, sodium hypochlorite > 10% concentration, and zinc chloride.

All containers, pipes, apparatuses, installations, and structures used in the manufacture, storage, transport, or use of these substances should be protected by suitable coatings impervious to corrosives. All containers or receptacles should be clearly labeled to indicate their contents and should bear the danger symbol for corrosives. In Australia, the labeling of these containers should be in accordance with the National Code of Practice for the Labeling of Workplace Substances, which replaces the National Occupational Health and Safety Commission's Guidance Note for the Labeling of Workplace Substances. Adequate ventilation and exhaust arrangements, whether general or local, should be provided whenever corrosive gases or dusts are present. The most satisfactory method of ensuring worker protection and safety is to prevent contact with corrosive substances and use suitable personal protective equipment (PPE). Students and workers using corrosive substances must always wear eye protection in the form of safety glasses.

2.2.7 Irritants

Irritants are chemical substances or agents that cause inflammation of the body surface on contact. Irritant chemical substances cause changes in the mechanics of respiration and lung function and may cause adverse effects to the eyes, skin, throat, and lungs (respiratory irritants).

2.2.7.1 Eye and Skin Irritants

Ammonia, alkaline dusts and mists, hydrogen chloride, hydrogen fluoride, halogens, nitrogen dioxide, ozone, phosgene, and phosphorous chloride can irritate the eyes and skin.

2.2.7.2 Lung and Respiratory Irritants

Lung irritants cause damage to the pulmonary tissue. These include but are not limited to acetic acid, acrolein, formaldehyde, and formic acid and are classified as primary and secondary irritants. The primary irritants exert local effects—for example, acid fumes cause burning effects on the lungs. Secondary irritants, such as mercury vapors, cause local irritation as well as systemic effects after absorption. Prolonged periods of lung irritation produce acute pulmonary edema. Symptoms include shortness of breath and coughing that produces large amounts of mucous. Reactions to some chemical substances also cause allergic sensitization with asthmatic-type symptoms. It is important that users note that short-term exposure to irritant

chemical substances is usually reversible and causes no permanent damage, while systemic poisoning may persist and cause permanent damage.

The solubility of irritant gases influences the degree of toxicity to lungs and parts of the respiratory tract. For instance, gases such as ammonia, hydrogen chloride, and sulfur dioxide are readily soluble and cause irritation of the upper respiratory tract. In contrast, insoluble gases such as carbon monoxide and phosgene travel deeply into the lungs and cause irritation of the bronchi and alveoli or air sacs. Soon after absorption into the blood stream, these gases cause deleterious effects to various organ sites. Exposure to chlorine and hydrogen sulfide, for instance, affects the entire respiratory tract.

2.2.8 Neurotoxic Chemicals

Exposure to neurotoxicants or neurotoxic chemical substances causes severe adverse health effects to the nervous system, which is very sensitive to organometallic compounds and sulfide compounds. These compounds disrupt the normal functioning of the central nervous system, peripheral nerves or sensory organs, and the conduction of nerve impulses. Thus, chemical substances are considered neurotoxicants when they induce a consistent pattern of neural dysfunction. The chemical substances include but are not limited to carbon disulfide, manganese, methyl mercury, organic phosphorous insecticides, tetraethyl lead, thallium, and trialkyl tin compounds.

2.2.9 Oxidizing Agents

Oxidizing chemicals are materials that spontaneously react and evolve oxygen at room temperature or with slight heating, or promote combustion. Oxidizing chemicals include peroxides, chlorates, perchlorates, nitrates, and permanganates. Strong oxidizers are capable of forming explosive mixtures when mixed with combustible, organic, or easily oxidized materials. These chemical substances require careful handling, storage, and disposal. These chemical substances cause hazards of fires, explosions, injuries, and even death because of carelessness or negligence during use.

It is well known that perchloric acid, a powerful oxidizing agent, reacts violently and explosively with any organic compound or reducing agent. Strong oxidizing agents, such as chromic acid, should be stored and used in glass or other inert, and preferably unbreakable, containers. Also, for the storage of perchloric acid, corks or rubber stoppers must never be used. Reaction vessels containing appreciable amounts of oxidizing materials should never be heated in oil baths, but rather on a heating mantle or sand bath. The primary hazard of oxidizing agents is the ability to act as an oxygen source, which is especially hazardous during fire situations. These materials present a fire and explosion hazard when in contact with organic or combustible materials. All contact with organic or combustible material must be avoided. In fact, the primary consideration in the storage of these materials is that they must be isolated from all flammable or combustible material. The common examples are chlorate, permanganate, inorganic peroxide, nitrocarbonitrate, or a nitrate that yields oxygen readily to stimulate the combustion of organic matter (see Tables 2.1 and 2.2).

TABLE 2.1
Oxidizing Chemical Substances and Agents

Aluminum nitrate	Ammonium permanganate
Ammonium perchlorate	Potassium nitrate
Ammonium persulfate	Potassium persulfate
Barium chlorate	Potassium permanganate
Potassium dichromate	Barium nitrate
Potassium bromate	Zinc peroxide
Silver nitrate	Sodium carbonate peroxide
Barium peroxide	Sodium chlorate
Bromine	Sodium perchlorate
Sodium chlorite	Sodium nitrate
Sodium peroxide	Sodium perborate
Sodium nitrite	Sodium perborate tetrahydrate
Dibenzoyl peroxide	Sodium dichloro-*s*-triazinetrione
Sodium dichromate	Sodium persulfate
Sodium perchlorate monohydrate	Calcium hypochlorite
Calcium chlorate	Calcium peroxide
Calcium nitrate	Chromic anhydride
Chlorine trifluoride	Cupric nitrate
Chromic acid	Fluorine
Hydrogen peroxide (8–27.5%)	Lithium hypochlorite
Lead nitrate	Magnesium nitrate
Lithium peroxide	Magnesium perchlorate
Magnesium peroxide	Strontium chlorate
Strontium nitrate	Strontium peroxide
Nickel nitrate	Zinc chlorate
Nitric acid (<70% concentration)	Nitrogen trioxide
Perchloric acid (<60% concentration)	

TABLE 2.2
Oxidizing Liquids and Solids

Bromine	Bromates
Chlorates	Chlorinated isocyanurates
Dichromates	Chromates
Hypochlorites	Hydroperoxides
Ketone peroxides	Inorganic peroxides
Nitric acid	Nitrates
Perborates	Nitrites
Perchloric acid	Perchlorates
Permanganates	Periodates
Peroxyacids	Peroxides
	Persulfates

2.2.10 Carcinogens, Mutagens, and Teratogens

Carcinogens are chemical substances capable of increasing the risk of cancer after prolonged periods of exposure. Teratogens are hazardous chemicals capable of causing an increased risk of birth defects in children of exposed workers. Precautions and prudent practices are very essential during the use of these chemical substances. Some chemical substances have been classified as known carcinogens and teratogens, while others are suspected carcinogens and teratogens. Students and workers must reduce direct exposure to these chemical substances at all levels of work through good work habits, responsibility, and common sense. Workers and work areas using carcinogens, mutagens, and teratogens should be well equipped with proper protocols for handling, storing, disposal, and emergency procedures.

2.2.11 Chemicals and Fire Hazards

Some of the flammable and combustible materials are categorized as:

class A: fires in ordinary combustible materials (e.g., wood, cloth, paper, rubber, and many plastics);
class B: fires in flammable liquids, oils, greases, tars, oil-base paints, lacquers, and flammable gases;
class C: fires that involve energized electrical equipment where the electrical conductivity of the extinguishing medium is of importance; when electrical equipment is de-energized, extinguishers for class A or B fires may be safely used; and
class D: fires in combustible metals such as potassium, sodium, lithium, magnesium, titanium, and zirconium.

2.3 CONCLUSION

More information on different chemical substances, as well as the categorization, kinds of uses, and possible health effects, is available in other chapters of this book and in other published literature.[3,4,10,13,16–18] To protect themselves and the living environment, students and workers must be well aware of potential toxicity and the implications of negligence and improper use. The different chapters of this book discuss specific chemical substances and their uses, toxicity, health effects on animals and humans, and the importance of taking precautions during use.

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3 Elements of Toxicology and Chemical Safety

3.1 INTRODUCTION

Toxicology is the branch of science concerned with understanding the gross and intrinsic capabilities of a chemical substance on biological systems—that is, on plants, animals, and humans. Toxicology is a multidisciplinary science and closely interrelated with many other branches of science. Chemical substances are required for health, progress, and societal development. In the very close linkage with an array of chemical substances and societal development, human health cannot be ignored. Therefore, thinkers of the past and present around the world framed regulations about the manners and methods of use of chemical substances. There are no safe chemical substances and all are toxic in one way or the other. No chemical substance is absolutely safe. In fact, the safety of a chemical substance depends upon the concentration and manner of exposure and use. This is important and should be very well understood and remembered by all students, industrial workers, and household users who handle, store, transport, and dispose of different chemical substances. Improper and negligent use and management of chemical substances cause injury, death, and disaster. The present chapter focuses on and briefly discusses the elements of toxicology vis-à-vis effects of chemical substances and their use.

Chemical substances as and when they are marketed for human use in the form of drugs, food additives, cosmetics, and many others items require safety data and detailed quality evaluations. To generate quality data about the candidate chemical substance, different countries and international regulatory agencies have framed elaborate procedures. By understanding the basics of toxicology and correctly adhering to regulations and observing precautions, the benefits of chemicals would enrich human society and free it from hunger and disease.

3.2 TOXICOLOGY STUDIES

Toxicological studies are essential to understanding the possible adverse effects that a candidate chemical or combination of chemicals may cause to animals, humans, fauna, and flora, and to make relevant, reliable, reproducible predictions. The generation of toxicological data after conducting experiments with short- and long-term exposure in species of organisms and laboratory animals using different routes of exposure provides substantial and basic guidance to establish safe levels of chemicals. Depending on route of exposure, the duration of exposure, and the quantity of the test chemical, the experimental animals develop signs and symptoms of toxicity. The test provides information about

- the nature of toxicity of the test chemical substance;
- the dose and concentration of the chemical substance that cause adverse effects in the animal;
- the toxicity profile in male and female test animals, oral, dermal, and respiratory routes;
- the immediate and long-term health effects; and
- the effects of two or more chemicals as additives or synergistic effects.

3.2.1 History of Toxicology

What is toxicology? What is the history of toxicology? What is the importance of toxicology to modern society? The answers to these questions can provide a better and more meaningful understanding of the management of chemical substances to protect health. Toxicology is a scientific discipline many thousands of years old. Reports trace the history of toxicology dating from 3000 BC to the Middle Ages (476–1453) to the periods of the Renaissance (1400–1600) and subsequent years. The history of toxicology needs to be traced along with the global development. To trace and document the history of toxicology to certain parts of the world alone is both incomplete and incorrect. It is therefore necessary to know the origin and global development of the science of toxicology.

The science of toxicology has a very solid and authentic historical base. In fact, elementary knowledge about toxicology dates back to early times of human history and civilization. India is well known as the birth place of ayurveda, the very ancient Indian system of medicine and human health care. Although recent documents indicate ayurveda's origin as ca. 5000 BC, according to the Indian scriptures, which have stood the test of time, dates extend to much earlier periods of human history. The ayurveda system of medicine and health care has valid links to the ancient books of wisdom—the *Vedas*. The word *Veda* in Sanskrit (*Samskruta*) means knowledge, and the language is Samskruta/Sanskrit, or *Devanagari* script. The term *ayurveda* comes from two words: *ayuh* (meaning life) and *veda* (meaning knowledge—the knowledge of longevity and life). Thus, ayurveda originated in India long ago in the prevedic period—the *Rigveda and Atharva-veda* (5000 years BC). The texts of ayurveda, such as Charak Samhita and Sushruta Samhita were documented about 1000 years BC. As has been documented elsewhere, ayurveda is one of the oldest systems of health care, describing both the preventive and curative aspects of different herbal medicines for improvement in the quality of life. Ayurveda in a most comprehensive way describes medication for human ailments and bears a close similarity to the principles of health care of the modern era propounded by the World Health Organization.

The ancient seers of India in the *Astanga Hrudaya of Vagbhata* and others have paved the way for the understanding of the concept of human health. Human ailments, including poisoning, are the areas covered by ayurveda. In brief, ayurveda discusses the combination of four essential parts of the system—namely, human body, mind, senses, and the soul—and unravels the effect of toxic chemical substances on the body and the manner of its elimination by adopting different processes. Further, the history of indigenous Indian medical science along with the

Indus Valley civilization dates back to more than 3000 BC. The most well planned cities of Harappa and Mohenjodaro exemplify not only the rich cultural heritage of India, but also its advanced systems of hygiene and human health care.[1–4]

For the people of the Indian subcontinent in particular the way of life and the association with food and drink was quite different and stringent as compared to the human populations in occidental regions of the world. The elementary knowledge about the use and restricted use of certain substances and food items and drinks was the guiding principle for the maintenance of good health. This is very evident in the dictum of the native language of India, Samskruta. The dictum may be grouped under health and hygiene or the Yoga system of philosophy—a path to lead a life of righteousness. The dictum in Samskruta runs as follows: *ati sarvatra varjayet,* meaning avoid excess in eating, drinking, and/or other activities, anywhere, anytime. Even *nector* (ambrosia), the drink of the angels, when consumed in excess can cause adverse effects! There are many regulations well documented for human health care. The dictum *langanam parmaushadham,* meaning fasting or moderate food before bed at night, is the best medicine to maintain a proper and good health and *madyam na pibeyam* means not to be alcoholic. In fact, *Rigveda,* the ancient scriptures of India, clearly mention *visha,* a term in Sanskrit for poison. Similar references are also made in hymns to poison liquids that produce ecstasy. In the Purana legends of India (ancient scriptures), mention of poison is made during the mythological process of churning the cosmic ocean before the drink (*amruta*) of immortality is won.

Much later (1493–1541), Paracelsus, the father of modern toxicology, pronounced a dictum of his own: *Sola dosis facit veneum* ("only the dose makes the poison"). "All substances are poisons, there is none which is not a poison. The right dose differentiates a poison from a remedy." In other words, no substance is absolutely safe. What a glorified commonness between ancient thinkers from India very much earlier in history and of the West in later periods, without knowing each other during the periods of world history. This is the glorious saga of the global history of toxicology.[4]

In the Western world the ancient Greeks were probably the first to dissociate medicine from magic and religion. Important and valuable contributions of several thinkers improved the quality of human health and our understanding in toxicology. Some of the important ones include:

- Shen Nung, 2696 BC: the father of Chinese medicine, noted for tasting 365 herbs. He wrote the treatise *On Herbal Medical Experiment Poisons* and died of a toxic dose.
- Ebers Papyrus, 1500 BC: the oldest well preserved medical document from ancient Egyptian records dated from approximately 1500 BC contains 110 papyrus pages on anatomy and physiology, toxicology, spells, and treatment.
- Homer, 850 BC: wrote of the use of arrows poisoned with venom in the epic tales of *The Odyssey* and *The Iliad.* The Greek word *toxikon* is arrow poison.
- Hippocrates, 460 BC: a Greek physician born on the island of Cos, Greece. He became known as the founder or father of modern medicine and was regarded as the greatest physician of his time. A person of many talents, he named cancer using the Greek word *karkinos* (crab) because of the creeping,

clutching, crab-claw appearance of cancerous tissue spreading into other tissue areas. He moved medicine toward science and away from superstition He was also noted for his oath of ethics still used today.

- Plato, 427–347 BC: reported the death of Socrates (470–399 BC) by hemlock (*Conium maculatum*).
- Socrates' death by ingesting hemlock, 399 BC: Socrates was charged with religious heresy and corrupting the morals of local youth. The active chemical used was the alkaloid coniine, which, when ingested, causes paralysis, convulsions, and potentially death.
- Aristotle, 384–322 BC: familiar with the venom of jellyfishes and scorpion fishes.
- Mithridates VI, 131–63 BC: from a young age, fearful of being poisoned. He went beyond the art of poisons to systematically study how to prevent and counteract poisons. He used both himself and prisoners as "guinea pigs" to test his poisons and antidotes. He consumed mixtures of poisons to protect himself, which is the origin of the term "mithridatic." The term *Mithridatism* is well known in pharmacology. It is named after Mithridates when he was king of Pontus (112–63 BC) and an enemy of the Roman Empire. To avoid his assassination, he took small doses of poison to immunize himself against it. He was the first to develop antidotes in his quest of the universal antidote.
- Sulla, 82 BC: *Lex Cornelia de sicariis et veneficis*—law against poisoning people, including prisoners; it was forbidden to buy, sell, or possess poisons.
- Aulus Cornelius Celsus (25 BCE–AD 50: promoted cleanliness and recommended the washing of wounds with an antiseptic such as vinegar. He published *De Medicina,* which contained information on diet, pharmacy, surgery, and preparation of medical opiods.
- Pedanius Dioscorides, 40–90 CE: Greek pharmacologist and physician in the time of Nero who wrote *De Materia Medica,* the basis for the modern pharmacopeia that was used until 1600 CE.
- Devonshire Colic, 1700s, Devonshire, England: High incidence of lead colic among those who drank contaminated cider. The apple press was constructed partly of lead. Discovered and described in the 1760s by Dr George Baker.
- Ramazzini, 1700: documented the possible preventive measures to control industrial hazards among workers.
- John Jones, 1701: extensively researched the medical effects of opium.
- Richard Meade, 1673–1754: wrote first English language book dedicated to poisonous snakes, animals, and plants.
- Percivall Pott, 1775: born in 1714 and apprenticed to Edward Nourse, made some groundbreaking discoveries in the fields of cancer research and surgery techniques. He discovered the link between occupational carcinogens and scrotal cancer in chimney sweeps and wrote multiple scientific articles in his lifetime.
- Friedrich Serturner, 1783–1841: first successful scientist in isolating morphene crystals from the poppy plant—in effect, creating a much stronger and more effective painkiller.

- Francois Magendie, 1783–1855: born in France, researched the different motor functions of the body in relation to the spine, as well as nerves within it. In addition, he researched the effects of morphine, quinine, strychnine, and a multitude of alkaloids. Noted as the father of experimental pharmacology.
- Louis Lewin, 1854–1929: German scientist who took up the task of classifying drugs and plants in accordance with their psychological effects. The classifications were Inebriantia (inebriants), Exitantia (stimulants), Euphorica (euphoriants), Hypnotica (tranquilizers), and Phantastica (hallucinogens).
- Serhard Schrader, 1903–1990: Born in Germany, chemist Schrader accidentally developed the toxic nerve agents sarin, tabun, soman, and cyclosarin while attempting to develop new insecticides. As a result, these highly toxic gases were utilized during World War II by the Nazis. He is sometimes called the "father of the nerve agents."

For more information, refer to the literature.[5,5b]

3.2.2 Branches of Toxicology

Chemicals are used extensively in industries, homes, and crop fields to meet growing challenges for healthy living. It has been reported, however, that a vast majority of chemicals lack basic toxicity data and this has caused concern. Generation of quality data on the toxicity and safety of chemical substances, proper evaluations, and meaningful interpretations to human health and environmental safety demand the support of specialized branches of science. In simple terms, the chemical substance under test has to pass through different branches for evaluation. These are (1) analytical toxicology, (2) aquatic toxicology, (3) biochemical toxicology, (4) clinical toxicology, (5) ecotoxicology, (6) environmental toxicology, (7) epidemiological toxicology, (8) genetic toxicology, (9) immunotoxicology, (10) nutritional toxicology, (11) mammalian toxicology, and (12) regulatory toxicology and many other related branches.

Recent advances in toxicology and technology have now taken yet another important turn with the emerging discipline of nanotechnology and nanotoxicology.[5a] In fact, nanotechnology is one of the top research priorities of the U.S. government. Nanotechnology involves research and technology development at the atomic, molecular, or macromolecular level, in the length scale of approximately 1–100 nm. This technology creates and uses structures, devices, and systems that have novel properties and functions because of their small and/or intermediate sizes and their novel ability to be controlled or manipulated on the atomic scale.

The nanomaterials thus manufactured in different industries—particularly drugs and pharmaceuticals—might pose risks to human health and other organisms due to their composition, reactivity, and unique size. Nanotechnology research and development, particularly in medical research, work at the micro- and nanoscale levels to develop new drug delivery methods, therapeutics, and pharmaceuticals. In such areas of research it is equally important to consider the potential interactions of nanomaterials with the environment and the associated risks. This involves studying the effects of natural nanoparticles in the air and soil, life cycle aspects of manufactured nanomaterials, and their fate and transport. Risk assessment also includes studies

on the toxicity of natural and manufactured nanomaterials, as well as their routes of exposure to humans and other organisms and potential for bioaccumulation. Also, the nanoscale colloidal particles thus produced are involved in the transformation and transport of metals, toxic organic compounds, viruses, and radionuclides in the environment because nanomaterials have been found to cause toxic responses in test animal systems. In fact, data on the toxicology of nanoparticles and nanotubes (tiny carbon tubes) are very sketchy. The nanoparticles perhaps have undesirable effects on the lungs and other body systems. Nanoparticles in food may cross into the gut lymphatic system. Nanoparticles that are inhaled have been known to travel from nasal nerves to the brain and cause health disorders.

The nanomaterials and the structures thus formulated with characteristic dimensions (approximately 1–100 nm) contain a variety of unique and tunable chemical and physical properties. In fact, these properties have made the nanoparticles central components of the emerging global technologies. The use of nanotechnology is increasing. Its potentially adverse effects on biological systems with particular reference to human health, however, have not been adequately understood. In order to accurately conduct hazard assessments, there is a need to know the concepts that apply to pathways of dermal, oral, and respiratory exposure with reference to nanomaterials. This gains added importance in the study of biological systems that include but are not limited to membrane transfer, screening methods, and impact on major body organs and systems.

While there are differences in the methods of data generation from one branch to another, all branches are interrelated to provide complete data about the toxicity and safety of a candidate test chemical substance vis-à-vis human safety. Toxicity of a chemical is the result of several reactions and interactions between the candidate chemical and its metabolites and the cellular receptors. These include enzymes, glutathione, nucleic acids, hormone receptors, and the like. The degree of toxicity of a chemical could be explained as follows:

$$\text{Toxicity C Ar (chemical) (receptor)},$$

where

Ar = the specific affinity of the receptor for the toxic chemical C. The toxicity of a chemical can also be expressed as toxicity = k (C) (R) Ac, where toxicity is dependent upon C, R, and Ac
C = concentration of the candidate chemical in the tissue
R = concentration of the endogenous receptor of the tissue
Ac = affinity of the receptor for the chemical

The toxicological evaluations related to human safety of chemical substances are a very complex process involving the determination of the intrinsic toxicity and hazard of the test chemicals. Subsequently, this evaluation leads to determining and establishing a "no observed effect level" (NOEL): the highest dose level tested experimentally that did not produce any adverse effects. This dose level then is divided by a safety factor to establish an acceptable daily intake (ADI) of the candidate chemical substance. The ADI value is normally based on current research and

long-term studies on species of laboratory animals with several doses, including high doses, and observations of humans. Subsequently, the NOEL is scaled by a safety factor based on judgment, experience, and international convention. Typically, the safety factor ranges between 100 and 1000, depending on the biological relevance and severity of the observed effect and to extrapolate the differences between test animals and humans. This provides a substantially lower level and thus a large margin of safety for humans.

ADI is a measure of a specific chemical substance—the pesticide residue or a food additive—in food, beverages, or drinking water that can be ingested over a lifetime period and without an appreciable health risk. ADIs are expressed by body mass, usually in milligrams per kilogram of body mass per day. The higher the value of ADI is, the safer is the chemical substance in food or water and for regular ingestion. In fact the concept of ADI is a measure to indicate the toxicity from long-term exposure to repeated ingestion of chemical substances in foods. This concept was first introduced in 1957 by the Council of Europe and later the Joint Expert Committee on Food Additives (JECFA) of the U.N. Food and Agricultural Organization (FAO) and the World Health Organization. This internationally accepted concept is applied when estimating safe levels of food additives, pesticides, and veterinary drugs.

3.2.3 Types of Toxicological Studies

All kinds of chemical substances have the intrinsic property of toxicity in one way or another, depending on the quantities of the chemical substance involved, system conditions, and nature of the surroundings, to mention a few. The purpose of the toxicological studies is to define the biological effects of the different chemical substances commonly used by humans. Further, the studies are also required to understand the intrinsic properties of chemical substances on children, animals, and the living environment. The regulatory agencies of different countries require information on doses of the test chemical substance that produce adverse biological effects in species of test animals as well as doses that cause no significant toxicological or pharmacological effects (NOEL). The spacing of the doses also provides an assessment of the dose–response relationship.

3.2.3.1 Acute Toxicity

Acute toxicity tests in laboratory animals are conducted to generate data of the test chemical and its ability to cause systemic damage as a result of a one-time exposure to relatively large amounts through a specified route of exposure. The test substances in specific amounts either as one oral dose or multiples within 24 hours are administered to the animals. Chemical substances that are acutely toxic cause damage in a relatively short time (within minutes or hours). Exposure to a single concentrated test chemical substance induces irritation, burns, illness, and other signs and symptoms of toxicity, including death (Appendix 3.1). Commonly used chemicals, such as ammonia and chlorine, cause severe inflammation, shock, collapse, or even sudden death when inhaled in high concentrations. Corrosive materials such as acids and bases may cause irritation, burns, and serious tissue damage if splashed onto the skin or eyes. Exposure to chemical substances, development of symptoms of poisoning,

methods, standard procedures, and estimation of LD_{50} values are available in the literature.[4,4a,4b,8–14]

3.2.3.2 Chronic Toxicity

Chronic toxicity studies provide information on the long-term health effects of chemical substances. Adverse health effects in exposed animals and subsequent severe damage are known to occur after repeated exposure to low doses over a period of time. The slow accumulation of mercury or lead in the body or after a long latency period from exposure to chemical carcinogens is an example. Chronic or prolonged periods of exposure to chemical substances may also cause adverse effects on the reproduction and behavior of animals and humans. The symptoms caused after chronic exposure usually differ from those observed in acute poisoning from the same chemical. In fact, when exposed to low concentrations of chemical substances, as is the case with chronic toxicity studies, the industrial worker and common public are unaware of the exposure.

Chronic toxicity also includes exposure to embryotoxins, teratogenic agents, and mutagenic agents. The embryotoxins are substances that cause any adverse effects on the fetus (death, malformations, retarded growth, functional problems). Teratogenic compounds specifically cause malformation of the fetus. Examples of embryotoxic compounds include mercury and lead compounds. Mutagenic compounds can cause changes in the gene structure of the sex cells that can result in the occurrence of a mutation in a future generation. Approximately 90% of carcinogenic compounds are also mutagens.

The regulatory agencies of different countries of the world require toxicity profiles of candidate chemical substances. It is mandatory that all such data (1) be generated through a battery of genetic toxicity tests about the chemical substances, (2) involve a 90-day feeding study both in a rodent species (usually the rat) and in a nonrodent mammalian species (usually the dog), (3) show a two-generation reproduction study with a teratology component in rats, and (4) include other specialized testing studies to define adequately the biological effect of the test chemical substance. The specialized studies include testing for (1) neurotoxicity, (2) immunotoxicity, and (3) effects following in utero exposure. The regulatory agencies also advocate and require data on toxicity tests performed for safety evaluation of direct food additives, as well as color additives used in food and food products.

The Organization for Economic Co-Operation and Development (OECD) Guidelines for the Testing of Chemicals are a collection of the most relevant internationally agreed-upon testing methods used by governments, industries, and independent laboratories to assess the safety of chemical products to man and animals. These guidelines represent a basic set of important tools that are primarily for use in regulatory safety testing and subsequent chemical product notification and chemical registration in different governments around the world.[5b]

The details of several other toxicological tests (namely, repeated-dose toxicity, subchronic toxicity, chronic toxicity, genotoxicity, mutagenicity, teratogenicity, carcinogenicity, neurotoxicity, and ecotoxicology) and the methods, purposes, and importance of safety evaluation studies to achieve human health have been discussed

in the literature.[4,4a,9–14] Humans are exposed to chemical substances normally through contamination, food poisoning, accidental ingestion, skin absorption, and/or respiratory route. To generate toxicity data, species of laboratory animals are exposed to test chemicals through the three major routes. However, more often than not, chemical substances enter through more than one route (e.g., skin absorption, accidental ingestion, and inhalation) into the bodies of industrial workers who are negligent during work.

To generate data on the toxicity profile of the test chemical substance and for further extrapolation of the data to human situations, other routes of exposure have also been used in laboratory animals. These routes include (1) inhalation (breathing in), (2) absorption (through the skin or eyes), (3) oral ingestion (eating, swallowing), (4) transfer across the placenta to the unborn baby, (5) intravenous (injection into the vein), (6) intramuscular (injection into the muscle), (7) subcutaneous (injection under the skin), and (8) intraperitoneal (injection inside the membrane that lines the interior wall of the abdomen). These routes are advocated by the regulatory authorities of governments for the generation of quality data about chemical substances and drugs and subject to specific data requirements. The laboratory animals used for testing should represent the species in which the drug will be used. The most sensitive breed or class of test animal should be selected for testing. The species of test animals should be free of disease and not exposed to environmental conditions and environmental pollutants.

Additional experimental parameters should be included in the animal safety studies when they might reveal suspected adverse properties of the test chemical substance or product. This is to know the species sensitivity to the test product or related drug product. The test animals should be properly acclimated to the study environment. Subsequent studies should be adequately designed, well controlled, and conducted by qualified investigators to generate meaningful data. Further, the safety evaluation of the test chemical substances should be identical to the product intended to be marketed, meaning (1) the same chemical substance, (2) same particle size, and (3) the same formulation, if any. Because the Center for Veterinary Medicine (CVM) regulates the manufacture and distribution of food additives and drugs that are given to animals, a discussion between the sponsor and CVM prior to use of an alternative drug product is recommended.

The routes of administration should be the same as proposed in the protocol as well as by labeling. This, however, as in some of the studies, requires modifications (e.g., drench in lieu of medicated feeds). In order to minimize autolytic decomposition, necropsy should be performed promptly after death on all animals that die during the study. The necropsy should be performed by a qualified and experienced person. A complete physical examination should be performed, and baseline data should be collected by a qualified and trained worker. Data should be obtained prior to the start of the trial and at reasonable, predetermined intervals thereafter in accordance with the study protocol.

The clinical observations should be recorded twice daily, 7 days a week, during the entire study period, or according to the study protocol. Appropriate clinical pathologic procedures should be conducted on all test groups. This is required on all animals in each group or, when appropriate, on a representative number (usually

one half or a previously agreed upon number) of animals preselected at random from each group and at predetermined intervals and described in the study protocol.

After the completion of studies, tissues should be collected and preserved for histologic examination. Again, all animals or a representative number (usually one half or a previously agreed upon number) from each group is selected for further studies. All or selected tissues of test animals exposed to the highest dose treatment and from control groups should be examined for possible histological changes. Wherever microscopic lesions are observed, the corresponding tissues of the test group from the next lower treatment group should be examined until a NOEL is established.

Documentation of all studies should be made indicating the representative test conditions and the manner of use of the test chemical substance. It is very important to remember that more often than not, the toxicological effects observed in animals and humans caused by chemical substances involve various modulating factors. Over the years, the potential health risks that might be caused by chemical substances acting in combination have been found to be important. In fact, the interaction between chemical substances does take many forms. Such interactions between chemical substances have become very relevant to determine the potential health risks vis-à-vis human safety. Some of the known and common forms of interactions include the following four categories:

An *additive* effect is one in which the combined effect of two chemical substances is equal to the sum of the effects of each (2 + 2 = 4).

An *antagonistic* effect occurs when the toxic effect of the combination of chemical substances is less than what would be predicted from the individual toxicities. The antagonistic effect or antagonism is like adding 1 + 1 and getting 1 as the result.

A *synergistic* effect occurs when the combined toxic effect of two chemical substances is much greater or worse than the sum of the effects of each by itself. Synergism is similar to adding 2 + 2 and getting 5 as the result.

Potentiation is the ability of one chemical substance to enhance or increase the simple summation of the two expected activities (1 + 0 = 1).

The toxicological interactions among chemical substances depend on the chemicals present, their mode of action, and their concentrations. Of the four types of interactions, additive effects are the most plausible. This requires that the chemicals act through similar mechanisms and affect the same target tissue. For instance, the (combined) action of two or more chemicals causing irritation effects is often an added effect rather than attributable to any one candidate chemical substance.

It is also important to remember that while tissue irritation studies in laboratory animals are conducted using different chemical substances including products of cosmetics or injectable drugs, the protocol should include data on the product vehicle and at least two times the use level concentration of the active ingredient. The same volume of both preparations should be administered to all animals of the experimental groups. Observation should be made about tissue inflammation, swelling, necrosis, and other reactions.

3.2.4 Influencing Factors

The toxicological effect of any chemical substance is dependent on a number of factors. In other words, toxicological tests using species of laboratory animals and generation of data are modulated by different important influencing factors. The data so generated offer valuable guidance for the interpretations and extrapolation of laboratory animal data to human situations in the workplace and elsewhere. In brief, these include but are not limited to (1) species and strains of test animals, (2) sex of the test species, (3) age of the test animal, (4) dose of the test chemical substance, (5) nutritional and health status of the test animal, (6) routes of exposure, (7) mode of interactions of two or more chemicals to cause synergistic effects and produce toxic effects that are much greater in combination or individual effect, (8) additive effect, and/or (9) antagonistic effect.

3.2.4.1 Dose–Time Relationship

The most important factor is the dose–time relationship. The amount of a substance that enters or contacts a person is called a dose. An important consideration in evaluating a dose is body weight. Dose is the quantity of a chemical substance that a surface, plant, or animal is exposed to. Time means how often one is exposed to or the duration of exposure to a chemical substance. In simple terms, the dose–time relationship provides information on how much of the test substance is involved and how often the exposure to the test substance occurs. This relationship gives rise to two different types of toxicity of a chemical substance—namely, acute toxicity and chronic toxicity.

3.2.4.2 Routes of Exposure and Toxicity Tests

The major routes through which the toxic chemicals enter the body under normal workplace conditions are by inhalation (respiratory route), through skin absorption (dermal route), or through ingestion (oral route). Many chemicals are known to cause the most severe health effects and rapid responses to test chemicals as soon as they enter directly into the blood circulation of animals. Several routes are used to evaluate and determine the toxicity and safety of chemical substances using species of laboratory animals in experimental toxicology studies. These routes of exposure include:

- inhalation (breathing in);
- absorption (through the skin or eyes);
- ingestion, oral (eating, swallowing);
- transfer across the placenta to the unborn baby;
- intravenous (injection into the vein);
- intramuscular (injection into the muscle);
- subcutaneous (injection under the skin); and
- intraperitoneal (injection inside the membrane that lines the interior wall of the abdomen).

3.2.5 Parameters of Toxicity

Industrial workers and the general public are often and regularly exposed to a wide range of chemicals, depending upon the nature of work and workplace. Exposure to high concentrations of chemicals for a prolonged period causes health effects of different types:

- Primary irritants cause local effects such as irritation to eyes, skin, nose, and mucous membranes, as well as skin rashes and dermatitis.
- Lung irritants cause irritation or damage to pulmonary tissue.
- Asphyxiants cause interference with or prevent the uptake and transformation of oxygen in the body.
- Narcotics cause mild anesthesia reactions, damage of the CNS, loss of consciousness, and death.
- Neurotoxic chemicals interfere with the transfer of signals between nerves of the nervous system and collapse.
- Hepatotoxic chemicals cause liver damage, jaundice, and liver enlargement.
- Nephrotoxic chemicals cause kidney damage and renal failure.
- Hematopoietic chemicals interfere with the production of red blood cells and can cause anemia and leukemia.
- Reproductive toxins cause spontaneous abortions, birth defects, and sterility.
- The design of a toxicity study should meet the objectives intended and minimize the pain, distress, and suffering of the test animals. The study should gather as much information as possible about the substance to be tested.[4,4a,9–12]

3.2.5.1 Parameters and the Safety Evaluation of Chemicals and Drugs

Although the inherent toxicity of any chemical substance cannot be changed, it is possible to avoid poisoning by preventing and/or limiting the manner of exposure. For this purpose, chemical substances are subjected to different tests. These include but are not limited to (1) acute toxicity, (2) cumulative toxicity, (3) absorption from different routes, (4) elimination and accumulation/storage in deep compartments of the body system, (5) penetration of barriers, (6) carcinogenicity, (7) mutagenicity, (8) teratogenicity, (9) sensitization, and (10) local irritation. The risk of harm and danger of chemical substances is equal to how poisonous the substance is, multiplied by the amount and route of exposure:

$$\text{Risk} = \text{toxicity} \times \text{exposure}$$

3.3 GOOD LABORATORY PRACTICE AND REGULATIONS

Chemical substances of different classes and kinds play an important role in the maintenance and improvement of quality of life. The safety and the possible health hazards caused by chemical substances to animals, humans, and the living environment must be evaluated carefully. Good laboratory practice (GLP) offers valuable

avenues for the development and coordination of environmental health and safety activities. In fact, the primary objective of the OECD principles of GLP is to ensure the generation of high-quality and reliable test data related to the safety of industrial chemical substances and preparations in the framework of harmonizing testing procedures for the mutual acceptance of data (MAD).

Nonclinical laboratory studies in target animals should be conducted in accordance with GLP regulations (namely, 21 CFR Part 58).[5b] Nonclinical studies relevant to animal safety determinations are subject to the GLP regulations. Since animal husbandry requirements often differ between laboratory animals and domestic animals, the U.S. Department of Agriculture does not require that domestic animals, including poultry, be maintained under the same conditions as laboratory animals. The regulations include terms such as "when applicable" and "as required" for those situations where differences in acceptable husbandry practices exist. Each nonclinical laboratory study contained in the new animal drug application must be accompanied by a statement declaring whether or not the study was conducted in compliance with the GLP regulations. If the study was not conducted in compliance with such regulations, the statement must describe, in detail, differences between the practices used and those required in the regulations. Although clinical studies contribute data relative to the overall safety assessment of a drug product, GLP regulations do not apply to clinical studies.

3.3.1 Good Laboratory Practice

Good laboratory practice is concerned with the organizational processes involving all types of studies in a laboratory/test that should be planned, performed, monitored, recorded, and reported. By adhering to the principle of GLP, a laboratory ensures the proper planning of studies and the provision of adequate means to arrive at meaningful study conclusions. The studies carried out according to GLP assure the quality and the integrity of the data generated and allow their use by government regulatory authorities in hazard and risk assessment of chemicals. This prescribes GLP standards for conducting toxicology studies on agricultural chemicals. Compliance with these standards is intended to assure the quality and integrity of toxicological data. Primarily, GLP is intended to ensure the quality and integrity of data generated in a laboratory on a product. Any violation would occur if a set protocol were not followed. The U.S. EPA has regulations and guidelines suggesting what studies are required and how they are to be performed. In fact, today GLP standards are recognized throughout the world.[4,4a,4b]

To facilitate proper use of chemical substances, OECD is developing proposals for classification criteria and labeling of chemical substances in the area of health and environmental hazards and the U.N. Subcommittee of Experts on the GHS is playing a significant role. A Task Force on Harmonization of Classification and Labeling has been established to coordinate the technical work carried out by the experts.

To generate quality data of a chemical substance and to comply with good laboratory practice, many provisions are set by the OECD.[4,4a,4b] In brief, these include the following:

- a complete description of how the protocol objectives were accomplished;
- all raw data and an interpretation or analysis of the information collected, including procedures used to allocate animals to treatment groups;
- a prior history on all animals used, including source, previous illnesses, and vaccinations (if known);
- animal management practices (holding facilities, handling techniques, feeding regimen);
- a complete description of the diet of experimental animals;
- a description of all prophylactic measures and treatments used to prevent or control infectious disease if administered during or just prior to the acclimation period (if it is anticipated that animals will need to be treated for complicating diseases during the baseline period or during the trial, detailed plans for this treatment should be provided in the protocol);
- description of each treatment for each animal to include: (1) identification of the animal, (2) nature and severity of disease, (3) date of first observation and duration of disease, (4) nature of treatment and dates, and (5) outcome of treatments;
- documentation of protocol changes or any deviation from the protocol, which is a GLP requirement; and
- complete descriptions of equipment, testing, sampling, sample handling, and assay procedures, and statistical evaluation of studies.

3.3.2 Toxicology Test Report

Recordkeeping is essential and it begins with a protocol that delineates the objectives of the study and outlines the experimental design and methods. To comply with the GLP requirements, the final test report on the toxicological effects of the test chemical substance includes specific descriptions. These may be listed as:

- identification of the study, the test item and reference item;
- a descriptive title;
- identification of the test item by code or name;
- identification of the reference item by name;
- characterization of the test item, including purity, stability, and homogeneity;
- name and address of the sponsor;
- name and address of any test facilities and test sites involved;
- name and address of the study director;
- name and address of the principal investigator(s) and details, if applicable;
- name and address of scientists having contributed reports to the final report;
- experimental starting and completion dates;
- a quality assurance statement listing the details (types of inspections, dates, phases, results, reporting date to management and to the study director);
- description of methods and materials used;
- a summary of the results;
- all information and data required by the study plan;

- a presentation of the results, including calculations and determinations of statistical significance;
- an evaluation and discussion of the results and, where appropriate, conclusions;
- the locations where the study plan, samples of test and reference items, specimens, raw data, and the final report are to be stored;
- dated signature of principal investigators and/or scientists involved in the conduct of the study; and
- dated signature by the study director indicating acceptance of responsibility for the validity of the data and the extent of compliance with good laboratory practice.

Further, it is very important that any corrections and additions to the final test report should be in the form of amendments clearly indicating the reason for the corrections or additions with the signature and date of the study director.

In conclusion, the students and workers in different industries and workplaces must be aware of the basic knowledge about the proper use of chemical substances and adhere to regulations and precautions to achieve chemical safety.

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APPENDIX 3.1

Signs and Symptoms of Toxicity[a]

Clinical Side Effect	Yes/No	Clinical Side Effect	Yes/No
Drowsiness	Yes	Hypertension	Yes
Anorexia	Yes	Nausea	No
Insomnia	Yes	Depression	Yes
Dizziness	No	Fatigue	No
Increased appetite	Yes	Sedation	Yes
Constipation	Yes	Tremor	Yes
Dry mouth	Yes	Tinnitus	No
Perspiration	Yes	Nervousness	Yes
Weight gain	Yes	Dermatitis	Yes
Epigastric distress	No	Hypotension	Yes
Headache	No	Vertigo	No
Vomiting	Yes	Heartburn	No
Palpitation	Yes	Weakness	Yes
Diarrhea	Yes	Blurred vision	Yes
Skin rash	Yes	Lethargy	Yes

[a] Predictable from species of laboratory animal studies.

4 Industrial Solvents

4.1 INTRODUCTION

Organic solvents are chemical substances used routinely and extensively in commercial and other industries. Many chemical substances used to dissolve or dilute other substances and materials are called *solvents.* Industrial solvents are often mixtures of several individual substances. They can be found under a variety of trade names. Since the advent of the Industrial Revolution, the use of non-water-based chemicals has increased dramatically. According to the report of the National Institute of Safety and Health (NIOSH), more than 49 million tons of organic solvents were produced in the United States alone in 1984, and today much larger quantities of many solvents are produced around the world.

A solvent is a chemical substance that dissolves another chemical substance or substances to form a solution of homogeneous mixture. The solvent is the component in the solution that is present in the largest amount and determines the physicochemical form of the substance as either solid, liquid, or gas. Solvents are usually but not necessarily always liquids and can also be gases or solids. The chemical substances dissolved in the solvent are called the solute, and a solvent plus a solute form the solution. The organic solvents share a common structure; they are hydrophilic, volatile, and of low molecular weight; and exist in liquid form at room temperature. Industrial solvents may be grouped as (1) aliphatic-chain compounds, which include *n*-hexane; or (2) aromatic compounds with a six-carbon ring, which include benzene and xylene.

The aliphatic and aromatic hydrocarbons may contain a substituted halogen element and are often referred to as halogenated hydrocarbons. These include, for example, perchloroethylene, trichloroethylene, and carbon tetrachloride. Organic solvents are very useful and have extensive applications in industry because they help in the manufacture of oils, fats, resins, rubber, and plastics. In fact, the role of organic solvents increased in the latter half of the nineteenth century with the development of the coal-tar industry. The wide application of organic solvents grew and became diverse and global.

The introduction of chlorinated solvents in the 1920s led to reports of solvent toxicity. Although the variety and number of organic solvents range in the thousands, only a few have been well studied and tested to know the possible human health effects.

The term *organic solvent* refers to most other solvents that contain carbon. Solvents usually have a low boiling point and evaporate easily; they are used to extract soluble compounds from a mixture. Solvents are usually clear and colorless liquids and most of them have a characteristic odor. The concentration of a solution is the amount of compound that is dissolved in a certain volume of solvent. Solvents and

solutes can be broadly classified into polar (hydrophilic) and nonpolar (lipohilic). Polarity can be measured as the dielectric constant or the dipole moment of a compound. The polarity of a solvent determines what type of a compound it is able to dissolve and with what other solvents or liquid compounds it is miscible. As a rule of thumb, polar solvents dissolve polar compounds best and nonpolar solvents dissolve nonpolar compounds best.

4.2 SOLVENTS

The saturated hydrocarbons are used in industry as fuels, lubricants, and solvents. After undergoing processes of alkylation, isomerization, and dehydrogenation, they also act as starting materials for the synthesis of paints, protective coatings, plastics, synthetic rubber, resins, pesticides, synthetic detergents, and a wide variety of petrochemicals. The fuels, lubricants, and solvents are mixtures that may contain many different hydrocarbons

The array of chemical substances usually termed solvents is many. Solvents are substances that are capable of dissolving or dispersing one or more other substances. Organic solvents are carbon-based solvents—that is, they contain carbon in their molecular structure. Millions and millions of people come in close contact with organic solvents through the use of household and industrial products. The end products include but are not limited to paints, varnishes, lacquers, adhesives, glues, cleaning agents, and products to remove oils, greases, and like substances. Many organic solvents are recognized for their neurotoxicity (e.g., *n*-hexane, tetrachloroethylene, toluene), as carcinogens (i.e., benzene, carbon tetrachloride, trichloroethylene), and as reproductive hazards (e.g., 2-ethoxyethanol, 2-methoxyethanol, methyl chloride). Global industrialization has been very closely associated with the extensive use of a large variety of solvents. The numbers and groups of industrial solvents are very large. Industrial solvents have been classified under many names. In brief, these include:

aliphatic hydrocarbons;
alicyclic hydrocarbons;
alcohols;
glycols and derivatives;
ethers and epoxy compounds;
esters;
arboxylic acids and anhydrides;
aldehydes and ketones;
aliphatic halogenated hydrocarbons;
aliphatic amines;
cyanides and nitriles;
aromatic hydrocarbons;
phenols and phenolic compounds;
aromatic halogenated hydrocarbons;
aromatic amines;
nitro compounds;

organic nitrogen compounds;
organic chemicals; and
halogens.

Each group includes a very large number of chemical substances that have been used extensively in chemical laboratories, multiple industries, and homes. In fact, the list is very large. The following pages provide brief information on the uses, manner of exposure, toxicity, and health effects of some of the solvents. More information on different solvents is available in the literature.[1–5,16–18]

4.2.1 Flammable and Combustible Solvents

For purposes of safety, it is necessary that the worker, manager, and related groups managing industrial solvents should know and understand the requirements of the Occupational Safety and Health Administration (OSHA) in the management of safe storage of flammable and combustible liquids. The worker should know the difference between a flammable liquid and a combustible substance. A flammable liquid is one that has a flash point below 100°F (37.8°C), except for any mixture having components with flash points of 100°F (37.8°C) or higher, the total of which make up 99% or more of the mixture) (1910.106(a)(19)). There are three categories of flammable liquids:

class 1A: liquids having flashpoints below 73°F (22.8°C) and having boiling points below 100°F (37.8°C) (1910.106(a)(19)(i)) (e.g., acetaldehyde, ethyl ether, and cyclohexane);
class 1B: liquids having flash points below 73°F (22.8°C) and having boiling points at or above 100°F (37.8°C) (1910.106(a)(19)(ii)) (e.g., acetone, benzene, and toluene); and
class 1C: liquids having flash points at or above 73°F (22.8°C) and having boiling points below 100°F (37.8°C) (1910.106(a)(19)(iii)) (e.g., hydrazine, styrene, and turpentine).

In contrast, a combustible liquid has a flash point at or above 100°F (37.8°C) (1910.106(a)(18)). The combustible liquids are divided into two classes:

class 2: liquids having flash points at or above 100°F (37.8°C) and below 140°F (60°C), except any mixture having components with flash points of 200°F (93.3°C) or higher, the volume of which makes up 99% or more of the total volume of the mixture (1910.106(a)(18)(i)) (e.g., acetic acid, naphtha, and standard solvent); and
class 3: liquids having flash points at or above 140°F (60°C) (1910.106(a)(18)(ii)).

Class 3 liquids are subdivided into two subclasses:

class 3A: liquids having flash points at or above 140°F (60°C) and below 200°F, except any mixture having components with flash points of 200°F (93.3°C)

or higher, the total volume of which makes up 99% or more of the total volume of the mixture (1910.106(a)(18)(ii)(a) (e.g., cyclohexanol, formic acid, and nitrobenzene); and

class 3B: liquids having flash points at or above 200°F (93.3°C) (1910.106(a)(18)(ii)(b)) (e.g., formalin and picric acid).

According to 1910.106(a)(18)(ii)(b), class 3B liquids include those with flash points at or above 200°F (93.3°C). This section does not cover class 3B liquids. Where the term "class 3 liquids" is used in the section, it means only class 3A liquids. (Class 3B is used in this document for reference purposes only.)

It should be noted that whenever a combustible liquid is heated for use to within 30°F (16.7°C) of its flash point, it should be handled in accordance with the requirements for the next lower class of liquids (1910.106(a)(18)(iii)).

The flash point and boiling point determine the class of a liquid. However, these should not be the only criteria used to determine the hazards of a liquid. Many other factors should also be considered for the proper use and storage of hazardous liquids. These factors include ignition temperature, lower explosive limit (LEL) or upper explosive limit (UEL), vapor pressure, specific gravity, and vapor density.

Exposure to solvents and other organic liquids is one of the most common chemical health risks at workplaces. Most of the organic solvents are combustible and often highly volatile and extremely flammable; they require care and precaution during use. Some solvents produce vapors that are heavier than air. These may move on the floor or ground to a distant ignition source, a spark point from welding, or static electricity and result in disaster. Smoking could also cause the vapors to explode. Vapors of solvents are also known to accumulate in confined places and to cause risks to health and the workplace.

4.2.2 Uses of Solvents

The most common uses for organic solvents are chemical synthesis, dry cleaning of cloth, paint thinners, removers of nail polish and glue, detergents, and waste spots. Examples of different solvents include but are not restricted to tetra chloroethylene, toluene, turpentine, acetone, ethanol, methyl acetate, and ethyl acetate. Because of the multiple activities and prolonged use of solvents, the hazard to human health has increased extensively. Also, solvents find use in different phases of the electronics industry and primarily as removers of grease, inks, paints, waxes, and glues, as well as in total cleaning processes. There is a wide range of organic solvents, some very toxic and others only mildly toxic. The subgroups should be considered to have a better idea of specific hazard risks and uses. The aromatic compounds and the chlorinated hydrocarbons are perhaps the most dangerous groups of solvents because many of them are known to cause cancer and other serious diseases. The organic solvents are widely used in the manufacturing, transportation, and other industrial sectors. These compounds are used in the manufacture of paints, dyes, agricultural products, and many other products. Because organic solvents are ingredients of many products, such as paints and cleaning agents, they are also found in nonmanufacturing workplaces and nonwork settings.

4.2.3 Exposure to Solvents

Industrial workers and the general public become exposed to industrial solvents in a variety of ways—for instance, during the fabrication and manufacturing processes of different industrial products. These include but are not limited to products in engineering, textiles, paints, house building and construction, footwear, the food industry, woodworking, rubber, dry cleaning, plastics, manufacture of lacquers and varnishes, adhesives, printing inks and ink removers, pesticides, toiletries, drugs and pharmaceuticals, polymer, dyes and pigments, detergents, soaps and cleaning agents, hospital equipment, and many other associated activities.

Human exposure to a variety of industrial solvents and the subsequent health effects are modulated with the concentration of the solvent (as vapor, mist, or other) in the ambient air, poor ventilation in the workplace, and presence of higher vapor concentration. During prolonged periods of exposure (through inhalation), industrial solvents cause health disorders in workers. Organic solvents are lipid soluble and enter the body rapidly through skin absorption and blood; they cause skin irritation, central nervous system (CNS) depression, and other deleterious effects. High concentrations of benzene, for instance, are known to cause CNS depression or cardiac arrhythmias and fatal injury. Exposure through skin absorption produces dermatitis, while inhalation of high concentrations leads to bronchial irritation or pulmonary edema. Thus, if or when workers become negligent and do not practice proper safety regulations during handling of industrial solvents, they become the victims and suffer chronic health disorders.

Industrial workers and the general public are exposed to solvents through one route or a number of routes simultaneously, depending on the properties of the candidate solvent, the worker's capability, and duration of use. Most solvents are "volatile"—that is, they evaporate into the air very quickly. The fumes, dusts, gases, and vapors that result can then be breathed in and easily passed through the lungs into the bloodstream. Another route of entry into the body is by ingestion, where fine droplets of solvents enter the body through swallowing. Oral or mouth contact with contaminated hands, food, and cigarettes also leads to the ingestion of solvents. Yet another entry route of solvents to the human body is through skin absorption. Direct skin contact of solvents allows them to enter the bloodstream. Thus, the rapid manner of exposure to different industrial solvents in humans is by inhalation (respiratory), ingestion (oral), and skin (dermal) absorption at workplaces, as well as from a polluted atmosphere. The health effects of solvents on humans are modulated by several factors, for instance:

- how easily and quickly a solvent evaporates at the ambient temperature;
- characteristics of the solvent—namely, its solubility in water or fat;
- concentration of the solvent in the air at the work environment;
- nature of work associated with the solvent; and
- duration or exposure period of the worker to the solvent.

Contamination affecting community water supplies, food additives, or household chemicals is an important source of solvent exposure. Well-water sampling, both in

the United States and abroad, has revealed quantities of chlorinated hydrocarbons and other solvents. As discussed earlier, most of the organic solvents, depending on their volatility, are flammable or highly flammable. However, there are certain exceptions, like chlorinated solvents such as dichloromethane and chloroform. Mixtures of solvent vapors are very hazardous and can cause explosions. Solvent vapors are heavier than air; they sink to the bottom and can travel long distances. Solvent vapors found in empty drums, containers, and cans often pose hazards of flash fires; hence, empty containers of volatile solvents should be stored in open spaces upside down. For instance, ethers, diethyl ethers, and tetra hydrofuran (THF) form highly explosive organic peroxides on exposure to light and oxygen in the air. Ethers need to be stored in the dark and in closed canisters in the presence of stabilizers such as sodium hydroxide and BHT (butylated hydroxytoluene).

One potential hazard of solvents is flammability. It is therefore very important to take adequate precautions and timely care to contain fires and consequent fire hazards. In fact, hazardous liquids need special precautions during storage, handling, and transportation. Industrial workers and managers should be well aware of the rules and regulations of the National Fire Protection Agency (NFPA) and the International Fire Code Institute (IFCI). These organizations have developed uniform fire codes and guidelines for the safe storage and use of flammable and combustible liquids. These guidelines are not mandatory unless a federal, state, or local authority chooses to use them. In contrast, OSHA has developed mandatory regulations for the general industry (29 CFR 1910.106), construction industry (29 CFR 1926.152), and shipyard industry (29 CFR 1915.36).

4.3 DRUGS, PHARMACEUTICAL PRODUCTS, AND RESIDUAL SOLVENTS

Many solvents are in use in manufacture of drugs and pharmaceuticals (Table 4.1). The residual solvents are not completely removed by practical manufacturing techniques. The control of chemical impurities in drugs and pharmaceutical products has assumed significance in recent years. The presence of unwanted chemicals, even in small amounts, is known to influence the efficacy and safety of the drugs and pharmaceuticals. In view of this, the International Conference on Harmonization (ICH) has formulated workable guidelines to control the impurities. Accordingly, different pharmacopoeias—for instance, the British Pharmacopoeia (BP), the United States Pharmacopoeia (USP), and the Indian Pharmacopoeia—are slowly incorporating limits to allowable levels of impurities present in the active pharmaceutical ingredients (APIs) or formulations. The ICH guidelines have classified

TABLE 4.1
Solvents in Pharmaceutical Compounds

Solvent	USP Limit (ppm)	Standard Solution (μg/mL water)
Methylene chloride	500	10
Benzene	100	2
Trichloroethylene	100	2
Chloroform	50	1
1,4-Dioxane	100	

different impurities in drugs and pharmaceutical products as (1) organic impurities (during the processing for drugs), (2) inorganic impurities, and (3) residual solvents.

The residual solvents are organic volatile chemicals used during the manufacturing process or generated during production. Because residual solvents are toxic and do not provide any kind of therapeutic benefit, they should be removed, to the extent possible, to meet ingredient and product specifications, good manufacturing practices, and other quality-based requirements. Drug products should contain no higher levels of residual solvents than can be supported by safety data. Because of the possible adverse health effects that chemical substances may cause, international organizations have set limits of safety for different chemical substances and related data based on prolonged studies with laboratory animals and human exposure. Accordingly, the International Program on Chemical Safety (IPCS) describes exposure limits of toxic chemicals with the term *tolerable daily intake* (TDI). The World Health Organization uses the term *acceptable daily intake* (ADI). For meeting the requirements of drugs and pharmaceutical products and for more clarity, the permitted daily exposure (PDE) has also been put to practice. Therefore, based on safety regulations, solvents for the manufacture of drugs and pharmaceutical products are classified as follows:

TABLE 4.2
Class 1: Residual Solvents to Avoid Using

Solvent	Level[a]	Nature
1,2-Dichloroethane	5	Toxic
1,1-Dichloroethene	8	Toxic
1,1,1-Trichloroethane	1500	Environmental hazard

[a] Concentration limit (ppm).

Class 1 solvents comprise solvents to be *avoided,* including known carcinogens, suspected carcinogens, and solvents that cause hazards to the living environment (Table 4.2).

Class 2 solvents are to be *limited* and include nongenotoxic animal carcinogens and others that induce irreversible toxicity like neurotoxicity and teratogenicity, and solvents suspected of other significant but reversible toxicities (Table 4.3).

Class 3 solvents have *low toxic potential*. These solvents have no health-based exposure limits and have low levels of PDE of about 50 mg/day (Table 4.4).

4.4 SOLVENTS AND PRECAUTIONS

Solvents are frequently used in industrial processes, including pharmaceutical manufacturing, metal cleaning and degreasing, and paint remover manufacturing. Solvents used in industrial processes can be toxic and volatile, and they require careful handling. Methylene chloride is a popular solvent in industrial chemical manufacture, but it is a potential carcinogen. Other solvents that require special storage and usage include benzene, diethyl ether, and sodium hydroxide.

Occupational exposure is defined as chronic exposure in amounts less than the threshold limit value causing material symptoms. As with many teratogens, critical

TABLE 4.3
Class 2: Residual Solvents with Limited Use

Solvent	Limit (ppm)[a]
Acetonitrile	4.1 410
Chlorobenzene	3.6 360
Chloroform	0.6 60
Cyclohexane	38.8 3880
1,2-Dichloroethene	18.7 1870
1,2-Dimethoxyethane	1.0 100
N,N-dimethylacetamide	10.9 1090
N,N-dimethylformamide	8.8 880
1,4-Dioxane	3.8 380
2-Ethoxyethanol	1.6 160
Ethylene glycol	6.2 620
Formamide	2.2 220
Hexane	2.9 290
Methanol	30.0 3000
2-Methoxyethanol	0.5 50
Methylbutylketone	0.5 50
Methylcyclohexane	11.8 1180
Methylene chloride	6.0 600
N-methylpyrrolidone	5.3 530
Nitromethane	0.5 50
Pyridine	2.0 200
Sulfolane	1.6 160
Tetrahydrofuran	7.2 720
Tetralin	1.0 100
Toluene	8.9 890
Trichloroethylene	0.8 80
Xylene	21.7 2170

[a] PDE = permitted daily exposure: milligrams of concentration per day.

parameters that determine the level of the exposure include duration of exposure, route of exposure, and dosage of exposure. Occupational exposure may involve exposure by inhalation or by skin contact. The dosage of the solvent exposure, measured by airborne concentration or blood level, is often difficult to assess accurately. Therefore, precautions such as wearing protective clothing and gloves and working in an adequately ventilated environment are strongly recommended during use and disposal of solvents:

- Avoid the generation of solvent vapors by working in a fume hood or a well ventilated area and avoid inhalation of solvent vapors.
- Keep storage containers tightly closed.
- Never use open flames near flammable solvents; use electrical heating instead.

TABLE 4.4
Class 3: Residual Solvents with Low Toxic Potential (PDE)[a]

Acetic acid heptane	Methylisobutylketone
Acetone isobutyl acetate	Dimethyl sulfoxide pentane
Anisole isopropyl acetate	Dimethyl sulfoxide pentane
1-Butanol methyl acetate	Ethanol 1-pentanol
2-butanol 3-methyl-1-butanol	Ethyl acetate 1-propanol
Butyl acetate methylethylketone	Ethyl ether 2-propanol
tert-Butylmethyl ether	Ethyl formate propyl acetate
Cumene 2-methyl-l-propanol	Formic acid

[a] PDE = permitted daily exposure of about 50 milligrams per day.

- Never flush flammable solvents down the drain to avoid explosions and fires.
- Avoid contact of the solvent with the skin since many solvents are easily absorbed through the skin.
- Always use personal protective equipment (PPE) and protective clothing to cover exposed parts of the body and personal clothing.
- Always use boots, gloves, eye protection, and suitable respirators to prevent splashes, skin contact, and inhalation of vapors.
- While working with solvents, observe that all personal protective equipment is suitable for the particular chemical substance in the solvent.
- Provide safety information to workers handling solvents and improve their awareness.
- Store solvents in a cool place, away from any potential ignition sources, in a well ventilated and firmly secured area.
- Ensure that solvent containers have warning labels indicating the hazards of the substance and what should be done in case of an emergency.
- In cases of solvent spills or leak residues, contain them with sand or other appropriate absorbents. Do not allow spillages to enter drains or other waterways.

Working with and management of industrial solvents require adequate and proper controls of many factors. These include but are not limited to the encapsulation of machinery, properly planned cleaning, ventilation of the work area, local exhaust ventilation controls, and collection and removal of solvent vapors before they build up in the work environment.

The design or selection of effective exhaust ventilation systems in work areas must include:

- a hood that captures the solvent vapors at their point of generation;
- capture and emission of solvent vapors without their passing through the breathing zones of workers;
- a proper filter system in the hood through which the solvent-saturated air passes;
- a suitable fan or other device to extract and expel vapor and fumes;

- adequate replacement of air by permanent inlets, ensuring that replacement air must not contain organic solvents, which must be removed from exhausted air and properly disposed of; and
- an automatic alarm system that ensures the efficiency of the ventilation system.

4.5 EDUCATION AND TRAINING

Industrial workers and students in laboratories associated with the activities and management of chemical substances, particularly hazardous wastes, require particular training. Initial and refresher training are a must for all workers to protect health and safety of the work environment. Industrial workers likely to come into contact with solvents must be trained by the employer for proper management of harmful chemical substances. This requires cooperation of management, workers, and unions at the workplace. Educational courses should be designed by the relevant occupational health and safety bodies in conjunction with employers' and workers' organizations. Workers must have the right to remove themselves from danger when using chemicals. Women workers must have the right, in the case of pregnancy or lactation, to alternative work. Exercise of these rights should not affect other employment rights of the worker. The concentration of solvents in the air must be regularly monitored and controlled by independent bodies to ensure that occupational exposure limits are respected. Even when the occupational exposure limit (OEL) is respected, the employer must try to lower the exposure. Regular medical examinations must be considered as a worker's right.

4.6 TOXICITY AND HEALTH EFFECTS

There is no uniformity in the toxicity and related health effects among different solvents. Some of the most common and observable short-term effects in exposed workers include irritation of the eyes, lungs, and skin; headache; nausea; dizziness; and light-headedness. Further, different solvents, their vapors, and mists have various effects on human health. Many of the solvents are narcotic and cause fatigue, dizziness, and intoxication. Exposure to high concentrations of solvents for a prolonged period of time causes unconsciousness and even death. Exposure to large doses of solvents may slow down the reaction time and affect rational judgment. This may increase the risk of accidents at work and elsewhere, such as in traffic on the way home. Solvents irritate the eyes and the respiratory tract. While solvents are known to clean and degrease metal plates in industrial processes, they damage the skin of the industrial workers using them. This is a very common cause of skin disorders and dermatitis among workers. Some solvents even penetrate the skin and enter the blood circulation, leading to health disorders. Solvents are also known to cause deleterious effects on liver, kidneys, heart, blood vessels, bone marrow, and the nervous system. Many solvents alone, in combination, and after repeated exposure are known to cause adverse health effects in workers. Solvents are known to cause sudden loss of consciousness when they are inhaled, particularly for prolonged

periods of time. The majority of solvents are known as neurotoxicants and cancer-inducing chemicals.

Industrial workers and the general public are exposed to industrial solvents under different work conditions. After absorption, solvents get excreted in urine and sweat or they may be exhaled. Short-term exposure to solvents causes many health disorders, such as dermatitis or skin problems (drying, cracking, reddening, or blistering of the affected area), headaches, drowsiness, poor coordination, and nausea (feeling sick). These effects usually take place very quickly. Also, exposure to solvents in very high concentrations causes severe health disorders, including unconsciousness and fatalities. Similarly, prolonged periods of exposure to solvents also cause health effects such as dermatitis; damage to the brain and nervous system; damage to the liver, kidney, blood, and vascular system; fertility disorders in both men and women; and damage to the fetus in a pregnant woman (Appendix 4-2).

Attempts should be made to use alternate solvents for industrial processes. Solvents that pose and cause the most serious risk to human health should be replaced by less hazardous ones. If this is not possible, at least the work conditions and exposure to solvents should be adjusted to avoid or minimize the health risk. This may be achieved, for example, by using a closed process. Among solvents, the most hazardous ones identified are benzene, carbon disulfide, and carbon tetrachloride.

4.7 NEUROTOXICITY

There has been increasing attention to the damage to the nervous system caused after exposure to solvents. The period of exposure may be of short duration or long term. Chronic exposure to solvents causes degenerative changes in parts of the nervous system. The symptoms of neurotoxicity after a brief or acute exposure include dizziness, euphoria, poor coordination, unsteady gait, fits, and coma. In contrast, workers exposed to different solvents for a prolonged period in workplaces show personality changes, irritability, sleep disorders, short-term memory loss, reduced attention span, dementia, and peripheral neuropathy.

There are useful tests to identify toxic effects on the peripheral nerves. Studies such as nerve conduction tests (NCSs) and electromyographic tests (EMGs) are used to identify the tingling or numbness of the hands or feet or associated muscle weakness. A set of neuropsychometric tests has also been developed to find behavioral effects of solvents in humans. These include but are not limited to (1) motor speed; (2) hand steadiness; (3) perceptual speed; (4) reaction speed, eye–hand coordination, and manual dexterity; (5) verbal and visual memory and learning; and (6) cortical evoked potentials (electrical activity in the brain following sensory stimulation).[5a–6a]

4.8 SOLVENT SYNDROME AND FETAL DEFECTS

Forms of solvent abuse include sniffing paints, lacquers, glues, and gasoline to achieve a "high." These solvents are known to contain variable proportions of many solvents; the most common components are toluene, benzene, and xylene. Gasoline also contains methanol and petroleum ether. Case reports of mothers who sniffed

these substances describe a syndrome of birth defects analogous to fetal alcohol syndrome. This fetal solvent syndrome or fetal gasoline syndrome has also been associated with hypotonia, mental retardation, and poor postnatal head growth. In these instances, it is difficult to determine whether a primary solvent is responsible for the effects or if a combination of solvents was the cause for the embryopathy.

4.9 WORKPLACE CONTROLS AND WORK PRACTICES

Industrial workers should be trained regularly to observe and practice elementary work rules to achieve proper management of industrial solvents in workplaces for the following reasons:

- Good work practices and training help to reduce hazardous exposure. For most of the hazardous solvents, it is possible to find a substitute with the same characteristics but less drastic effects on health.
- Proper and adequate ventilation in the work area is important and should be considered carefully when using solvents.
- Equipment (fire extinguishers, absorbent material, etc.) should be considered and provided for situations such as spillage or emergencies.
- Personal protective equipment and clothing, such as aprons, gloves, and masks with filters, should be available where needed, and they should be used according to the recommendations. Storage of this equipment should be in a clean place away from possible contact with solvent vapors. The solvent containers and packages must be properly and legibly labeled with warning symbols and safety advice and should be made mandatory.

4.10 OCCUPATIONAL EXPOSURE LIMITS

There is no clear definition for the terms *safe exposure limit* (SEL) and *occupational exposure limit* (OEL), although the terms has scientific and legal interpretations and implications. The values of SEL or OEL vary from country to country around the world. It is well known that a rough rule of thumb is that the SELs and OELs are levels below which most industrial workers and the general population could get exposed to chemical substances on a regular basis with a low risk to health. It should be clearly understood that SEL and OEL are certainly *not* levels that are definitely safe and below which no harm is caused.

4.11 SOLVENTS AND TOXICITY PROFILE

The following pages provide brief information on a few selected solvents, including the manner of exposure and toxicological effects on laboratory animals and on humans. For purposes of easy and quick identification and reference by the user, the solvents are listed in alphabetical order rather than according to the chemical classes to which they belong. The chemical class of each solvent may be found in Appendix 4.1. For more detail on each of the chemical substances, refer to the literature.[3–5]

Acenaphthene (CAS no. 83-32-9)
Molecular formula: $C_{12}H_{10}$
Synonyms and trade names: 1,2-dihydroacenaphthylene, 1,8-ethylenenaphthalene
Use and exposure: Acenaphthene is a tricyclic aromatic hydrocarbon, crystalline solid at ambient temperature. Acenaphthene does not dissolve in water but is soluble in many organic solvents. Acenaphthene occurs in coal tar produced during the high-temperature carbonization or coking of coal. It is used as a dye intermediate in the manufacture of some plastics and as an insecticide and fungicide. Acenaphthene is an environmental pollutant and has been detected in cigarette smoke, automobile exhausts, and urban air; in effluents from the petrochemical, pesticide, and wood preservative industries; and in soils, groundwater, and surface waters at hazardous waste sites. This compound is one of a number of polycyclic aromatic hydrocarbons (PAHs) on the U.S. Environmental Protection Agency's (EPA) priority pollutant list.[1,4]
Toxicity and health effects: Studies on laboratory animals orally exposed to acenaphthene showed loss of body weight, peripheral blood changes (unspecified), increased aminotransferase levels in blood serum, and mild morphological damage to the liver and kidneys.[70] Human studies with acenaphthene are limited. Acenaphthene is irritating to the skin and mucous membranes of humans and animals. Oral exposure of rats to acenaphthene for 32 days produced peripheral blood changes, mild liver and kidney damage, and pulmonary effects.[8,9]

Acetaldehyde (CAS no. 75-07-0)
Molecular formula: C_2H_4O
Synonyms and trade names: acetic aldehyde, aldehyde, ethanol, ethylaldehyde
Use and exposure: Acetaldehyde is a highly flammable, volatile, colorless liquid with a characteristic and pungent odor. It is miscible in water. Exposure to acetaldehyde occurs during the production of acetic acid and various other industrial chemical substances—for instance, manufacture of drugs, dyes, explosives, disinfectants, phenolic and urea resins, rubber accelerators, and varnish.[10,13,16]
Toxicity and health effects: Exposure for a prolonged period to acetaldehyde liquids and vapors in work areas causes irritation to the eyes, skin, upper respiratory passages, and bronchi. Continued exposure is known to result in damage to the corneal epithelium, dermatitis, photophobia, a foreign body sensation, coughing, pulmonary edema, necrosis, damage to nasal mucosa and trachea, and persistent lacrimation. Acetaldehyde causes bronchitis and reduction in the number of pulmonary macrophage. The severity of lung damage increases with the buildup of fluid in the lungs (pulmonary edema) and respiratory distress in the worker.[10]
Acetaldehyde and cancer: Laboratory animal studies indicate that exposure through inhalation to vapors of acetaldehyde causes nasal tumors in rats and laryngeal tumors in hamsters. However, no adequate data are available regarding acetaldehyde as a human carcinogen. The U.S. EPA has classified acetaldehyde as group 2B; that is, it is a possible human carcinogen.[6,13,6]

Acetic anhydride (CAS no. 108-24-7)

Molecular formula: $C_4H_6O_3$

Synonyms and trade names: acetic acid anhydride, acetyl acetate, acetic oxide, acetyl oxide, ethanoic anhydride, acetyl ether, hydroxybiacetyl, acetanhydride, anhydride acetique, anhydrid kyseliny octove, anidride acetica, azijnzuuranhydride, octowy bezwodnik.

Use and exposure: Acetic anhydride is a colorless liquid with a strong, pungent odor. It is soluble in cold water, decomposes in hot water to form acetic acid, and is soluble in alcohol, chloroform, and ether. Exposure to acetic anhydride can occur via inhalation, ingestion, and eye or skin contact. Acetic anhydride also penetrates the skin very quickly. Acetic anhydride has applications in the manufacture of acetyl compounds, cellulose acetate, cellulose esters, chloroacetic acid, acetyl chloride, triacetate fibers, and vinyl acetate; processing of dyes, perfumes, explosives, and flavorings; electropolishing of metals; and processing of semiconductors. It is used as an acetylizer and solvent in examining wool fat, glycerol, fatty and volatile oils, and resins; in detecting rosins; as a dehydrating agent in nitrations, sulfonations, and other reactions where removal of water is necessary; in the manufacture of pharmaceuticals, including aspirin; as an intermediate in the synthesis of pesticides; and as an esterifying agent for food starch.[6,11]

Toxicity and health effects: Acetic anhydride is highly corrosive and causes severe irritation and burns of the eyes, mucous membranes, and skin of exposed animals. Exposure to acetic anhydride causes a burning sensation in the nose and throat, cough, pain in the chest, increased resistance to breathing, excessive tearing, redness, and pain. Contact with the skin causes burns and blisters. Workers exposed to acetic anhydride developed pulmonary edema, with coughing and difficulty breathing, and skin sensitization with redness and itching.[6,12–14]

Storage and protection: Acetic anhydride is a flammable liquid and harmful vapor. Accidental exposure and ingestion cause poisoning, skin burns, eye damage, and digestive and respiratory tract burns. The target organs include the CNS, eyes, skin, and mucous membranes. It should be stored in a cool, dry, well-ventilated area in tightly sealed containers that are labeled in accordance with OSHA's Hazard Communication Standard (29 CFR 1910.1200). It should be protected from physical damage and separated from water, alcohols, strong oxidizers, chromic acid, amines, strong caustics, heat, sparks, and open flame.[15]

Exposure limits: The Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and the American Conference of Industrial Hygienists (ACGIH) recommend permissible exposure limits (PELs) for acetic anhydride as 5 ppm as a ceiling limit.[16]

Acetone (CAS no. 67-64-1)

Molecular formula: $(CH_3)_2CO$

Synonyms and trade names: dimethyl ketone, 2-propanone, and beta-ketopropane

Use and exposure: Acetone is a manufactured chemical that is also found naturally in the environment. It is a colorless liquid with a distinct smell and taste. It evaporates easily, is flammable, and dissolves in water. Acetone is used to make plastic, fibers, drugs, and other chemicals. It is also used to dissolve other substances. It occurs naturally in plants, trees, volcanic gases, and forest fires, and as a product of the breakdown of body fat. It is present in vehicle exhaust, tobacco smoke, and landfill sites. Industrial processes contribute more acetone to the environment than natural processes do. People are exposed to acetone in a variety of ways—for instance, through contaminated air in the workplace, with the use of household materials like nail polish and paints, contaminated food, and repeated breathing of secondhand smoke.[1–4,17–19]

Toxicity and health effects: Acetone on inhalation causes irritation to nose, throat, lung, and eyes and headaches. Repeated exposure causes lightheadedness, confusion, increased pulse rate, nausea, vomiting, unconsciousness, and possibly coma. It also shortens the menstrual cycle in women. Laboratory animals after a prolonged exposure to acetone developed kidney, liver, and nerve damage and experienced increased birth defects and reproductive disturbances.[17–19]

Acetone and cancer: The U.S. EPA and the International Agency for Research on Cancer (IARC) have not classified acetone as a human carcinogen.[17]

Exposure limits: OSHA recommends the concentration limit of acetone in workplace air as 1000 ppm for an 8-hour workday time-weighted average (TWA), while NIOSH recommends the limit as 250 ppm in workplace air for a 10-hour workday (TWA).[17]

Acetylene (CAS no. 74-86-2)

Molecular formula: C_2H_2

Synonyms and trade names: ethine, ethyne, narcylene

Use and exposure: Acetylene is the simplest member of the unsaturated hydrocarbons called alkynes or acetylenes. Pure acetylene is a colorless gas with a pleasant odor; as prepared from calcium carbide, it usually contains traces of phosphine. Acetylene is a compressed gas that is used as a fuel and is stored in a liquid state. An acetylene cylinder should be stored and used in a vertical, valve-end-up position only. Using or storing the tank in any other position can be extremely dangerous. Acetylene is extensively used in industry for welding, cutting, flame scarfing, cutting, metalizing, and other metallurgical operations. Chemically, acetylene has uses in the manufacture of vinyl chloride, synthetic rubber, acronitile, acrylate, vinyl alkyl ethers, and many other substances.

Toxicity and health effects: Exposure to acetylene for a short period of time has not been reported to cause any kind of irritation to the skin or mucous membrane in workers. However, exposure to high concentrations of acetylene is known to cause mild narcotic effects and asphyxiation. In severe cases the exposed worker suffers poor muscular coordination, cyanosis, irregular pulse, nausea, vomiting, prostration, unconsciousness, convulsions, and

even death.[7] Proper ventilation in work areas and strict observance of industrial hygiene practices during welding, brazing, and metallurgical processing protect workers from acetylene-related health problems.

Acrolein (CAS no. 107-02-8)

Molecular formula: C_3H_4O

Synonyms and trade names: acrylic aldehyde, acraldehyde, allyl aldehyde, ethylene aldehyde

Use and exposure: Acrolein is a watery white or yellow liquid that burns easily, is easily volatilized, and has a disagreeable odor. Acrolein can be formed from the breakdown of certain pollutants found in outdoor air, from burning tobacco, or from burning gasoline. Exposure to airborne acrolein may occur from breathing contaminated air, from smoking tobacco or proximity to someone who is smoking, or from being near automobiles or oil or coal power plants. The general public is exposed to acrolein primarily through the inhalation of air, especially indoor air, containing environmental tobacco smoke. In fact, acrolein is included in the priority list of hazardous substances identified by the U.S. EPA.[1–4,20–22] The largest use for acrolein is as an intermediate in the manufacture of acrylic acid and its esters. Acrolein is also used in the manufacture of allyl alcohol, pyridines, tetrahydrobenzaldehyde, modified starch, synthetic glycerine, acrolein polymers, polyurethanes, and polyester resins.

Toxicity and health effects: Acrolein is toxic and causes irritation to eyes, nose, and throat and skin burns. Exposure to high levels (10 ppm) of acrolein for a very short period is fatal to humans. It has adverse health effects on the lungs, with severe symptoms such as upper respiratory tract irritation and congestion.[20–23] Prolonged periods of inhalation exposure to high concentrations of acrolein cause severe irritation to eyes, nose, and throat and lung congestion in humans. The target organs affected by acrolein include the respiratory tract, gastrointestinal tract, eyes, and skin.[22–26]

Acrolein and cancer: No information is available on the carcinogenic effects of acrolein in humans. The Department of Health and Human Services (DHHS) has not classified acrolein as to its carcinogenicity. The U.S. EPA observed that data on acrolein are inadequate for an assessment of human carcinogenic potential based on limited evidence of carcinogenicity in animals, the structural similarity of acrolein to substances possibly carcinogenic to humans, the carcinogenic potential of one of its metabolites, and the lack of human data.[20,24–26]

Acrylamide (CAS no. 79-06-1)

Molecular formula: $CH_2CHCONH_2$

Synonyms and trade names: propenamide, acrylic amide, acrylagel thylenecarboxamide, amresco acryl-40, optimum

Use and exposure: Acrylamide is an organic solid of white, odorless, flakelike crystals. The crystalline monomer is a colorless-to-white, free-flowing crystal that is very soluble in water, alcohol, and ether and insoluble in

benzene and heptane. It is stable at room temperature, but may polymerize violently when melted or in contact with oxidizing agents and under ultraviolet light. When heated to decomposition, acrylamide emits acrid fumes and nitrogen oxides. The polymer exists in many forms that are soluble and insoluble in water. The greatest use of acrylamide is as a coagulant aid in drinking water treatment, in treatment of oil wells, as paper-making aids, in thickeners, soil-conditioning agents, sewage and waste treatment, ore processing, permanent-press fabrics, making organic chemicals and dyes, sizing of paper and textiles, and construction of dam foundations and tunnels. It is also used as a chemical intermediate in the manufacture of polymers, in synthesis of dyes, as a cross-linking agent, in flocculants, in adhesives, and in paper and textile coatings.[27]

Toxicity and health effects: Prolonged periods of exposure to acrylamide through inhalation, skin absorption, and or eye contact cause irritation to the mucous membranes, the nose, and the eyes. Exposed workers also suffer from nausea, speech disorders, and weakness of legs and hands. It is a neurotoxin and disturbs the functions of the CNS, resulting in peripheral nerve damage.[27–29]

Acrylamide and cancer: Acrylamide is known to cause cancer in animals. Also, certain doses of acrylamide are toxic to the nervous system of both animals and humans. In April 2002 the Swedish National Food Authority reported the presence of elevated levels of acrylamide in certain types of food processed at high temperatures. Since then, acrylamide has been found in a range of cooked and heat-processed foods in other countries, including the Netherlands, Norway, Switzerland, the United Kingdom, and the United States. Previous concerns about acrylamide were focused on workers using it in their jobs and cigarette smoking. Thus, acrylamide is a confirmed animal carcinogen with unknown relevance to humans. There is sufficient evidence in experimental animals for the carcinogenicity of acrylamide, but the evidence in humans is inadequate. The IARC has classified acrylamide as a group 2A chemical, meaning that it is probably a human carcinogen.[29]

Exposure limits: Acrylamide has a threshold limit value (TLV) of 0.03 mg/m³ as TWA (skin). Australia recommends an 8-hour TWA exposure limit of 0.03 mg/m^3.[29]

Acrylonitrile (CAS no. 107-13-1)

Molecular formula: C_3H_3N

Synonyms and trade names: cyanoethylene, 2-propenenitrile, vinyl cyanide

Use and exposure: Acrylonitrile is a colorless, man-made liquid with a sharp, onion- or garlic-like odor. It can be dissolved in water and evaporates quickly. Acrylonitrile is used principally as a monomer in the manufacture of synthetic polymers, polyacrylonitriles, acrylic fibers, and other chemicals such as plastics and synthetic rubber. A mixture of acrylonitrile and carbon tetrachloride was used as a pesticide in the past.[1,9a] Acrylonitrile is highly flammable and toxic. It undergoes explosive polymerization. The

burning of acrylonitrile releases toxic fumes of hydrogen cyanide and oxides of nitrogen.

Toxicity and health effects: Prolonged periods of inhalation of high concentrations of acrylonitrile by workers cause mucous membrane irritation, headaches, nausea, feelings of apprehension and nervous irritability, low-grade anemia, leukocytosis, kidney irritation, and mild jaundice. The exposed worker also develops throat irritation, tightness in the chest, difficulty breathing, dizziness, weakness, impaired judgment, and convulsions. However, these symptoms have been found to disappear with the cessation of further exposure. Spillage on the skin burns it and produce redness and blisters. Laboratory studies showed that acrylonitrile caused accumulation of fluid in the lungs, weakness, and paralysis.[9a,9b]

Acrylonitrile and cancer: Reports have indicated that acrylonitrile may reasonably be anticipated to cause cancer in people. Studies of people are inconclusive, while animal studies have shown cancers of the brain and mammary glands.[9a] The U.S. EPA has classified acrylonitrile as a group B1, meaning that it is a probable human carcinogen.[9a–9c]

Exposure limits: For acrylonitrile, OSHA has set a limit of 2 ppm per 8-hour TWA, while NIOSH recommends a level of 1 ppm in the average workplace air over a period of 10 hours.[9a]

Alcohols

The alcohols are hydrocarbons with one or more hydrogen atoms substituted by hydroxyl (–OH) groups. A compound with one hydroxyl group is an alcohol, while with two the group is called glycols and with three hydroxyls it is called glycerols. Alcohols are used extensively in industry as solvents for the manufacture of a variety of products. Generally, all alcohols cause irritation to the mucous membrane with mild narcotic effects. There are important classes of alcohols—namely, allyl alcohol, amyl alcohol, *n*-butyl alcohol, methyl alcohol, ethyl alcohol, and propyl alcohol.

Allyl alcohol (CAS no. 107-18-6)

Molecular formula: C_3H_6O

Synonyms and trade names: vinyl carbinol, propenyl alcohol, 2-propeno-1, propenol-3

Use and exposure: Allyl alcohol is used in the manufacture of allyl esters as monomers and prepolymers for the manufacture of resins and plastics. It has a large use in the preparation of pharmaceutical products, in organic synthesis, and as a fungicide and herbicide. Workers engaged in industries such as the manufacture of drugs, pesticides, allyl esters, organic chemicals, resins, war gas, and plasticizers are often exposed to this alcohol.[1,4]

Toxicity and health effects: Exposure to high concentrations of allyl alcohol vapors causes irritation to eyes, skin, and upper respiratory tract. Laboratory studies with animals have shown the symptoms of local

muscle spasms, pulmonary edema, tissue damage to liver and kidney, convulsions, and death. In view of these findings, industrial workers should be allowed to work with protective clothing.[1,4]

Amyl alcohol (CAS no. 75-85-4)

Molecular formula: $C_5H_{11}OH$

Synonyms and trade names: pentanols, pentyl alcohols, fusel oil, and potato spirit

Use and exposure: Amyl alcohols are produced during the fermentation of grains, potatoes, and beets, as well as during the acid hydrolysis of petroleum fraction. Application of amyl alcohol in industry is very large (and includes manufacturing of lacquers, paints, varnishes, perfumes, pharmaceuticals, plastics, rubber, explosives, hydraulic fluids; extraction of fats; and petroleum refining.[1,4]

Toxicity and health effects: Vapors of amyl alcohol cause mild irritation to mucous membrane of the eyes, nose, throat, and upper respiratory tract and to the skin. Acute and long-term exposures to amyl alcohol cause nausea, vomiting, headache, vertigo, and muscular weakness. Prolonged exposure may also cause narcotic effects.[1,4]

***n*-Butyl alcohol** (CAS no. 71-36-3)

Molecular formula: $CH_3CH_2CH_2CH_2OH$

Synonyms and trade names: *n*-butanol, butyl hydroxide, *n*-propylcarbinol, and butyric hydroxybutane

Use and exposure: *n*-Butyl alcohol is used extensively in a large number of industries. For instance, it is used as a solvent in industries associated with the manufacturing of paints, varnishes, synthetic resins, gums, pharmaceuticals, vegetable oils, dyes, and alkaloids. *n*-Butyl alcohol finds use in the manufacture of artificial leather, rubber and plastic cements, shellac, raincoats, perfumes, and photographic films.[1,4]

Toxicity and health effects: *n*-Butyl alcohol is a highly refractive liquid and burns with a strongly luminous flame. Exposure to *n*-butyl alcohol causes irritation to eyes, nose, throat, and the respiratory system. Prolonged exposure results in symptoms of headache, vertigo, drowsiness, corneal inflammation, blurred vision, photophobia, and cracked skin. It is advised that workers coming in contact with *n*-butyl alcohol should use protective clothing and barrier creams.[1,4]

Ethyl alcohol (CAS no. 64-17-5)

Molecular formula: C_2H_5OH

Synonyms and trade names: absolute alcohol, absolute ethanol, anhydrous alcohol, anhydrol, cologne spirit, molasses alcohol, potato ethanol, grain alcohol, spirit of wine, cologne spirit

Use and exposure: Ethyl alcohol is a flammable, colorless, and mildly toxic solvent. It is a versatile solvent and miscible in all proportions with water and many organic solvents; it is incompatible with strong

oxidizing agents, peroxides, acids, acid chlorides, acid anhydrides, alkali metals, ammonia, and moisture. It forms explosive mixtures with air and is hygroscopic. Ethyl alcohol is the most common solvent used in chemical synthesis of a large variety of products in different industries (e.g., in the manufacturing of pharmaceuticals, plastics, lacquers, polishes, plasticizers, perfumes, adhesives, rubber accelerators, explosives, synthetic resins, nitrocellulose, inks, and preservatives and as a fuel). Ethyl alcohol or ethanol is used in medical wipes and is the most common antibacterial hand senitizer.[1,4]

Toxicity and health effects: Prolonged exposure to vapors of ethyl alcohol causes irritation to eyes and the upper respiratory tract, besides causing headache, drowsiness, fatigue, and mild to severe tremor.[1,4] Ethyl alcohol is a CNS depressant and has significant psychoactive effects in sublethal doses. Ethyl alcohol itself is not a carcinogen, but it causes effects on the liver and influences immune suppression. As such, ethanol consumption can be an aggravating factor in cancers resulting from other causes.[1,4]

Methyl alcohol (CAS no. 67-56-1)

Molecular formula: CH_3OH

Synonyms and trade names: methanol, carbinol, wool alcohol, and wood spirit

Use and exposure: Methyl alcohol is a clear, colorless liquid with a slight alcoholic odor. It is used in the synthesis of formaldehyde, methylamine, ethylene glycol, methacrylates, and as an industrial solvent for a large number of products such as inks, resins, adhesives, and dyes for straw hats. Methyl alcohol is an important ingredient commonly used to prepare grease and dirt remover. It is also used in the manufacture of photographic films, plastics, celluloid, textile soaps, wood stains, coated fabrics, paper coatings, artificial leather, and other industrial products. It is incompatible with strong oxidizing agents such as nitrates, perchlorates, or sulfuric acid, and reacts and attacks some forms of plastics, rubber, coatings, and metallic aluminum.[1,4]

Toxicity and health effects: Exposure to vapor of methyl alcohol causes irritation to the mucous membranes. Toxic effects are exerted upon the nervous system, particularly the optic nerve. Once absorbed into the body, it is very slowly eliminated. Symptoms of overexposure include but are not limited to headache, drowsiness, nausea, vomiting, blurred vision, blindness, drunkenness, insomnia, abdominal pains, coma, and death. Oral ingestion of large amounts of methyl alcohol has caused nausea, giddiness, and loss of consciousness in humans.[1,4]

Propyl alcohol (CAS no.71-23-8)

Molecular formula; $CH_3CH_2CH_2OH$ (*n*-propyl alcohol); $CH_3CHOHCH_3$ (isopropyl alcohol)

Synonyms and trade names: *n*-propyl alcohol, 1-proponal, isopropyl alcohol, isoproponal, and 2-propona

Use and exposure: Propyl alcohol is a clear, colorless, volatile, flammable, fragrant liquid miscible with water and used as a solvent and antiseptic. It has two isomers: *n*-propyl alcohol and isopropyl alcohol. These alcohols have extensive use as chemical intermediates in a variety of industries—manufacturing, pharmaceuticals, perfumes, cosmetics, skin lotions, hair tonics, mouthwashes, and liquid soaps. They are also used as lacquers, dental lotions, polishers, and surgical antiseptics.[1,4]

Toxicity and health effects: Propyl alcohol is not known to cause toxicity to animals and humans unless used improperly. The vapor of propyl alcohol in high concentrations causes mild irritation to eyes, conjunctiva, and mucous membrane of the upper respiratory tract and depression of the CNS.[1,4]

Aliphatic hydrocarbons

Aliphatic hydrocarbons form a very important group of compounds in the chemical industry. Saturated aliphatic hydrocarbons are present naturally in swamp gas, natural gas, paraffin, and crude oil fractions. It is also found in coal, natural resins of plants, and in the fats of animals. These are released to the environment in the exhaust of gasoline and diesel engines, in the flue gas of municipal waste incinerators, and from vulcanization and extrusion processing operations. The industrial uses are often in mixtures— for instance, natural gas, petroleum naphtha, gasoline, kerosene, and mineral spirits. The major uses of aliphatic hydrocarbons include but are not limited to fuels, refrigerants, propellants, dry cleaning agents, lubricants, solvents, and a large number of chemical intermediates. Many are the industrial applications of paraffin wax—for instance, fuels, solvents, lubricants, degreasers, protective coatings, refrigerants, propellants, the application processes of pesticides, intermediates in the synthesis of organic chemicals, and food additives. Industrial applications of aliphatic hydrocarbons, which include alkanes, alkenes (olefins), and alkynes, are not in the scope of these discussions and details may be found in the literature.[1,4]

The most common members of aliphatic hydrocarbons are methane, ethane, *n*-propane, *n*-butane, *n*-pentane, *n*-hexane, *n*-heptane, *n*-octane, *n*-nonane, and *n*-decane. In general, after repeated exposure, these compounds cause nausea, vomiting, abdominal discomfort, asphyxia, and chemical pneumonitis. In high concentrations as gas or vapor, these compounds trigger CNS depression and axonopathy. Keeping up the essential requirements of chemical safety to industrial workers, the ACGIH and OSHA have set the threshold limits for many of the aliphatic hydrocarbons.[1,4]

***n*-Butane** (CAS no. 106-97-8)

Molecular formula: C_4H_{10}

n-Butane is found in exhausts of gasoline engines and in waste disposal sites. Butane as a gas is highly inflammable and explosive; pure butane

has several applications in industries and processing associated with aerosol propellants, fuel source, solvents, rubber, plastics, food additives, and refrigeration. Occupational exposure by direct contact to liquefied butane causes severe adverse health effects such as skin burns or frostbite, injury to the eyes and mucous membrane, and CNS depression.[1,4]

Ethane (CAS no. 74-84-0)
Molecular formula: C_2H_6
Ethane is an extremely flammable gas present in the exhausts of diesel and gasoline engines, municipal incinerators, and from the combustion of gasoline. Inhalation and other exposure cause CNS depression in mammals. Ethane in liquid form results in frostbite. In high concentrations, ethane causes asphyxiation. The symptoms include loss of mobility and consciousness. The victim may not be aware of asphyxiation. In low concentrations it may cause narcotic effects. Symptoms may include dizziness, headache, nausea, and loss of coordination. Remove the victim to an uncontaminated area while wearing a self-contained breathing apparatus. Keep the victim warm and rested.[1,4]

***n*-Heptane** (CAS no. 142-82-5)
Molecular formula: C_7H_{16}
n-Heptane is a flammable liquid present in crude oil and widely used in the automobile industry—for example, as a solvent, a gasoline knock testing standard, automotive starter fluid, and paraffinic naphtha. *n*-Heptane also causes adverse health effects in industrial workers such as CNS depression, skin irritation, and pain.[5,6] Other compounds such as *n*-octane ($CH_3(CH_2)_6CH_3$), *n*-nonane ($CH_3(CH_2)_7CH_3$), and *n*-decane ($CH_3(CH_2)_8CH_3$) also have different industrial applications. Industrial workers exposed to these compounds also show adverse health effects. In principle, management of these aliphatic compounds requires proper handling and disposal to avoid health problems and to contain chemical risk to workers and the living environment.[1,4]

***n*-Hexane** (CAS no. 110-54-3)
Molecular formula: C_6H_{14}
n-Hexane is a highly flammable liquid usually isolated from crude oil and has extensive industrial application as a solvent in adhesive bandage factories and other industries. It is highly toxic, triggering several adverse health effects in animals and humans—for instance, nausea, skin irritation, dizziness, numbness of limbs, CNS depression, vertigo, and respiratory tract irritation. Occupational exposure has been demonstrated to cause motor polyneuropathy in industrial workers. Workers associated with glue sniffing for a long time showed adverse effects in the form of degeneration of axons and nerve terminals.[1,4]

Methane (CAS no. 74-82-8)
Molecular formula: CH_4
Methane is a natural gas present in coal mines, marsh gas, and sludge degradations. Although at low concentrations it causes no toxicity, high doses lead to asphyxiation in animals and humans. Displacement of air by methane gas is known to cause shortness of breath, unconsciousness, and death from hypoxemia. Also, incomplete combustion of gas produces carbon monoxide. Methane is stable and extremely flammable and has a low flash point. Mixtures with air constitute an explosion hazard. It reacts violently with interhalogens and is incompatible with strong oxidizing agents, halogens, interhalogens, and oxygen. High-purity methane is burned to form a high-quality carbon black that is used in a variety of electronic components. Other chemicals derived from methane include methanol, chloroform, carbon tetrachloride, and nitromethane.[1,4]

***n*-Pentane** (CAS no. 109-66-0)
Molecular formula: C_5H_{12}
n-Pentane is a flammable liquid. It has diverse uses in industry—for instance, as an aerosol propellant and as an important component of engine fuel. *n*-Pentane is a CNS depressant. Laboratory studies in dogs indicate that prolonged exposure to high concentrations of *n*-pentane induces cardiac sensitization, poor coordination, and inhibition of the righting reflexes. NIOSH has recommended limits of *n*-pentane for working areas.[1,4]

***n*-Propane** (CAS no. 74-98-6)
Molecular formula: C_3H_8
n-Propane is released to the living environment from automobile exhaust, burning furnaces, natural gas sources, and during combustion of polyethylene and phenolic resins. Propane is both highly inflammable and explosive and needs proper care and management at workplaces. Its use in industry includes source for fuel and propellant for aerosols. Industrial workers exposed to liquefied propane have demonstrated skin burns and frostbite. Propane also causes CNS depression.[1,4]

Aniline (CAS no. 62-53-3)
Molecular formula: C_6H_7N
Synonyms and trade names: aminobenzene, aminophen, arylamine, benzenamine, aniline oil, phenylamine
Use and exposure: At room temperature, aniline, the simplest aromatic amine, is a clear to slightly yellow, oily liquid that darkens to a brown color on exposure to air with a characteristic odor and taste. It has a low vapor pressure at room temperature. Aniline is slightly soluble in water and is miscible with most organic solvents. It does not readily evaporate at room temperature. Aniline is slightly soluble in water and mixes readily with most

organic solvents. Aniline is used to make a wide variety of products, such as polyurethane foam, agricultural chemicals, synthetic dyes, antioxidants, stabilizers for the rubber industry, herbicides, varnishes, and explosives. Aniline is synthesized by catalytic hydrogenation of nitrobenzene or by ammonolysis of phenol. In industry, aniline is an initiator or intermediary in the synthesis of a wide variety of products, most notably polyurethane foam, agricultural chemicals, analgesics, synthetic dyes, antioxidants, stabilizers for the rubber industry, and hydroquinone for photographic developing. Aniline has been used as an octane booster in gasoline. Aniline in air will be broken down rapidly by other chemicals and by sunlight. The general population may be exposed to aniline by eating food or drinking water containing aniline, but these amounts are usually very small. A worker in a place that makes products like dyes, varnishes, herbicides, and explosives may be exposed to aniline. Aniline has also been detected in tobacco smoke, so people who smoke or breathe secondhand smoke may also be exposed to aniline. People living near uncontrolled hazardous waste sites may be exposed to higher than normal levels of aniline.[1,8,30]

Toxicity and health effects: Aniline becomes toxic on inhalation, ingestion, and through skin contact. Exposure to liquid aniline causes mild irritation to skin or eyes. Absorption of aniline through skin results in systemic toxicity and damages the hemoglobin, eventually leading to the development of methemoglobinemia. The symptoms of aniline toxicity include cyanosis, dizziness, headaches, irregular heart beat, convulsions, coma, and death.[30–31a]

Aniline and cancer: The U.S. EPA has determined that aniline is a probable human carcinogen.[30] The IARC has observed that aniline may be categorized as group 3, meaning that it is not classifiable as a human carcinogen, although laboratory rats exposed to aniline for a lifetime developed cancer of the spleen.[31a]

Exposure limits: OSHA has set the exposure limit for aniline as 5 ppm in workplace air for 8 hours (TWA).

Benzene (CAS no. 71-43-2)

Molecular formula: C_6H_6

Synonyms and trade names: benzene, benzine, benzol, aromatic hydrocarbon

Uses and exposure: Benzene is a colorless, flammable liquid with a pleasant odor. It is used as a solvent in many industries, such as rubber and shoe manufacturing and in the production of other important substances such as styrene, phenol, and cyclohexane. It is essential in the manufacture of detergents, pesticides, solvents, and paint removers. It is present in fuels such as in gasoline up to the level of 5%. There are several uses for benzene.[1–4,32–34]

Toxicity and health effects: Exposure to low concentrations of benzene vapor or to the liquid causes dizziness, light-headedness, headache, loss of appetite and stomach upset, and irritation to the nose and throat. Prolonged exposure to high concentrations of benzene leads to functional irregularities in the

heart beat and, in severe cases, death. Benzene is a known carcinogen to humans. It causes leukemia and blood disorders such as aplastic anemia. The major types of leukemia related to benzene exposure are acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (also called chronic myeloid leukemia [CML]), chronic lymphocytic leukemia (CLL), and hairy cell leukemia (HCL).[1–4,32–34] Occupational exposure to benzene is frequent, such as in road-tanker drivers and Chinese glue and shoe-making factory workers. Exposure to benzene has also been linked to lymphoma and rare blood diseases.

AML: Acute myelogenous leukemia (also known as acute myeloid leukemia or acute nonlymphocytic leukemia) is a blood cancer that develops in specific types of white blood cells (granulocytes or monocytes). White blood cells are used by the body to fight infections. The blood cells affected, granulocytes and monocytes, are created from stem cells (hematopoietic stem cells that will turn into different blood cells). These blood stem cells originate in a person's bone marrow. With the development of acute myelogenous leukemia, the normal development of white blood cells becomes disturbed and they do not grow properly. Possibly due to some sort of change or damage to their genetic material or DNA, the cells are prevented from growing beyond a certain point. This disturbs their development, and affects the differentiation process of cells into functional types of white cells.[32–36]

ALL: Acute lymphocytic leukemia is a malignant cancer that develops in a person's white blood cells, called lymphocytes. White blood cells are used by the body to ward off disease and infection. Under normal circumstances, ALL is rare among adults—only about 1500 adults get the disease each year in the United States. However, ALL is the prevalent form of leukemia in children. Nearly 85% of leukemia in children is ALL. In adults, the disease may be related to genetics or exposure to solvents containing benzene. In people who develop ALL (and other types of acute leukemia), white blood cells do not grow properly. Because of some change or damage to their genetic material or DNA that scientists do not fully understand, the cells are prevented from growing beyond a certain point early in their development, and they cannot differentiate into functional types of white cells.

Long-term exposure to benzene increases the risks of getting cancer; however, cancer linked to benzene has been discovered in people exposed for less than 5 years. Workers exposed for decades are at increased risk for these rare forms of leukemia and long-term exposure may also adversely impact bone marrow and blood production. Still other workers have been diagnosed with aplastic anemia, a group of disorders that prevent bone marrow from producing all three types of blood cells: red blood cells, white blood cells, and platelets.[32–37]

Exposure limits: The U.S. EPA has set the maximum permissible level of benzene in drinking water at 5 ppb of water. OSHA has set limits of 1 ppm of workplace air for 8 hours (TWA).[32] NIOSH recommends that the benzene be treated as a potential human carcinogen and that the exposure limit be regulated as a potential human carcinogen.[32]

Benzene and TLVs: The exposure limit for benzene has been set as 0.5 ppm for 8 hours (TWA) and 2.5 ppm for 15-minute short-term exposure limit (STEL) on skin.[32]

Benzidine (CAS no. 92-87-5)

Molecular formula: $C_{12}H_{12}N_2$

Synonyms and trade names: 4,4-biphenyldiamine, 4,4-diaminobiphenyl, *p*-diaminodiphenyl

Use and exposure: Benzidine is a white, grayish-yellow, or slightly reddish crystalline solid or powder with extensive applications in industry. It is used for the synthesis of dyes like Congo red, dye intermediates, and as a hardener in rubber manufacturing industries. The predominant use for benzidine is in the production of dyes, especially azo dyes in the leather, textile, and paper industries.[37a]

Toxicity and health effects: Benzidine is known to be acutely toxic to humans by ingestion. The symptoms of acute poisoning by ingestion include but are not restricted to cyanosis, headache, mental confusion, nausea, and vertigo. Dermal exposure may cause skin rashes and irritation. There is no information available on the acute effects of benzidine in humans via inhalation exposure. Animals exposed for a prolonged period of time developed effects on the blood, liver, kidney, and CNS. Chronic exposure caused bladder injury among workers.[37a]

Benzidine and cancer: Industrial workers exposed to benzidine developed increased risk of bladder cancer. The U.S. EPA has classified benzidine as group A, meaning a human carcinogen. Benzidine is a well known carcinogen in animals and the IARC has classified it as group 1 meaning a human carcinogen.[37a]

1,1′-Biphenyl (CAS no. 92-52-4)

Molecular formula: $C_{12}H_{10}$

Synonyms and trade names: diphenol, 1,1′biphenyl, phenylbenzene

Use and exposure: 1,1′-Biphenyl is a clear, colorless liquid with a pleasant odor; it is the most thermally stable organic compound. It is combustible at high temperatures, producing carbon dioxide and water when combustion is complete. Partial combustion produces carbon monoxide, smoke, soot, and low molecular weight hydrocarbons. It is used extensively in the production of heat-transfer fluids, for example, as an intermediate for polychlorinated biphenyls, and dye carriers for textile dyeing. It is also used sometimes as a mold retardant in citrus fruit wrappers and in formation of plastics, optical brighteners, and hydraulic fluids.[37b,37c]

Toxicity and health effects: The acute effects of biphenyl include polyuria, accelerated breathing, lacrimation, anorexia, weight loss, muscular weakness, coma, fatty liver cell degeneration, and severe nephrotic lesions. Exposure to biphenyl fumes for short periods of time causes nausea, vomiting, irritation of the eyes and respiratory tract, and bronchitis. Breathing small

amounts of biphenyl over long periods of time causes damage to the liver and nervous system of exposed workers. The finely dispersed particles form explosive mixtures in air.[37b,37c]

Exposure limits: OSHA recommends the PEL for biphenyl as 0.2 ppm (TWA). Similarly, the ACGIH recommends a TLV of 0.2 ppm (TWA).[37b,37c]

sec-Butyl acetate (CAS no. 105-46-4)

Molecular formula: $C_6H_{12}O_2$

Synonyms and trade names: acetic acid, 1-methylpropylacetate, 1-methylpropyl acetate acetic acid, 2-butyl ester, acetic acid, sec-butyl ester, sec-butylacetate, butyl acetate.

Use and exposure: Sec-butyl acetate is a colorless liquid with a pleasant odor. The vapor mixes well with air and it becomes an explosive mixture. It reacts with strong oxidants, strong bases, and strong acids and nitrates, causing fire and explosion hazards.[38,39]

Toxicity and health effects: Prolonged occupational exposure to sec-butyl acetate affects health. The symptoms of toxicity include irritation of the skin and eyes. Exposure to high concentrations of sec-butyl acetate irritates the nose and throat, causing coughing and respiratory distress, headache, nausea, vomiting, dizziness, drowsiness, and coma. After prolonged exposure to sec-butyl acetate, industrial workers show symptoms of severe irritation to eyes, headache, drowsiness, dryness in the upper respiratory system and skin, and narcosis.[38,39]

Exposure limits: The legal airborne PEL is 200 ppm averaged over an 8-hour work shift. NIOSH-recommended airborne exposure limit is 200 ppm averaged over a 10-hour work shift (TWA). The ACGIH-recommended airborne exposure limit is 200 ppm averaged over an 8-hour work shift.[38,39]

***n*-Butylamine** (CAS no. 109-73-9)

Molecular formula: $C_4H_9NH_2$

Synonyms and trade names: 1-aminobutane, 1-butanamine, butylamine, mono-*n*-butylamine (MNBA), monobutylamine

Use and exposure: *n*-Butylamine is a clear, colorless liquid with a pungent fish- or ammonia-like odor; it is an extremely flammable liquid and is miscible with water and ethanol. It is used extensively in industries as an intermediate in organic synthesis, to make insecticides, in leather and synthetic tanning, antioxidants, photography, plastics, dyestuffs, rubber chemicals and many emulsifying agents, and pharmaceuticals.[39a]

Toxicity and health effects: Studies have shown that exposure to vapors causes irritation to the eyes, severe burns, loss of vision, irritation to the nose and throat, headache, and pulmonary edema. Exposure to excessive vapor concentrations may cause nausea, vomiting, faintness, coughing, chest pains, dizziness, depression, convulsions, narcosis, and possibly unconsciousness. Exposure of this nature is unlikely, however, because of the irritating properties of the vapor. Any direct skin contact with liquid *n*-butylamine causes

severe primary irritation and deep second-degree burns (blistering) in humans. Nose, throat, and eye irritation and headaches can also occur.[39a]

Exposure limits: The airborne PEL for *n*-butylamine has been set by OSHA as 5 ppm and the ACGIH has set the TLV at a 5 ppm ceiling (skin).[39a]

Carbon disulfide (CAS no. 75-15-0)

Molecular formula: CS_2

Synonyms and trade names: carbon bisulfide, dithiocarbonic anhydride

Use and exposure: Pure carbon disulfide is a colorless liquid with a sweet, chloroform-like odor (threshold of 0.05 mg/m^3) and an odor threshold of 0.05 mg/m^3. The impure carbon disulfide that is usually used in most industrial processes is a yellowish liquid with an unpleasant odor, like that of rotting radishes. Carbon disulfide evaporates at room temperature, and the vapor is more than twice as heavy as air. It easily explodes in air and also catches fire very easily.[1–3,40,41] Carbon disulfide as a solvent has been in use for a long time in the manufacture of sulfur matches and in the extraction of fats. More recently, it has been used in the cold vulcanization of rubber, and today it is used in converting cellulose into rayon fiber and cellophane; xanthogenats (viscose foil); soil disinfectants; electronic vacuum tubes; solvent for phosphorus, sulfur, bromine, iodine, selenium, fats, resins, and rubber; and chemical processes in industry. Direct uses include as a flame lubricant in cutting glass and for generating petroleum catalysts. Food-related uses of carbon disulfide include preservation of fresh fruit, in adhesive compositions for food packaging, and as a solvent in the extraction of growth inhibitors.[40,41]

Toxicity and health effects: Exposure to high concentrations of carbon disulfide causes deleterious effects that include headaches, nausea, vomiting, dizziness, fatigue, chest pains, blurred vision, delirium, neurophysiological changes, reduced nerve conduction velocity, peripheral neuropathy, polyneuropathy, convulsions, and problems with brain, liver, heart. After pregnant rats breathed carbon disulfide in the air, some of the newborn rats died or had birth defects. High concentrations of carbon disulfide have caused skin burns when the chemical accidentally touched people's skin.[1–3,40,41]

Carbon disulfide and cancer: There are no confirmed reports indicating that carbon disulfide is carcinogenic to animals and humans. The U.S. DHHS, the IARC, and the U.S. EPA have not classified carbon disulfide as a human carcinogen.[40,41]

Care and precautions: Handling of carbon disulfide requires proper clothing; eye protection and respiratory protection are important under trained management. On contact with eyes, immediately flush with large amounts of water for at least 15 minutes, occasionally lifting upper and lower lids. Call for medical attention immediately. On skin contact, quickly remove contaminated clothing.

Exposure limits: OSHA has set a PEL for carbon disulfide of 20 ppm for an 8-hour workday (TWA); similarly, NIOSH has recommended a limit for workroom air well within 1 ppm for a 10-hour workday (TWA).[40,41]

Carbon tetrachloride (CAS no. 56-23-51)[1,4,5]

***p*-Chloronitrobenzene** (CAS no. 100-00-5)

Molecular formula: $C_6H_4ClNO_2$

Synonyms and trade names: 4-chloronitrobenzene; *p*-chloronitrobenzene; PCNB; PNCB; *p*-nitrochlorobenzene; 1-chloro-4-nitrobenzene; 4-nitrochlorobenzene; 4-chloronitrobenzene: $C_6H_4ClNO_2$ (nitrobenzol, oil of mirbane); nitrobenzene: $C_6H_5NO_2$ (nitrobenzol, oil of mirbane); *o*-nitrotoluene: $CH_3C_6H_4NO_2$ (*m*-nitrotoluene, *p*-nitrotoluene)

Use and exposure: *p*-Chloronitrobenzene is used extensively in industry as an intermediate in the manufacture of dyes, rubber, and agricultural chemicals. It is incompatible with strong oxidizers and alkalis. It serves as an intermediate in the manufacture of dyes, rubber, and agricultural chemicals.[42,43]

Toxicity and health effects: Repeated exposure to high concentrations of *p*-chloronitrobenzene causes adverse health effects with symptoms of toxicity such as anoxia, unpleasant taste, anemia, methemoglobinemia in animals, hematuria (blood in the urine), spleen, kidney, and bone marrow changes, and reproductive effects (potential occupational carcinogen). The target organs of *p*-chloronitrobenzene-induced toxicity include blood, liver, kidneys, cardiovascular system, spleen, bone marrow, and reproductive system.[42,43]

p-Chloronitrobenzene and cancer: Evaluations by IARC (1996) reported that data and evidence on the carcinogenicity of *p*-chloronitrobenzene in laboratory animals and humans are inadequate and grouped the solvent as 3—not classifiable as a human carcinogen.[42,43]

Exposure limits: OSHA has set the PEL as 1 mg/m^3 (skin) (TWA) and the immediately dangerous to life or health (IDLH) limit has been identified as approximately 100 mg/m^3.[42]

Cyclohexane (CAS no. 110-82-7)

Molecular formula: C_6H_{12}

Synonyms and trade names: benzenehexahydride, hexahydro-benzene, ciclohexano, hexamethylene, exanaphthene, cykloheksan

Use and exposure: Cyclohexane is colorless and highly flammable and readily forms explosive mixtures with air. It is a mobile liquid with a sweet odor that resembles that of chloroform or benzene. Cyclohexane occurs naturally in crude oil and may be released wherever petroleum products are refined, stored, and used. It is insoluble in water and soluble in alcohol, ether, and almost all organic solvents. Cyclohexane is noncorrosive and quickly volatilizes. Cyclohexane derivatives can be used for the synthesis of pharmaceuticals, dyes, herbicides, plant growth regulators, plasticizers, rubber chemicals, cycloamines, and other organic compounds. Any kind of contact between cyclohexane and oxidizing agents such as perchlorates, peroxides, permanganates, chlorates, and nitrates should be avoided. On heating or mixing with liquid nitrogen dioxide, cyclohexane causes explosion.[3,5,6,44]

Toxicity and health effects: Cyclohexane is harmful if swallowed or inhaled, as well as through skin contact. It causes irritation to the skin and eyes and can cause

irritation to the mucous membranes in workers. On repeated and prolonged contact with skin, cyclohexane may cause dermatitis among workers.[3,5,6,44,45]

Cyclohexane and cancer: There are no adequate data about cyclohexane and induction of cancer in animals or in humans. The U.S. EPA has observed that the data are inadequate for an assessment of cyclohexane as a human carcinogen.[45]

Dinitrotoluene (CAS no. 25321-14-6)

Molecular formula: $C_7H_6N_2O_4$

Synonyms and trade names: dinitrotoluene, 2,4-dinitrotoluol, DNT, 2,4-DNT, 4-methyl-1,3-dinitrobenzene

Use and exposure: Technical grade dinitrotoluene is an oily liquid and easily combustible. Dinitrotoluenes are used primarily as chemical intermediates in the production of toluene diamines, diisocyanates, polyurethane foams, dyes, propellants, and polymers, and in the explosives industry.[4,45a,45b]

Toxicity and health effects: Dinitrotoluene is known to cause adverse health effects on the blood, liver, kidney, and CNS in laboratory animals after an acute oral exposure. The animals also showed cyanosis and ataxia. Prolonged periods of exposure caused muscular weakness, poor muscular coordination, tremors, convulsions, ataxia, and paralysis. Industrial workers have developed headache, appetite loss, giddiness, dizziness, nausea, insomnia, and tingling pains in the extremities after chronic exposure to dinitrotoluene.[45a,45b]

2,4- and 2,6-Dinitrotoluenes and cancer: The IARC has reported that there is sufficient evidence in experimental animals for the carcinogenicity of 2,4-dinitrotoluene and 2,6-dinitrotoluene and that evidence is inadequate in humans. Therefore, these have been classified as group 2B, meaning that they are possibly carcinogenic to humans. In view of the inadequate evidence in experimental animals for the carcinogenicity of 3,5-dinitrotoluene, the compound has been listed as group 3, meaning it is not classifiable as a human carcinogen.[45a,45b]

1,4-Dioxane (CAS no. 123-91-1)

Molecular formula: $C_4H_8O_2$

Synonyms and trade names: 1,4-dioxacyclohexane, diethylene dioxide, 1,4-diethylene dioxide, glycol ethylene ether 8, ethylene glycol ethylene ether, diox

Use and exposure: Technical 1,4-dioxane is a clear liquid with an ether-like odor. It is highly flammable and forms explosive peroxides in storage (rate of formation increased by heating, evaporation, or exposure to light). 1,4-Dioxane is incompatible with oxidizing agents, oxygen, halogens, reducing agents, and moisture.[46] It is used as a solvent for cellulose acetate, ethyl cellulose, benzyl cellulose, resins, oils, waxes, some dyes, paper, cotton, and textile processing; and for various organic and inorganic compounds and products. It is also used in automotive coolant liquid, in shampoos and other cosmetics as a degreasing agent, and as a component of paint and varnish. Human exposure to 1,4-dioxane has been traced to multiple occupations

and breathing of contaminated workplace air and drinking polluted water. Industrial uses of 1,4-dioxane are many. For instance, it is used as a solvent for celluloses, resins, lacquers, synthetic rubbers, adhesives, sealants, fats, oils, dyes, and protective coatings; as a stabilizer for chlorinated solvents and printing inks; as a wetting and dispersing agent in textile processing, agrochemicals, and pharmaceuticals; in different solvent-extraction processes; and in the preparation and manufacture of detergents.[1–4,46–48]

Toxicity and health effects: Laboratory studies in experimental animals indicated that repeated exposure to large amounts of 1,4-dioxane in drinking water, in air, or on the skin causes convulsions, collapse, and damage to liver and kidney. On inhalation of 1,4-dioxane, workers suffered from severe poisoning. The symptoms among industrial workers have included coughing, irritation of eyes, drowsiness, vertigo, headache, anorexia, stomach pains, nausea, vomiting, irritation of the upper respiratory passages, coma, and death. 1,4-Dioxane also caused hepatic and renal lesions, demyelination, and edema of the brain.[1–4,46–48]

1,4-Dioxane and cancer: Laboratory studies with animals exposed to 1,4-dioxane showed induction of nasal cavity and liver carcinomas in rats, liver carcinomas in mice, and gall bladder carcinomas in guinea pigs. NIOSH has observed that dioxane is a potential occupational carcinogen and, on the basis of weight-of-evidence characterization, the U.S. EPA classified 1,4-dioxane as group B2, meaning 1,4-dioxane as group B2, which means probable human carcinogen.[46–48]

Exposure limits: NIOSH has set the recommended exposure limit (REL) as 1 ppm for 30 minutes. OSHA has set the PEL as 100 ppm (skin) (TWA) and the IDLH limit as 500 ppm.[46–48]

Ethylene glycol dinitrate (CAS no. 628-96-6)

Molecular formula: $C_2H_4N_2O_6$

Synonyms and trade names: ethylene dinitrate, glycol dinitrate, dinitroglycol, EGDN

Use and exposure: Ethylene glycol dinitrate, also called nitroglycol, is a colorless to yellow, oily liquid. It reacts with acids and is used in the manufacturing of explosives to lower the freezing point of nitroglycerin, in order to produce dynamite for use in colder weather.

Toxicity and health effects: Exposure to ethylene glycol dinitrate causes poisoning and adverse health effects among industrial workers. These include but are not limited to nausea, vomiting, dizziness, throbbing head, abdominal pain, hypotension, flushing of the face, palpitations, methemoglobinemia, delirium, CNS depression, angina, and skin irritation. In laboratory animals ethylene glycol dinitrate caused anemia, mild changes in the liver, and kidney damage.[48a,48b]

Precautions and storage: On exposure to heating, ethylene glycol dinitrate may cause violent combustion or explosion in work areas and release toxic fumes and nitrogen oxides. Also, it may explosively decompose on shock, friction, or concussion. Storage of ethylene glycol dinitrate requires areas

of a fireproof, separate building away from acids, food, and foodstuffs. The storage areas must be kept cool and properly closed.[48a,48b]

Exposure limits: For ethylene glycol dinitrate, OSHA has set a PEL of 0.2 ppm. NIOSH has set the REL as 0.1 mg/m^3 STEL (skin), and the ACGIH has set the TLV as 0.05 ppm.[48a,48b]

Ethylene oxide (CAS no. 75-21-8)

Molecular formula: C_2H_4O

Synonyms and trade names: EO, EtO, alkene oxide, ethylene oxide 1,2-epoxyethane, dihydrooxirene oxacyclopropane, dimethylene oxide, oxidoethane, epoxyethane

Use and exposure: Ethylene oxide is the simplest cyclic ether. It is a colorless gas or liquid and has a sweet odor. Ethylene oxide is a flammable, very reactive, and explosive chemical substance. On decomposition, vapors of pure ethylene oxide mix with air or inert gases and become highly explosive. Large-scale use of ethylene oxide, however, is as an intermediate in the production of monoethylene glycol, diethylene glycol, triethylene glycol, poly(ethylene) glycols, ethylene glycol ethers, ethanolamine, ethoxylation products of fatty alcohols, fatty amines, alkyl phenols, cellulose, and poly(propylene glycol). It is also used as a fumigant for food and cosmetics and in hospital sterilization of surgical equipment and heat-sensitive materials.[49,50]

Toxicity and health effects: Ethylene oxide is toxic by inhalation. Symptoms of overexposure include headache, dizziness, lethargy, behavioral disturbances, weakness, cyanosis, loss of sensation in the extremities, reduction in the sense of smell and or taste, progressing with increasing exposure to convulsions, seizure and coma. Ethylene oxide is also an irritant to skin and the respiratory tract, and inhaling the vapors may cause the lungs to fill with fluid several hours after exposure. Inhalation may cause dizziness or drowsiness. Liquid contact may cause frostbite and allergic skin reactions. After ingestion of ethylene oxide, laboratory animals showed adverse effects in blood, damage to liver and kidney, reproductive effects, miscarriages, spontaneous abortion, and cancer.[49,50]

Ethylene oxide and cancer: Prolonged exposure of laboratory animals to ethylene oxide increased the incidence of liver cancer. OSHA classifies ethylene oxide as a carcinogenic agent. The ACGIH classifies ethylene oxide as "A2," meaning that it is a suspected human carcinogen. The National Toxicology Program (NTP) classifies ethylene oxide as a known human carcinogen. While NIOSH classifies ethylene oxide as a potential human carcinogen, the IARC classifies ethylene oxide as group 1, meaning a human carcinogen.[49,50]

Exposure limits: OSHA and ACGIH have set a limit of 1 ppm for ethylene oxide. NIOSH recommends that average workplace air should contain less than 0.1 ppm ethylene oxide. The U.S. Food and Drug Administration (FDA) has set a tolerance limit of 50 ppm of ethylene oxide in ground spices.[49,50]

Storage and precautions: Ethylene oxide is dangerously explosive under fire conditions; it is flammable over an extremely large range of concentrations

in air and burns in the absence of oxygen. Ethylene oxide is usually stored as a pressurized or refrigerated liquid. At room temperature and pressure, it rapidly evaporates, potentially causing frostbite in cases of skin exposure. Always treat any ethylene oxide leak as an emergency.

Methyl ethyl ketone (CAS no. 78-93-3)
Molecular formula: C_4H_8O
Synonyms and trade names: 2-butanone
Use and exposure: Methyl ethyl ketone (MEK) is a colorless volatile liquid that is soluble in water. MEK is a high-production volume chemical primarily used in commercial and industrial settings, but it is rarely found in commercial products. The major use of MEK is as a solvent and chemical intermediate. As a solvent, MEK is used in surface coatings, adhesives, inks, traffic marking paints, cleaning fluids, and dewaxing agents. Its largest use is in vinyl lacquers, but nitrocellulose lacquers also consume large volumes of MEK. It is used for the solubilization of acrylic coatings in the surface-coatings industry. MEK is also commonly used as a solvent for rubber cements and other natural or synthetic resins for adhesive use. Thus, its primary use is as a solvent in processes involving gums, resins, cellulose acetate, and cellulose nitrate; in the synthetic rubber industry; in the production of paraffin wax; and in household products such as lacquer and varnishes, paint remover, and glues.[49a,49b]
Toxicity and health effects: Inhalation exposure to MEK causes irritation to the eyes, nose, and throat; CNS depression; headache; and nausea. There are no long-term studies with animals breathing MEK. It may contribute to the formation of photochemical smog. MEK has been shown to be of a low order of toxicity following acute oral, dermal, and inhalation exposure. Dermatitis has been reported in humans following dermal exposure to MEK. However, it has not been shown to produce skin sensitization.[49a,49b]
MEK and cancer: The U.S. EPA has listed MEK in group D, meaning that it is not classifiable as a human carcinogen.[49a,49b]

Nitrobenzene (CAS no. 98-95-3)
Molecular formula: $C_6H_5NO_2$
Synonyms and trade names: nitrobenzol, oil of mirbane, essence of mirbane
Use and exposure: Nitrobenzene is a colorless to pale yellow liquid. It has been used extensively in a variety of industries—for instance, the manufacture of aniline dyes and soaps; as solvent for paints; for refining lubricating oils, such as those used in motors and machinery; as shoe polish, floor polish, and dressings for leather products; and to produce lubricating oils such as those used in motors and machinery. A small amount of nitrobenzene is used in the manufacture of drugs, pesticides, synthetic rubber, and explosives.[50a]
Toxicity and health effects: Nitrobenzene is highly toxic to animals and humans. The acute oral LD_{50} to rats has been reported as 640 mg/kg. Industrial workers exposed to nitrobenzene are prone to adverse effects on skin and mucous membranes. These include headache, fatigue, giddiness, vomiting,

weakness, tachycardia, depression, and coma. Studies have indicated that nitrobenzene could trigger pathomorphological lesions in liver and spleen among industrial workers. Severe disturbances during embryogenesis and organogenesis have been reported in nitrobenzene-exposed animals.[50a]

Nitrobenzene and cancer: No suitable cancer bioassays or epidemiological studies are available to assess the carcinogenicity of nitrobenzene. However, the IARC has observed that there is sufficient evidence in experimental animals for the carcinogenicity of nitrobenzene, but the evidence for the carcinogenicity of nitrobenzene in humans is inadequate. The overall evaluations of the IARC classified nitrobenzene as group 2B, meaning that it is possibly carcinogenic to humans.[50b] In contrast, the U.S. EPA has placed nitrobenzene in weight-of-evidence group D, meaning it is not classifiable as a human carcinogen.

2-Nitropropane (CAS no. 79-46-9)

Molecular formula: $CH_3CH(NO_2)CH_3$

Synonyms and trade names: dimethylnitromethane, isonitropropane, nitroisopropane, Ni-Par S-20TM (a commercial grade 2-NP), and NiPar S-30TM (mixtures of 1-nitropropane and 2-NP)

Use and exposure: 2-Nitropropane is a clear, colorless liquid with a pleasant odor that is soluble in many organic solvents, including chloroform. Its vapors may form an explosive mixture with air. 2-Nitropropane is primarily used as a solvent for organic compounds and coatings; with vinyl resins, epoxy paints, nitrocellulose, and chlorinated rubber; in printing inks, adhesives, and printing as flexographic inks; maintenance with traffic markings on roads and highways; shipbuilding; and general maintenance. It also has limited use as a paint and varnish remover. 2-Nitropropane is also used as a solvent in food processing industries for fractionation of a partially saturated vegetable oil. Because of its large-scale use pattern, human exposure to 2-nitropropane has become a health concern.[51–53]

Toxicity and health effects: Laboratory rats exposed to 2-nitropropane in high concentrations (207 ppm) developed adverse liver changes like hepatocellular hypertrophy, hyperplasia, necrosis, and liver carcinoma. It has been reported that prolonged exposure to concentrations of 20–45 ppm of 2-nitropropane caused nausea, vomiting, diarrhea, anorexia, and severe headaches among workers. Industrial workers handling 2-nitropropane for the application of epoxy resins to the walls of a nuclear power plant developed toxic hepatitis.[6,6a,51–53]

2-Nitropropane and cancer: 2-Nitropropane has been classified by the U.S. EPA as group B2, meaning that it is a probable human carcinogen.[53] There is sufficient evidence in experimental animals for the carcinogenicity of 2-nitropropane, but the evidence in humans is inadequate. In its overall evaluation, the IARC classified 2-nitropropane as group 2B, meaning it is possibly carcinogenic to humans.[53a]

Care and precautions: In view of its potential toxicity, 2-nitropropane should be handled in the workplace as a potential human carcinogen. Strict chemical management should be observed at all levels. Industrial workers should be provided with approved personal respiratory protective devices and full-body clothing for protection against splashes.[1–3,6,6a,51–53]

Exposure limits: OSHA has set a PEL for 2-NP of 25 ppm for 8-hour workplace air (TWA).[51–53]

***o*-Nitrotoluene** (CAS no. 88-72-2)

Molecular formula: $C_7H_7NO_2$

Synonyms and trade names: nitrotolul, methylnitrobenzene, 2-nitrotoluene, 2-NT

Use and exposure: *o*-Nitrotoluene is a light, yellow colored, oily, combustible liquid with a characteristic odor of aromatic nitro compounds. It is sparingly soluble in water. *o*-Nitrotoluene is used for the synthesis of a variety of industrial products, such as azo dyes, agricultural chemicals, explosives, sulfur dyes, and rubber chemicals.[4,53b]

Toxicity and health effects: Exposure to *o*-nitrotoluene causes adverse effects in animals and humans. Acute and chronic exposure causes headache, skin irritation, flushing of face, dizziness, dyspnea, hypoxia, cyanosis, nausea, vomiting, muscular weakness, increased pulse and respiratory rate, irritability, and convulsions.[53b]

Care and precautions: *o*-Nitrotoluene is incompatible with oxidizing agents, strong bases, sulfuric acid, reducing agents, hydrogen, and sodium. It undergoes decomposition and produces toxic fumes, causing a fire and explosion hazard. Also, it attacks some forms of plastic, rubber, and coatings. On combustion, *o*-nitrotoluene forms nitrogen oxides and carbon monoxide.[4,53b]

Perchloroethylene (CAS no. 127-18-4)

Molecular formula: C_2Cl_4

Synonyms and trade names: tetrachloroethylene, tetrachloroethene, ethylene tetrachloride, PERC, perchlorcarbon dichloride, 1,1,2,2-tetrachloroethylene

Use and exposure: Perchloroethylene (also called tetrachloroethylene) is a clear, colorless, nonflammable liquid. The smell is known to be sweetish and resembles that of ether. Exposure to perchloroethylene can occur in the workplace or in the living environment following releases to air, water, land, or groundwater. Perchloroethylene (PERC) is a man-made chemical substance with extensive uses in industry for dry cleaning fabrics and textiles and for metal-degreasing operations. In the United States, PERC is the most commonly used dry cleaning solvent and is also occasionally used as a spotting agent. PERC can enter the human body through both respiratory and dermal exposure. Although nonflammable, if PERC is heated sufficiently, thermal decomposition will result in the formation of hydrogen chloride and phosgene gases. Symptoms of perchloroethylene exposure include but are not limited to depression of the CNS, liver and kidney damage, impaired memory, confusion, dizziness, headache, drowsiness, and

eye, nose, and throat irritation. Repeated dermal exposure may result in dry, scaly skin and fissured dermatitis.[54–56]

Toxicity and health effects: Exposure to perchloroethylene causes both mild and severe poisoning among industrial workers. The symptoms of poisoning include but are not limited to severe nausea, confusion, vomiting, slurred speech, dizziness, fatigue, loss of balance, headache, weakness, and poor coordination. In high concentrations in air, particularly in closed, poorly ventilated areas, single exposure to tetrachloroethylene causes diverse effects on the CNS. The symptoms include but are not restricted to dizziness, headache, sleepiness, confusion, nausea, difficulty in speaking and walking, fatigue, headaches, slurred speech, sweating, poor coordination, memory loss, and possibly unconsciousness and death.[54–57]

Perchloroethylene and cancer: Based on the data in laboratory animals, tetrachloroethylene is capable of causing cancer to humans. Studies of NIOSH revealed elevated risk of cancer of the urinary tract, esophagus, and pancreas among individuals who worked in dry cleaning establishments. Because the studies involved exposure to various other solvents in addition to perchloroethylene, no clear conclusions on PERC exposure alone could be made. Although PERC has been known for a long time to be an animal carcinogen, the IARC did not find adequate evidence to classify PERC as a possible human carcinogen. In 1995 the IARC classified PERC in group 2A, meaning that it was probably a human carcinogen. The IARC also has recently classified use of PERC in dry cleaning under group 2B, meaning that it is possibly carcinogenic to humans.[54–59]

Exposure limits: OSHA has recommended the PEL for perchloroethylene as 100 ppm for 8 hours (TWA). The acceptable ceiling concentration is 200 ppm for 5 minutes in any 3-hour period, not to exceed a maximum peak of 300 ppm.[54–56]

Care and precautions: Precautions and strict management are necessary in the handling of perchloroethylene. It should not be used around an open flame, welding arc, intense ultraviolet light source, or smoke. Like most solvents containing chlorine, perchloroethylene also breaks down and releases very hazardous compounds such as phosgene, hydrochloric acid, and chlorine.

Picric acid (CAS no. 88-89-1)

Molecular formula: $C_6H_3N_3O_7$

Synonyms and trade names: picronitric acid, 2,4,6-trinitrophenol, trinitrophenol

Use and exposure: Picric acid is a white to yellowish crystalline substance and highly flammable. It is used in the manufacture of fireworks, matches, electric batteries, colored glass, explosives, and disinfectants. Pharmaceutical, textile, and leather industries also make use of picric acid. Bouin's picro-formol is used as a preservative solution for biological specimens in laboratories.[4,59a]

Toxicity and health effects: Picric acid causes different adverse effects on the skins of animals and humans, like allergies, dermatitis, irritation, and sensitization. Absorption of picric acid by the system causes headache, fever, nausea, diarrhea, and coma. In high concentrations, picric acid is known to

cause damage to erythrocytes, the kidney, and the liver. In 1916 the shock-sensitive metal picrates caused chemical hazards at a French ammunition factory because of fire. The molten picric acid flowed onto the concrete floor and the calcium picrate thus formed detonated and killed about 170 people.[4,59a]

Precautions:

Care and caution are essential in the use and storage of picric acid at workplaces because shock-sensitive metal picrates are hazardous.

Picric acid must always be kept wet.

Do not open a new bottle until needed.

Check the hydration of picric acid kept in bottles at least every 6 months and add distilled water as necessary.

Do not use metal spatulas to remove the material from the stored bottles.

Clean the bottle neck, cap, and threads with a wet cloth before resealing.

Discard old bottles of picric acid with metal caps.

Avoid storage of large amounts of picric acid at workplaces and dispose of picric acid every 2 years.

Waste disposal of old picric acid must be done with the advice of explosives experts.

Styrene (CAS no. 100-42-5)

Molecular formula: C_8H_8

Synonyms and trade names: vinyl benzene, cinnamene, styrol, ethenylbenzene, phenethylene, phenylethene

Use and exposure: Styrene is a colorless liquid with a sweet smell. Styrene is primarily a synthetic chemical used extensively in the manufacture of plastics, rubber, and resins. It is also used as an intermediate in the synthesis of materials used for ion exchange resins and to produce copolymers.[4,59b,59c]

Toxicity and health effects: Acute exposure to styrene causes respiratory effects, such as mucous membrane irritation, eye irritation, and gastrointestinal effects. Styrene causes subjective complaints of headache, fatigue, dizziness, confusion, drowsiness, malaise, difficulty in concentrating, and a feeling of intoxication. Chronic exposure to styrene affects CNS depression and dysfunction, hearing loss, and peripheral neuropathy.[4,59b,59c]

Styrene and cancer: The IARC has classified styrene as a group 2B, meaning that it is a possible human carcinogen.[4,59b,59c]

Toluene (CAS no. 108-88-3)

Molecular formula: C_7H_8

Synonyms and trade names: methacide, methylbenzene, phenylmethane, toluol, toluene (dissolved)

Use and exposure: Toluene is a clear, colorless liquid with an aromatic odor. It is a natural constituent of crude oil and is produced from petroleum refining and coke-oven operations. It is used in household aerosols, nail polish, paints and paint thinners, lacquers, rust inhibitors, adhesives, and solvent-based cleaning agents. Toluene is also used in printing operations, leather tanning, and chemical processes. Benzene and other PAHs are common

contaminants of toluene. Toluene is added to gasoline, used to produce benzene. The major source of toluene exposure for workers and for the general population is gasoline, which contains 5–7% toluene by weight.[64–66] Workers associated with several kinds of activities are at risk, such as manufacturing of dyes and printing inks, painting, automobile mechanics, gasoline manufacturers, shippers, retailers, adhesive and coating manufacturers and applicators, audio equipment production, the chemical industry, coke-oven processes, fabric manufacturers (fabric coating), hazardous waste sites, linoleum manufacturers, pharmaceutical manufacturers, printing, shoe manufacturing, and production of styrene producers.[64–68]

Toxicity and health effects: Workers exposed to moderate levels of toluene demonstrate signs and symptoms of poisoning. These include fatigue, confusion, weakness, drunken-type actions, memory loss, nausea, loss of appetite and hearing, and disturbed vision. However, these symptoms of toxicity disappear with cessation of further exposure. In contrast, repeated human exposure to high levels of toluene leads to severe poisoning, unconsciousness, and even death. Humans with a history of cardiovascular, respiratory, and liver disease are at greater risk of toluene toxicity. Similarly, like other organic solvents, toluene is a respiratory tract irritant and workers with a history of respiratory tract disorders like asthma, chronic obstructive pulmonary disease (COPD), or reactive airways dysfunction syndrome (RADS) are more vulnerable to toluene toxicity.[64–68] Reports have indicated that workers who abuse pure toluene for prolonged periods of time (6–14 years) suffer from cerebellar dysfunction, mental retardation, abnormal encephalograms, brain atrophy, and visual impairment. Similarly, clinical studies of toluene sniffers suggest that ototoxicity as well as vestibular deficits may occur after prolonged inhalation exposure.[68]

Toluene and cancer: Studies in humans and animals generally indicate that toluene does not cause cancer. The U.S. EPA observed that toluene is not classifiable for its carcinogenicity. In view of the inadequate evidence for the carcinogenicity of toluene in humans and lack of evidence on carcinogenicity in experimental animals, the IARC classified toluene under group 3, meaning that it is not classifiable as to human carcinogenicity.[64,66,67]

Exposure limits: The U.S. EPA has set a limit of 1 mg/L of drinking water. Discharges, releases, or spills of more than 1000 lb of toluene must be reported to the National Response Center. OSHA has set a limit of toluene at 200 ppm of workplace air.[64,67]

2,4-Toluene diisocyanate (CAS no. 584-84-9)

Molecular formula: $C_9H_6N_2O_2$

Synonyms and trade names: toluene-2,4-diisocyanate, 2,4-diisocyanato-1-methylbenzene, diiso-cyanatotoluene, TDI, creorcinol diisocyanate, *m*-toluene diisocyanate, 4-methyl-1,3-phenylene diisocyanate.

Use and exposure: Toluene diisocyanate exists in two isomeric forms (2,4-toluene diisocyanate and 2,6-toluene diisocyanate), which have similar properties and effects. Toluene diisocyanate is produced commercially as an 80:20

(2,4-toluene diisocyanate:2,6-toluene diisocyanate) mixture of the two isomers. At room temperature, the mixture is a clear, pale yellow liquid with a sharp, pungent odor. It should be stored under refrigeration, away from light and moisture in a tightly closed container under an inert atmosphere. Toluene diisocyanate is insoluble in water and miscible with most common organic solvents;[60] it is made by reacting toluene diamine with carbonyl chloride (phosgene).Toluene diisocyanate is commonly used as a chemical intermediate in the production of polyurethane foams, elastomers, and coatings; paints; varnishes; wire enamels; sealants; adhesives; and binders. It is also used as a cross-linking agent in the manufacture of nylon polymers.

Toxicity and health effects: Toluene diisocyanate is severely irritating to tissues, especially to mucous membranes. Inhalation produces euphoria, ataxia, mental aberrations, vomiting, abdominal pain, respiratory sensitization, bronchitis, emphysema, and asthma. The mechanism by which toluene diisocyanate produces toxic symptoms is not known, but the compound is highly reactive and may inactivate tissue biomolecules by covalent binding. Acute and chronic exposure to toluene diisocyanate produces health disorders on the skin, respiratory system, CNS, and gastrointestinal tract. A number of occupational studies have reported that chronic exposure to toluene diisocyanate reduces lung function among workers associated with the production of polyurethane foam. Exposure to toluene diisocyanate produces severe respiratory problems; individuals with pre-existing breathing difficulties may be more susceptible to its effects. It causes irritation of the respiratory tract. Concentration-dependent effects occur, often after a delay of 4–8 hours, and may persist for 3–7 days. High-concentration inhalation can lead to chest tightness, cough, breathlessness, and inflammation of the bronchi with sputum production and wheezing. Accumulation of fluid in the lungs can also occur.[60–63] Previously exposed persons may develop inflammation of the lungs when re-exposed to extremely low levels of toluene diisocyanate. Flu-like symptoms such as fever, malaise, shortness of breath, and cough can develop 4–6 hours after exposure and persist for 12 hours or longer. Chest x-rays may indicate lung changes. In sensitized individuals, asthmatic attacks can occur after exposure to extremely low toluene diisocyanate air concentrations (0.0001 ppm). Asthmatic reactions can be immediate, delayed (4–8 hours), or both. Exposure to toluene diisocyanate can lead to reactive airway dysfunction syndrome (RADS), a chemically or irritant-induced type of asthma. Children may be more vulnerable because of relatively increased minute ventilation per kilogram and failure to evacuate an area promptly when exposed.[60–63]

2,4-Toluene diisocyanate and cancer: The DHHS has observed that toluene diisocyanate may reasonably be anticipated to be a carcinogen. However, the U.S. EPA has not classified 2,4-toluene diisocyanate as a human carcinogen. Animal studies have reported significantly increased incidence of tumors of the pancreas, liver, and mammary glands. The IARC has classified 2,4-toluene diisocyanate as group 2B, meaning that it is a possible human carcinogen.[60,61] Toluene diisocyanate has not undergone a complete

evaluation and determination under the U.S. EPA's integrated risk information system (IRIS) program for evidence of human carcinogenic potential.

Safe exposure limits: OSHA has set the PEL for toluene diisocyanate as 0.02 ppm and the NIOSH has set the IDLH as 2.5 ppm.[63]

Care and medical protection: Use and storage of toluene diisocyanate require precautions. It polymerizes under the influence of bases, tertiary amines, and acyl chlorides with fire or explosion hazard. On combustion, it forms toxic vapors and gases, including nitrogen oxides and isocyanates. It reacts readily with water, acids, and alcohols, causing pressure and increasing the hazard of explosion. In the case of development of any unusual signs or symptoms, such as headache, increased pain or a discharge from the eyes, increased redness or pain or a pus-like discharge in the area of a skin burn within 24 hours of an exposure to toluene diisocyanate, there is a need for immediate medical support to the exposed worker.[60,62]

Xylenes (CAS no. 1330-20-7): *o*-xylene (CAS no. 95-47-6); *m*-xylene (CAS no. 108-38-3); *p*-xylene (CAS no. 106-42-3)

Molecular formula: C_8H_{10}

Synonyms and trade names: dimethyl benzene, xylol, methyl toluene, 1,4-dimethyl-benzene

Use and exposure: There are three forms of xylene: *meta*-xylene, *ortho*-xylene, and *para*-xylene (*m*-, *o*-, and *p*-xylene). These different forms are referred to as isomers. Xylene is a colorless, sweet-smelling liquid that catches fire easily. It occurs naturally in petroleum and coal tar. Chemical industries produce xylene from petroleum. Xylene is used as a solvent in the printing, rubber, and leather industries. It is also used as a cleaning agent, a thinner for paint, and in paints and varnishes. It is found in small amounts in airplane fuel and gasoline. Xylene is used extensively in the manufacture of many other chemicals, such as plastics, synthetic fibers, pesticides, insect repellents, and leather goods.[69]

Toxicity and health effects: Xylene is irritating to the skin, eyes, and respiratory tract. It can cause systemic toxicity by ingestion or inhalation. The most common route of exposure is via inhalation. Symptoms of xylene poisoning include CNS effects (headache, dizziness, ataxia, drowsiness, excitement, tremor, and coma), ventricular arrhythmias, acute pulmonary edema, respiratory depression, nausea, vomiting, and reversible hepatic impairment. Prolonged periods of exposure to high concentrations of xylene cause severe health disorders among workers. These include but are not limited to fatigue, irritability, poor coordination, difficulty concentrating, loss of memory, personality changes like increased anxiety and nervousness, pulmonary edema, injury to the liver and kidneys, and neurotoxicity.[69] The effects of xylene on the nervous system may be briefly categorized as

100–200 ppm: nausea, headache;

200–500 ppm: weakness, irritability, vomiting;

800–10,000 ppm: giddiness, confusion, clumsiness, slurred speech, loss of balance, ringing in the ears; and
>10,000 ppm: sleepiness, loss of consciousness, respiratory failure, death.

Xylene and cancer: The IARC has observed that there is inadequate evidence for the carcinogenicity of xylene in humans. No conclusions have been drawn from the available animal information. The overall evaluation of the IARC listed xylene as group 3, meaning that it is not classifiable as a human carcinogen. The list of industrial solvents is large and information on others may be found in the literature.[1–6,16]

4.12 CONCLUSION

Organic solvents of different kinds are used extensively in industry. The solvents are used for extracting, dissolving, or suspending materials such as fats, waxes, and resins that are not soluble in water. They are also used in paints, adhesives, glues, coatings, and degreasing/cleaning agents, and in the production of dyes, polymers, plastics, textiles, printing inks, agricultural products, and pharmaceuticals. Many different classes of chemicals can be used as organic solvents, including aliphatic hydrocarbons, aromatic hydrocarbons, amines, esters, ethers, ketones, and nitrated or chlorinated hydrocarbons. Several solvents have been the cause of health disorders among workers exposed in workplaces through skin contact, breathing in vapors, splashes in the eye, and, in extreme cases, ingestion. Solvents cause the skin to dry out and to be prone to blistering and cracking.

Several studies as well as NIOSH have recognized that many solvents, such as benzene, carbon tetrachloride, trichloroethylene, 2-ethoxyethanol, 2-methoxyethanol, methyl chloride, *n*-hexane, tetrachloroethylene, toluene, and others, are known to cause severe health disorders. Epidemiologic studies of various groups of solvent-exposed workers have demonstrated statistically significant chronic changes in peripheral nerve function (sensory and motor nerve conduction velocities and electromyographic abnormalities) that persisted for months to years. Chronic exposure to benzene, *o*-toluidine, aniline, and other solvents in workplaces has been implicated in the development of cancer in workers. Therefore, proper use and management of solvents are essential and require knowledge about basics of chemical safety.

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APPENDIX 4.1

Classes of Different Chemical Substances and Solvents

Aliphatic hydrocarbons	Acetylene
Alicyclic hydrocarbons	Cyclopropane C_3H_6, cyclohexane C_6H_{12}, cyclohexene C_6H_{10}, methylcyclohexane C_7H_{14}, $_{1,3}$-butadiene $H_2C{=}CH{-}CH{=}CH_2$, gasoline, *n*-hepane, *n*-hexane, kerosene, naphtha, paraffin, turpentine
Alcohols	Allyl alcohol, amyl alcohol, *n*-butyl alcohol, ethyl alcohol, ethylenechlorhydrin, methyl alcohol, propyl alcohol
Glycols	Ethylene glycol, ethylene glycol ethers
Ethers and epoxy compounds	*bis* (Chloromethyl) ether $ClCH_2OCH_2Cl$, chloromethyl methyl ether $ClCH_2OCH_3$, dichloroethyl ether $ClCH_2CH_2OCH_2CH_2Cl$, dioxane $OCH_2CH_2OCH_2CH_2$, epichlorohydrin CH_2OCHCH_2Cl, ethylene oxide H_2COCH_2, ethyl ether $CH_3CH_2OCH_2CH_3$
	Esters
Acetates	Ethyl acetate $CH_3COOC_2H_5$, *n*-butyl acetate $CH_3COOC_4H_9$, ethyl silicate $(CH_2H_5O)_4$, Si
Formates	Methyl formate, ethyl formate, carboxylic acids and derivatives, acetic acid CH_3COOCH, acetic anhydride $CH_3COOCOCH_3$, formic acid HCOOH, oxalic acid HOOCCOOH, phthalic anhydride $C_8H_4O_3$
Aldehydes and ketones	Acetaldehyde CH_3CHO, acrolein $H_2C{=}CHCHO$, formaldehyde HCHO, furfural $C_5H_4O_2$
Ketones	Acetone CH_3COCH_3, methyl ethyl ketone $CH_3COCH_3CH_3$

Aliphatic halogenated hydrocarbons	Carbon tetrachloride CCl_4, chloroform, $CHCl_3$, chloroprene $H_2C{=}CCl{-}CH{=}CH_2$, 1,2-dibromoethane $BrCH_2CH_2Br$, 1,2-dichloroethane $ClCH_2CH_2Cl$, 1,2-dichloroethylene ClCH=CHCl, ethyl chloride CH_3CH_2Cl
Fluorocarbons	Methyl bromide CH_3Br, ethyl bromide C_2H_5Br, methyl chloride CH_3Cl, methylene chloride CH_3Cl_2, propylene dichloride $CH_3CHClCH_2Cl$, tetrachloroethane $CHCl_2CHCl_2$, tetrachloroethylene $Cl_2C{=}CCl_2$, 1,1,1-trichloroethane CH_3CCl_3, 1,1,2-trichloroethane $CH_2ClCHCl_2$, trichloroethylene $ClC{=}CCl_2$, vinyl chloride $CH_2{=}CHCl$
Aliphatic amines	*n*-Butylamine $CH_3{-}CH_2{-}CH_2{-}CH_2{-}NH_2$
Ethanolamines	Monoethanoamine, diethanolamine, ethylenediamine $H_2N{-}CH_2{-}CH_3{-}NH_2$
Cyanides and nitriles	Acetonitrile $CH_3{-}CN$, acrylonitrile $CH_2{=}CH{-}CN$, calcium cyanamide N=Ca, *o*-chlorobenzylidene malonitrile $ClC_6H_4CH{=}C\ (CN)_2$, hydrogen cyanide HCN
Isocyanates	Toluene diisocyanate (TDI), methylene bisphenyl isocyanate (MDI)
Aromatic hydrocarbons	Benzene C_6H_6, diphenyl $C_6H_5C_6H_5$, naphthalene $C_{10}H_8$, styrene $C_6H_5CH{=}CH_2$, toluene $C_6H_5CH_3$, xylene $C_6H_4\ (CH_3)_2$
Phenols and phenolic compounds	Cresol $CH_3C_6H_4OH$, creosote, hydroquinone $C_6H_4\ (OH)_2$, phenol C_6H_5OH, quinone $C_6H_4O_2$
Aromatic halogenated hydrocarbons	Benzyl chloride $C_6H_5CH_2Cl$, chlorodiphenyls and derivatives $C_{12}H_{10}$-XClX, chlorinated benzenes, chlorinated naphthalenes $C_{10}H_8$-xCl
Aromatic amines	2-Acetylaminofluorene $CCH_2C_6H_4C_6H_3NHCOCH_3$, aminodiphenyl $C_6H_5H_6H_4NH_2NH_2$, aniline $C_6H_5NH_2$, benzidine and salts, 3,3-dichlorobenzidine and salts $_6H_3ClNH_2C_6H_3ClNH_2$, 4-dimethyl amino azobenzene $C_6H_5NNC_6H_4N\ (CH_3)_2$, 4,4(-methylene *bis*(2-chloroaniline) $CH_2\ (C_6H_4ClNH_2)_2$, alpha-naphthalamine $C_{10}H_7NH_2$, beta-naphthalamine $C_{10}H_7NH_2$
Nitro compounds	Dinitrobenzene $C_6H_4\ (NO_2)_2$, dinitro-*o*-cresol (DNOC) $CH_3C_6H_2\ (NO_2)_2OH$, dinitrophenol (DNP), dinitrotoluene (DNT), dinitrobenzene $C_6H_5NO_2$, 4-nitrobiphenyl $C_6H_5C_6H_4NO_2$, nitroglycerin $C_3H_5(ONO_2)_3$, ethylene glycol dinitrate $O_2NOCH_2OCH_2ONO_2$
Nitroparaffins	Nitrophenol $NO_2C_6H_4OH$, picric acid $C_6H_2(NO_2)_3OH$, tetryl, trinitrotoluene (TNT)
Organic nitrogen compounds	Acridine $C_{13}H_9N$, *N,N*-dimethylformamide HCON $()CH_3)_2$, ethyleneimine H_2CNHCH_2, hexamethylenetetramine $(CH_2)_6N_4$
Hydrazine and derivatives	Hydrazine ($H_2N{-}NH_2$), *N*-nitrosodimethylamine $(CH_3)_2NN{=}O$, pyridine C_5H_5N, *N,N*-dimethylacetamide $CH_3CON\ (CH_3)_2$
Organic chemicals	Beta-propiolactone OCH_2CH_2CO, tricresyl phosphates (TCP), carbon disulfide CS_2, dimethyl sulfate $(CH_3)_2\ SO_4$
Mercaptans	Methyl mercaptan CH_3SH, ethyl mercaptan CH_3CH_2SH, n-butyl mercaptan $CH_3(CH_2)_2CHSH$, tetramethylthiuram disulfide $C_6H_{12}N_2S_4$
Halogens	Bromine HBr, chlorine Cl, fluorine HF, hydrogen chloride HCl

Sources: Flick, E. W. 1998. *Industrial Solvents Handbook,* 5th ed. Park Ridge, NJ: Noyes Publications; Andrew, L. S., and Snyder, R. 1991. In *Casarett and Doull's Toxicology,* 4th ed., ed. M. O. Amdur, J. Doull, and C. D. Klassen, 681–722. New York: Pergamon Press.

APPENDIX 4.2

Health Hazards of Solvents upon Inhalation

Acetone	Vapors mildly irritating to eyes and respiratory tract; a CNS depressant at high levels; ataxia and seizures have been reported
Chloroform	Vapors slightly irritating to eyes and respiratory tract; a CNS depressant; mild to moderate systemic toxicity, including headache, nausea, vomiting, confusion, and drunkenness; more severe exposures may cause respiratory arrest and coma; a carcinogen in animals
n-Hexane	Vapors mildly irritating to eyes and respiratory tract; light-headedness, giddiness, nausea, and headache; greater exposure may cause unconsciousness and death
Toluene	Acute exposure results in euphoria, excitement, dizziness, headache, nervousness, ataxia, convulsion, and coma; deaths have been recorded from acute exposure to toluene in "sniffers"
Trichloroethane	A respiratory and CNS depressant; symptoms of acute inhalation may include nausea, euphoria, ataxia, dizziness, agitation, and lethargy; severe exposure will lead to respiratory arrest, seizures, and coma
Xylene	Dizziness, excitement, flushing of the face, drowsiness, poor coordination, tremor, confusion, respiratory depression, and coma

5 Metals and Metal Compounds

5.1 INTRODUCTION

The contribution of different metals and metal compounds to society through socioeconomic development and improvement in the quality of life needs no emphasis. In fact, over the ages, human civilization has witnessed the role of metals in the civilized world as exemplified in the Stone Age, Copper Age, and Bronze Age. Metals and metal compounds have offered benefits to society and their improper use has caused harmful health effects to mankind.

Process metallurgy is one of the oldest applied disciplines of the sciences. Its history can be traced back to 6000 BC. Admittedly, its form at that time was rudimentary, but, to gain a perspective, it is worthwhile to spend a little time studying the initiation of mankind's association with metals. Currently, there are 86 known metals. Before the nineteenth century, only 24 of these metals had been discovered and, of these metals, 12 were discovered in the eighteenth century. Therefore, from the discovery of the first metals (gold and copper) until the end of the seventeenth century, only 12 metals were known. Four of these metals—arsenic, antimony, zinc, and bismuth—were discovered in the thirteenth and fourteenth centuries, while platinum was discovered in the sixteenth century. The other seven metals, known as the metals of antiquity, were the metals upon which civilization was based, known to the Mesopotamians, Egyptians, Greeks, and Romans. Of the seven metals, five can be found in their native states—namely, gold, silver, copper, iron (from meteors), and mercury. However, the occurrence of these metals was not abundant and the first two metals to be used widely were gold and copper. In fact, in human history, discovery of metals and growth and development of a variety of global industries are all unbreakable linkages lasting over the centuries.

5.2 DISCOVERY OF METALS

The discovery of metals and metal compounds is closely linked to the history of human civilization and advancement of industrial growth and development around the world. How human civilization has passed through centuries and the contribution of different metals and metal compounds for the human development and improvement of quality of life is beyond description and praise. Some of the metals are now known as the metals of antiquity—that is, those metals upon which human civilization took early origin, profusely grew, and is still making advanced growth. The following list shows different metals and metal compounds and the time in history when they were discovered.

Gold (ca. 6000 BC)
Copper (ca. 4200 BC)
Silver (ca. 4000 BC)
Lead (ca. 3500 BC)
Tin (ca. 1750 BC)
Smelted iron (ca. 1500 BC)
Mercury (ca. 750 BC)
Cobalt (1735)
Nickel (1751)
Manganese (1774)
Molybdenum (1781)
Tellurium (1782)
Tungsten (1783)
Uranium (1789)
Zirconium (1789)
Titanium (1791)
Yttrium (1794)
Beryllium (1797)
Chromium (1797)
Niobium (1801)
Tantalum (1802)
Iridium, palladium, rhodium (1803)
Potassium, sodium (1807)
Boron, barium, calcium, magnesium, strontium (1808)
Cerium (1814)
Lithium, cadmium, selenium (1817)
Silicon (1823)
Aluminum (1827)
Thorium (1828)
Vanadium (1830)
Lanthanum (1839)
Erbium, terbium (1843)
Ruthenium (1844)
Cesium, rubidium (1860)
Thallium (1861)
Indium (1863)
Gallium (1875)
Holmium, thulium, scandium, samarium, gadalinium, praseodynium, neodynium, dysprosium (1878–1885)
Germanium (1886)
Polonium, radium (1898)
Actinium (1899)
Europium (1901)
Lutetium (1907)
Protactinium (1917)
Hafnium (1923)
Rhenium (1924)
Technetium (1937
Francium (1939)
Promethium (1945)

Exposure of humans and animals to a variety of metals and environmental contamination has become a major issue. Essentially, all metals and related compounds, barring a few, cause adverse health effects to humans at sufficiently high concentrations and after a prolonged period of exposure. Interestingly, certain metals essential to human life, such as copper and zinc, are also known to cause adverse health effects. Thus, metals like Co, Cr, Cu, Fe, Mg, Ni, Mo, Se, and Zn are essential, while metals like As, Ag, Au, Be, Cd, Cs, Li, Hg, and Pb have been considered as nonessential for human health. There is much human exposure to metals and metal compounds, for instance, during mining, in extraction from their ores, manufacturing and metallurgical processes, transportation, packaging, and waste disposal. Metals are very important because they are good conductors of heat and electricity.

5.3 DIFFERENT METALS

The Earth's crust is composed of a vast number of different compounds containing both metal and nonmetal elements called ores: aluminum, antimony, arsenic, barium, beryllium, bismuth, calcium, cadmium, chromium (VI), cobalt, copper, iron, manganese, magnesium, mercury, lithium, osmium, potassium, silver, thorium, tin, uranium, vanadium, and zinc.

5.3.1 Metals and Alloys

Metals are mixed together to create alloys. These alloys have better physical properties than the individual metals, such as higher melting points, greater mechanical strength, or increased resistance to corrosion. Steel is an alloy. A few other common alloys are bronze, a mixture of copper and tin; brass, an alloy produced with a mixture of copper and zinc; and solder and pewter, which are mixtures of tin and lead. Gold is alloyed with other metals such as zinc or nickel to produce normal gold as well as white gold. There are several elements that may be grouped:

Alkali metals: lithium, sodium, potassium, rubidium, cesium, and francium. Metals such as sodium and potassium (the alkali metals) react violently with water—too violently to conduct experiments. The group 2 metals (also called alkaline earth metals) react less readily and can be used in the laboratory.
Alkaline earth metals, including beryllium, magnesium, calcium, strontium, barium, and radium.
Transition metals.
Metalloids.
Nonmetals.
Halogens.
Noble gases.
Rare earth elements.

The alkaline earth elements are metallic elements found in the second group of the periodic table. They include beryllium, magnesium, calcium, strontium, barium, and radium. Metals and metal compounds cause adverse health effects to animals and humans when they are not metabolized and are accumulated in the soft tissues of the body. Occupational and environmental exposure for prolonged periods of time to high concentrations of metals in the form of vapors, dusts, fumes, and/or constant skin absorption results in health effects. Accidental ingestion and suicidal or homicidal attempts using metals and metal compounds and their health effects are not the scope of this discussion. The following pages discuss, in brief, some of the most commonly encountered toxic metals and metal compounds, their uses, and thir possible health effects on man and animals.[1–4]

5.4 METAL POISONING AND SYMPTOMS

Prolonged periods of exposure to metals are known to cause poisoning. Symptoms include but are not limited to memory loss, increased allergic reactions, high blood pressure, depression, mood swings, irritability, poor concentration, aggressive behavior, sleep disorders, fatigue, speech disorders, cholesterol, triglycerides, vascular occlusion, neuropathy, autoimmune diseases, and chronic fatigue. Toxic heavy metals may lead to a decline in the mental, cognitive, and physical health of the individual. The degree to which a system, organ, tissue, or cell is affected by a heavy metal toxin depends on the toxin itself and the individual's degree of exposure to the toxin.

The toxicity, health effects, and related symptoms of poisoning caused by different metals and metal compounds in humans is modulated by many factors. In a large number of instances, poisoning from metal compounds is because of the persistence of the metal dusts and fumes present in the workplace, as well as the properties of each metal, the pattern or route of exposure, the form and nature of the metal, and the quantity or concentration of the metal compound ingested, inhaled, or absorbed into the system. The health status of a worker modulates its toxicity. Toxic metals cause severe poisoning and skin diseases such as melanosis, leukomelanosis, keratosis, nonpitting edema, gangrene, and skin cancer.

Industrial workers often complain of nausea, vomiting, diarrhea, stomach pain, headache, sweating, and a metallic taste in the mouth. Depending on the metals in question, there may be blue-black lines in the gum tissues and impairment of cognitive, motor, and language skills. The expression "mad as a hatter" comes from the mercury poisoning prevalent in seventeenth century France among hat makers, who soaked animal hides in a solution of mercuric nitrate to soften the hair.

Poisoning and toxicity from metals and metal compounds have been traced to their extra accumulation in the body tissues and blood, eventually leading to health disorders. When several metals are present in the body, they cause synergistic toxicity. Over a period of time, accumulation of metals causes poisoning and fatal injuries. The common metals associated with poisoning and fatalities among workers and the general public are aluminum, arsenic, cadmium, lead, and mercury. Industrial workers are heavily exposed to metals and related compounds in workplaces and show symptoms of toxicity and poisoning, which include but are not limited to:

- pain throughout the muscles and tendons and soft tissues of the body;
- discomfort, fatigue, dizziness, and illness;
- migraines, headaches, forgetfulness, confusion, and hearing loss;
- impaired facial recognition and gingivitis;
- visual disturbances, lack of eye contact, and impaired visual fixation;
- gastrointestinal discomfort: indigestion, diarrhea, and constipation;
- mood swings, depression, and/or anxiety;
- neurological effects: burning sensation of extremities, numbness, tingling, paralysis, and electrifying feeling throughout the body;
- abnormal sensations in the mouth and extremities;
- slurred speech, unintelligible speech, and impaired reaction time;
- poor concentration, uneven performance on IQ tests, and low IQ scores;

- presenile and senile dementia;
- irritability and aggressive behaviors;
- difficulty walking, swallowing, and talking, myoclonal jerks, and unusual postures; and
- decreased locomotor activity, abnormal gait and posture, poor coordination, loss of balance.

While several symptoms and health disorders are common to many metals, some of the metals produce specific symptoms and health effects (see Appendix 5.1).

Aluminum (CAS no. 7429-90-5) and aluminum compounds
Molecular formula: Al
Synonyms and trade names: aluminum wire, aluminum foil, aluminum shot
Use and exposure: Aluminum is the most commonly available element in homes and workplaces. It is readily available for human ingestion through the use of food additives, antacids, buffered aspirin, astringents, nasal sprays, and antiperspirants, and from drinking water, automobile exhaust and tobacco smoke, and using aluminum foil, aluminum cookware, cans, ceramics, and fireworks. The association of aluminum toxicity with Alzheimer's disease in humans has not been well confirmed. Some data support the association and some do not because the evidence suggesting aluminum as the primary cause of the disease is inadequate and inconclusive. Prolonged periods of exposure to aluminum and its dust cause coughing, wheezing, shortness of breath, memory loss, learning difficulty, loss of coordination, disorientation, mental confusion, colic, heartburn, flatulence, and headaches. Chronic exposure to aluminum dust causes irritation to eyes, skin, and the respiratory system; pulmonary fibrosis; and lung damage.[4–8]
Toxicity and health effects: Occupational exposure to aluminum dust and fumes during welding provides suggestive evidence that there may be a relationship between chronic aluminum exposure and subclinical neurological effects such as impairment on neurobehavioral tests for psychomotor and cognitive performance. The inhalation exposure has not been associated with overt symptoms of neurotoxicity. Prolonged exposure to high concentrations of aluminum and its accumulation causes disturbances in renal function, dialysis, and encephalopathy syndrome—a degenerative neurological syndrome characterized by the gradual loss of motor, speech, and cognitive functions.[4–8]
Aluminum and cancer: The Department of Health and Human Services (DHHS) and the U.S. Environmental Protection Agency (EPA) have not evaluated the carcinogenic potential of aluminum in humans. Aluminum has not been shown to cause cancer in animals.[1] However, the International Agency for Research on Cancer (IARC) has classified aluminum under group 1, meaning that it is a known human carcinogen.[5,6]

Antimony (CAS no. 7440-36-0)
Molecular formula: Sb

Antimony trichloride (CAS no. 10025-91-9); molecular formula: $SbCl_3$

Use and exposure: Antimony is a silvery-white metal found in the Earth's crust. Antimony ores are mined and later mixed with other metals to form antimony alloys used in lead storage batteries, solder, sheet and pipe metal, bearings, castings, and pewter. Antimony oxide is added to textiles and plastics to prevent them from catching fire. It is also used in paints, ceramics, and fireworks, and as enamels for plastics, metal, and glass.

Toxicity and health effects: Exposure to antimony and its compounds causes poisoning to the worker. The symptoms include irritation to eyes, skin, nose, and throat; ulceration of nasal septum and larynx; and dermatitis as characterized by antimony spots. The exposed individual suffers from coughing, dizziness, seizures, headache, anorexia, nausea, vomiting, diarrhea, stomach cramps, bloody stools, insomnia, inability to smell properly, metallic taste, cardiovascular disturbances, pulmonary edema, pharyngitis, tracheitis, pneumoconiosis, slow and shallow respiration, coma, and death.[4,9–11] Antimony fumes and dusts inhaled by industrial workers are associated with the development of benign tumors of the lungs, dermatitis, and, less commonly, effects on the heart and kidneys. Laboratory animals exposed to antimony by inhalation or ingestion exhibit effects similar to those noted in humans. However, there is insufficient evidence to suggest that antimony compounds cause malignant tumors by inhalation in humans or animals.[9–11]

Antimony and cancer: Prolonged periods of exposure of experimental animals (rats) to high concentrations of antimony trioxide and trisulfide increased the incidence of lung tumors. However, the DHHS, IARC, and U.S. EPA have not classified antimony as to its human carcinogenicity. The IARC has grouped antimony trioxide under group 2B, meaning as a possible human carcinogen; the ACGIH has included antimony trioxide under group A2, meaning that it is a suspected human carcinogen.[9–11]

Precautions and warnings: Antimony trioxide is incompatible with bromine trifluoride, strong acids, strong bases, reducing agents, perchloric acid, and chlorinated rubber. The release of deadly gas (stibine) and its inhalation cause adverse effects on the respiratory, gastrointestinal, and cardiovascular systems. Workers must wear impervious protective clothing, including boots, gloves, lab coats, aprons, or coveralls, as appropriate, to prevent skin contact.

Arsenic and arsenic compounds (CAS no. 7440-38-2)

Synonyms and trade names: arsenic black, arsenicals, arsenic-75, colloidal arsenic, gray arsenic, metallic arsenic

Arsenic compounds: Molecular formula—arsenic (As), arsenic acid (H_3AsO_4), arsenous acid (H_3AsO_3), arsenic trioxide (As_2O_3), arsine, arsenic trihydride (AsH_3), cadmium arsenide (Cd_3As_2), gallium arsenide (GaAs), lead hydrogen arsenate ($PbHAsO_4$)

Arsenic is a steel gray, very brittle, crystalline, semimetallic solid; it tarnishes in air, and when it is heated it rapidly oxidizes to arsenous oxide, which

smells of garlic. Arsenic and its compounds are poisonous. Arsenic is a metalloid widely distributed in the Earth's crust. Arsenic and its compounds occur in crystalline, powder, amorphous, or vitreous forms. It occurs in trace quantities in all rock, soil, water, and air. Arsenic is present in more than 200 mineral species, the most common of which is arsenopyrite.

Use and exposure: Arsenic is the most common metal known in history for poisoning. Human exposure to arsenic has been usually associated with suicidal, malicious, homicidal, and occupational handling. Arsenic compounds are used in medicine, glass manufacture, pigment production, rodent poisons, insecticides, fungicides, weed killers, semiconductor manufacture, and tanning processes. Arsenic enters the environment by several industrial activities—for instance, during the smelting process of copper, zinc, and lead, and in the manufacture of chemicals, pesticides, paints, and glasses. The most important compounds are white arsenic, the sulfide, Paris green, calcium arsenate, and lead arsenate, which have been used as agricultural insecticides and poisons. The use of arsenic in the preservation of timber has also led to contamination of the environment. Contamination of drinking water with arsenic caused a serious and massive epidemic of poisoning in Bangladesh.[16–18]

Toxicity and health effects: It is known that arsenic causes poisoning to animals and humans. The symptoms of arsenic poisoning include but are not limited to violent stomach pains in the region of the bowels, tenderness and pressure, vomiting, a sense of dryness and tightness in the throat, thirst, hoarseness and difficulty of speech, greenish or yellowish matter vomited (sometimes streaked with blood), diarrhea, convulsions, cramps, clammy sweats, eyes red and sparkling, delirium, and death. Arsenic causes deleterious effects to blood, kidneys, and central nervous, digestive, and skin systems; skin and nail changes; hyperkeratosis; hyperpigmentation; exfoliative dermatitis; sensory and motor polyneuritis; headache; drowsiness; confusion; stocking-glove distribution of numbness and tingling; distal weakness; moderate hemolytic anemia; leucopenia; slight proteinuria; liver function abnormalities; inflammation of respiratory mucosa; peripheral vascular insufficiency; elevated risk of skin cancer; and cancers of lung, liver, bladder, kidney, and colon.[16–18]

Arsenic and cancer: Reports have indicated that arsenic caused lung and kidney cancers and tumors in laboratory animals and workers. Also, several other studies have shown that ingestion of inorganic arsenic can increase the risk of skin cancer and cancer in the lungs, bladder, liver, kidney, and prostate. Inhalation of inorganic arsenic can cause increased risk of lung cancer. The DHHS has determined that inorganic arsenic is a known carcinogen. The IARC and U.S. EPA have determined that inorganic arsenic is carcinogenic to humans. The IARC has classified arsenic and arsenic compounds as carcinogens under the group 1, while the EU has classified arsenic trioxide, arsenic pentoxide, and arsenate salts under category 1, meaning that evidence is sufficient to establish that it is carcinogenic to man.[16–18]

Inorganic arsenic compounds (As_{+3} and As_{+5}) cause ulceration of nasal septum, nasal septum perforation (as seen in miners), dermatitis, gastrointestinal disturbances, peripheral neuropathy, respiratory irritation, and hyperpigmentation of skin. Acute exposure causes fever, anorexia, hepatomegaly, melanosis, ischemic heart disease, cardiac arrhythmias, and cardiovascular failure. These compounds also cause jaundice; cirrhosis; acites; enlargement of liver (hemmorachic necrosis and fatty degeneration); kidney damage, with effects on capillaries, tubules, and glomeruli; peripheral neuropathy (sensory and motor); axonal degeneration; encephalopathy; and hearing loss due to effects on auditory nerves. They are potential occupational carcinogens.

Arsine (CAS no. 7784-42-1)

Molecular formula: AsH_3

Synonyms and trade names: arsenic trihydride, arsenic hydride, hydrogen arsenide

Use and exposure: Arsine is a colorless, highly toxic gas that has a garlic odor. It is soluble in water, benzene, and chloroform. It is extremely flammable and explosive when exposed to heat, sparks, or flames. Arsine decomposes on heating and under the influence of light and moisture, producing toxic arsenic fumes. Arsine reacts with strong oxidants, causing an explosion hazard and may explosively decompose on shock, friction, or concussion. Workers in the metallurgical industry involved in the production process and the maintenance of furnaces and workers in the microelectronics industry can be affected. Arsine is extensively used in the semiconductor industry and in the manufacture of microchips.[12–15]

Toxicity and health effects: Arsine is a highly toxic gas. It is a potent hemolytic agent and causes acute intravascular hemolysis, rapid red blood cell destruction, and renal failure. Arsine is highly soluble in body fat or lipids and hence can easily cross the alveolo-capillary membrane into the red blood cells. Arsine causes chemical burns. Exposure to arsine causes headaches, malaise, weakness, dizziness, dyspnea, abdominal and back pain, nausea, vomiting, diarrhea, bronze skin, hematuria (hemoglobin in urine), jaundice, liver enlargement, fever, anxiety, disorientation, delirium, shivering, muscular cramps, tachypnea, tachycardia, anemia, hyperkalemia, electrocardiographic changes, burning sensations, peripheral neuropathy (focal anesthesia and paresthesia), agitation, and hallucinations. The exposed individual soon develops a sensation of cold and paresis in the limbs, hemoglobinuria, a garlic-like odor in the breath, multi-organ failure, and massive hemolysis and kidney failure. Studies have indicated that occupational exposure to arsine causes an increased rate of miscarriage among women associated with the semiconductor industry. Reports have indicated that arsine and arsenic compounds are mutagenic. Cytogenetic effects such as chromosomal aberrations, sister chromatid exchanges, and endo reduplication have been observed in Syrian hamster embryo cells exposed to sodium arsenite.[12–15]

Arsine and cancer: Arsine and airborne arsenic compounds have been associated with carcinogenicity.[64] An increased risk of lung cancers has been reported in several epidemiological studies. Arsine is a human carcinogen. The IARC has classified arsenic and arsenic compounds as group 1, meaning carcinogenic to humans.[12–15]

Barium (CAS no. 7440-39-3)

Molecular formula: Ba

Use and exposure: Barium is a silvery-white metal that exists in nature only in ores containing mixtures of elements. It combines with other chemicals such as sulfur or carbon and oxygen to form barium compounds. Barium compounds are used by the oil and gas industries to make drilling muds, which make it easier to drill through rock by keeping the drill bit lubricated. They are also used to make paint, bricks, ceramics, glass, and rubber. Barium sulfate is used to perform medical tests and to take x-rays of the gastrointestinal tract in humans.[19]

Toxicity and health effects: The health effects of the different barium compounds depend on how well the compound dissolves in water or in stomach contents. Barium compounds that do not dissolve well, such as barium sulfate, are not generally harmful. Barium has been found to potentially cause gastrointestinal disturbances and muscular weakness when people are exposed to it at levels above the U.S. EPA drinking water standards for relatively short periods of time. Some people who eat or drink amounts of barium above background levels found in food and water for a short period may experience vomiting, abdominal cramps, diarrhea, difficulties in breathing, increased or decreased blood pressure, numbness around the face, and muscle weakness. Eating or drinking very large amounts of barium compounds that easily dissolve can cause changes in heart rhythm or paralysis and possibly death.[19]

Barium and cancer: The DHHS and IARC have not classified barium as to its carcinogenicity. The U.S. EPA has determined that barium is not likely to be carcinogenic to humans following ingestion and that there is insufficient information to determine whether it will be carcinogenic to humans following inhalation exposure.[19]

Beryllium (CAS no. 7440-41-7)

Molecular formula: Be

Use and exposure: Beryllium is a metal that is found in nature, especially in beryl and bertrandite rock. It is a hard, grayish metal naturally found in mineral rocks, coal, soil, and volcanic dust. It is extremely lightweight and hard, is a good conductor of electricity and heat, and is nonmagnetic. These properties make beryllium suitable for many industrial uses, including metal working. Beryllium compounds are commercially mined and the beryllium is purified for use in nuclear weapons and reactors, aircraft and space vehicle structures, instruments, x-ray machines, and mirrors. Beryllium ores are used to make specialty ceramics for electrical and high-technology

applications. Beryllium alloys are used in automobiles, computers, sports equipment (golf clubs and bicycle frames), and dental bridges. Beryllium dust enters the air from burning coal and oil and will eventually settle over the land and water. It enters water from erosion of rocks and soil, and from industrial waste. Some beryllium compounds will dissolve in water, but most stick to particles and settle to the bottom. Most beryllium in soil does not dissolve in water and remains bound to soil. Beryllium does not accumulate in the food chain. The general population is exposed to normally low levels of beryllium in air, food, and water. People working in industries where beryllium is mined, processed, machined, or converted into metal, alloys, and other chemicals may be exposed to high levels of beryllium. People living near these industries may also be exposed to higher than normal levels of beryllium in air. People living near uncontrolled hazardous waste sites may be exposed to higher than normal levels of beryllium.[20]

Toxicity and health effects: Beryllium can be harmful if a person breathes it. The effects depend on how much one is exposed to and for how long. If beryllium air levels are high enough (>1000 $\mu g/m^3$), an acute condition can result. This condition resembles pneumonia and is called acute beryllium disease. Occupational and community air standards are effective in preventing most acute lung damage. Acute effects include allergic dermatitis and chemical pneumonia. Chronic effects include berylliosis and granulomatous lung disease. Chronic beryllium disease (CBD) primarily affects the lungs. CBD may occur among people who are exposed to the dust or fumes from beryllium metal, metal oxides, alloys, ceramics, or salts. Beryllium contact with skin that has been scraped or cut may cause rashes or ulcers.[20]

Beryllium and cancer: Long-term exposure to beryllium can increase the risk of developing lung cancer in people. The DHHS and IARC have determined that beryllium is a human carcinogen. The U.S. EPA has determined that beryllium is a probable human carcinogen. Also, studies of workers exposed to beryllium have demonstrated significantly elevated risks of lung cancer. The IARC, the expert cancer agency of the World Health Organization (WHO), has concluded that exposure to beryllium can cause lung cancer in humans.[20]

Cadmium (CAS no. 7440-43-9) and cadmium compounds

Molecular formula: Cd

Use and exposure: Cadmium is a natural element in the Earth's crust. It is usually found as a mineral combined with other elements. Cadmium combines with oxygen to form cadmium oxide, with chlorine to form cadmium chloride, and with sulfur to form cadmium sulfide or cadmium sulfate. Cadmium has many uses, including in batteries, pigments, metal coatings, and plastics. Primarily, exposure to cadmium and cadmium compounds occurs in workplaces during mining, smelting, processing, product formulations, and battery manufacturing; nonoccupational exposure comes from various foods and tobacco smoke. Cadmium is used primarily in the production of nickel-cadmium batteries and for metal plating. It is used in alloys for

soldering, brazing, and electrical contacts. Cadmium pigments and stabilizers are important additives in certain specialized plastics, glasses, ceramics, rubbers, paints, inks, and enamels to achieve bright colors.[1,4,21,22]

Toxicity and health effects: Humans exposed to cadmium suffer with nausea, vomiting, abdominal cramping, diarrhea, increased salivation, hemorrhagic gastroenteritis, headache, dizziness, cough, dyspnea, chills (metal fume fever), alopecia, anemia, arthritis, cirrhosis of the liver, renal cortical necrosis, and cardiomyopathy. Acute inhalation of cadmium causes nasopharyngeal irritation, chest pain, enlarged heart, pulmonary edema, pulmonary fibrosis, emphysema, bronchiolitis, alveolitis, and renal cortical necrosis, particularly necrosis of proximal tubule cell. Prolonged periods of exposure to high concentrations of cadmium cause adverse effects to the skeletal system, arthritis, cardiovascular system/hypertension. Cadmium is a human carcinogen. In laboratory animals, it causes cancer of the lung, prostate, testes, hematopoietic system, liver, and pancreas. In industrial workers, exposure to cadmium has resulted in tumors of the lung and prostate.[21,22]

Chromium (CAS no. 7440-47-3)

Molecular formula: Cr

Use and exposure: Chromium is unique among regulated toxic elements in the environment. There has been widespread commercial use in the form of various alloys and compounds for more than 100 years. Chromium exists in three common stable valence states; in order of generally increasing toxicity, these states are chromiums (0), (III), and (VI). Early applications included chrome pigments and tanning liquors. In recent decades, chromium has also been widely used in chromium alloys and chrome plating. Several million workers worldwide are exposed to airborne fumes, mists, and dust containing chromium or its compounds.[23] Of the occupational situations in which exposure to chromium occurs, highest exposure to chromium (VI) occurs during chromate production, welding, chrome pigment manufacture, chrome plating, and spray painting. Highest exposure to other forms of chromium occurs during mining, ferrochromium and steel production, welding, and cutting and grinding of chromium alloys. Chromium (VI) and chromium (III) are used for chrome plating, dyes and pigments, leather tanning, and wood preserving. Chromium is released to air primarily by combustion processes and metallurgical industries. Occupational exposure to chromium through inhalation occurs more with stainless steel welding, chromate production, chrome plating, and chrome pigment industries, primarily to hexavalent chromium (Cr VI). In several other occupations, workers are exposed to both trivalent chromium (Cr III) and chromium (VI) as soluble and insoluble materials.[23]

Toxicity and health effects: Occupational exposure to chromium through inhalation occurs more with stainless steel welding, chromate production, chrome plating, and chrome pigment industries, primarily to hexavalent chromium. Chromium (III) is an essential nutrient that helps the body use

sugar, protein, and fat. Breathing high levels of chromium (VI) can cause irritation to the nose, such as runny nose, nosebleeds, ulcers, and holes in the nasal septum. Ingesting large amounts of chromium (VI) can cause stomach upsets and ulcers, convulsions, kidney and liver damage, and even death. Skin contact with certain chromium (VI) compounds can cause skin ulcers. Some people are extremely sensitive to chromium (VI) or chromium (III). Allergic reactions consisting of severe redness and swelling of the skin have been noted.[23,24]

Chromium and cancer: Several studies have shown that chromium (VI) compounds can increase the risk of lung cancer. Animal studies have also shown an increased risk of cancer. The WHO has determined that chromium (VI) is a human carcinogen. The DHHS has observed that certain chromium (VI) compounds are known to cause cancer in humans. The U.S. EPA has reported that chromium (VI) in air is a human carcinogen.[23–25]

Cobalt (CAS no. 7440-48-4) metal, dust, and fumes (as Co)

Molecular formula: Co

Use and exposure: Cobalt compounds have been used for centuries to impart a rich blue color to glass, glazes, and ceramics. Cobalt is used to produce alloys used in the manufacture of aircraft engines, magnets, grinding and cutting tools, and artificial hip and knee joints. Radioactive cobalt is used for commercial and medical purposes. ^{60}Co (read as cobalt 60) is used for sterilizing medical equipment and consumer products, as well as radiation therapy for treating cancer patients.

Toxicity and health effects: Human exposure to cobalt and cobalt compounds causes cough, tight chest, pain in chest on coughing, dyspnea, malaise, chilling, sweating, shivering, and aching pain in back and limbs. After more days of exposure to high concentrations of cadmium, the worker develops more severe pulmonary responses such as severe dyspnea, wheezing, chest pain and precordial constriction, persistent cough, weakness and malaise, anorexia, nausea, diarrhea, nocturia, abdominal pain, diffuse nodular fibrosis, respiratory hypersensitivity, asthma, sensation of hotness, cardiomyopathy, lung damage, hemoptysis, prostration, and death.[1,2,4,26]

Cobalt and cancer: Nonradioactive cobalt has not been found to cause cancer in humans or animals. However, cancer has been shown in animals that breathed cobalt or when cobalt was placed directly into the muscle or under the skin. The IARC reported that cobalt and cobalt compounds are possibly carcinogenic to humans. Exposure to high levels of cobalt radiation can cause changes in the genetic materials within cells and may result in the development of some types of cancer.[26]

Copper (CAS no. 7440-50-8) dusts, fumes, and mists

Molecular formula: Cu

Use and exposure: Copper occurs naturally in elemental form and as a component of many minerals. It is classified as a noble metal. Copper is a reddish-colored

metal with very high thermal and electrical conductivity. Copper salts, such as sulfate, carbonate, cyanide, oxide, and sulfide, are used as fungicides, as components of ceramics and pyrotechnics, for electroplating, and for numerous other industrial applications.[1,27] Copper is an essential trace mineral that is vitally important for both physical and mental health. It is closely related with nerve conduction, connective tissue, the cardiovascular and immune systems, and estrogen metabolism, and it is required for women's fertility and to maintain pregnancy. Copper stimulates production of the neurotransmitters epinephrine, norepinephrine, and dopamine. It is also required for monoamine oxidase, an enzyme related to serotonin production.

Toxicity and health effects: High levels of copper are found in liver, kidneys, brain, bones, and cornea of patients with Wilson's disease (a genetic disorder characterized by impaired copper metabolism). Industrial workers exposed to copper, fumes, dust, and mists in work areas develop symptoms of poisoning. Copper can be absorbed by oral, inhalation, and dermal routes of exposure. It is an essential nutrient that is normally present in a wide variety of tissues. Prolonged exposure to copper causes irritation to mucous membrane, nasal and pharyngeal irritation, nasal perforation, eye irritation, metallic or sweet taste, and dermatitis. Health effects also include anemia, adverse effects to lung and liver, and kidney damage. The exposed worker also suffers from metal fume fever, chills, muscle aches, nausea, fever, dry throat, coughing, weakness, lassitude, irritation of eyes and the upper respiratory tract, discolored skin and hair, and acute lung damage. Copper compounds as dust cause irritation to eyes, skin, and the respiratory tract; gastrointestinal disturbances; headache; vertigo; drowsiness; and hepatomegaly. Vineyard workers chronically exposed to Bordeaux mixture (copper sulfate and lime) exhibit degenerative changes of the lungs and liver.[1,27]

Copper and target organs: The target organs and health disorders closely associated with copper toxicity are the respiratory system (pulmonary copper deposition, fibrosis, and granulomas of the lung), the liver, the gastrointestinal tract (Kupffer cells, fibrosis and cirrhosis, anorexia, hepatomegaly, nausea), and the nervous system (headache, vertigo, and drowsiness).

Copper deficiency: Copper imbalance causes health disorders that include arthritis, fatigue, adrenal burnout, insomnia, scoliosis, osteoporosis, heart disease, cancer, migraine headaches, seizures, fungal and bacterial infections, gum disease, tooth decay, skin and hair problems, and female organ conditions including uterine fibroids and endometriosis. Copper deficiency is associated with atherosclerosis and other cardiovascular conditions, aneurysms, gout, and anemia.[1,2,27]

Iron oxide fume (CAS no. 7439-89-6)

Molecular formula: Fe

Use and exposure: Iron is required for the normal body functions of animals and humans and of all living cells. It is essential for basic metabolic processes such as oxygen transport, DNA synthesis, cytochrome P-450 enzyme oxidative

metabolism, and electron transport. With its unique ability, iron serves both as an electron donor and acceptor. Iron is the most abundant trace mineral in the body and is an essential element in most biological systems.[2,3,28,29]

Toxicity and health effects: The toxicity of iron is governed by absorption. Chronic iron overload is an insidious toxicity that often does not produce obvious symptoms until substantial tissue damage to vital organs has occurred. Large amounts of free iron in the circulation are known to cause damage to critical cells in the liver, heart, and other metabolically active organs. Industrial workers exposed to fumes of iron compounds show potential symptoms of poisoning such as irritation of eyes, skin, and respiratory system; cough; metal fume fever (MFF); severe vomiting; diarrhea; abdominal pain and dehydration; and siderosis (a benign pneumoconiosis). Reports have indicated that severe siderosis leads to myocardial disease and death. Iron toxicity is usually the result of more chronic iron overload syndromes associated with genetic diseases, repeated transfusions, or other causes. As a result of iron storage disease, the liver becomes cirrhotic. Hepatoma, the primary cancer of the liver, has become the most common cause of death among patients with hemochromatosis. Workers and the general public with hemochromatosis absorb iron very efficiently, which can result in a buildup of excess iron and cause organ damage such as cirrhosis of the liver and heart failure.[28,29]

Lead (CAS no. 7439-92-1)

Molecular formula: Pb

Use and exposure: Lead is a naturally occurring bluish-gray metal found in small amounts in the Earth's crust. Lead is a very corrosion resistant, dense, ductile, and malleable metal that has been used for at least 5000 years. Early uses of lead included building materials, pigments for glazing ceramics, and pipes for transporting water. Exposure to lead has been associated with several human activities—for instance, burning fossil fuels, mining, manufacturing, industrial shielding in medical analysis and video display equipment, and as an additive in gasoline.[4,30–32] The sources of lead in the environment include lead-based paint in homes, lead pipes, lead solder on pipes and water heaters, enameled or ceramic pots and dishware and improper glazing, paper wrappings, food packages, polythene plastic bags, cardboard boxes with dyes, and candy packaging. Sources for lead contamination include bone meal, canned fruit or juice, car batteries (lead acid), ceramic glazes, cigarette ash, eating utensils, auto exhaust, leaded gasoline, hair dyes, lead crystal dishes and glassware, lead refineries, lead smelters, lead water pipes, mascara, milk, newsprint, organ meats, lead-based paint, pesticides, porcelain-glazed sinks and bathtubs, PVC containers, tobacco, toothpaste, toys, and vinyl miniblinds.

Occupations and exposure to lead: The following occupations can expose workers to lead: ammunition manufacturers (guns and bullets), auto body repairs, auto radiator repair shops, battery workers, brass/copper foundries, bridge and highway construction, cable makers, gas stations, glass manufacturers,

industrial machinery and related works, inorganic pigment manufacturers, lead miners, smelters, refiners, plastic manufacturers, painters, and printers, plumbers and fitters, pottery and ceramic workers, rubber product manufacturers, shipbuilders and shipyard workers, stained-glass makers, steel welders, textile workers, and welders and related workers.[4,30]

Toxicity and health effects: Exposure to lead causes adverse health effects to humans and animals of all ages; the effects have been found to be most serious in young children. Lead is recognized as a major environmental health risk throughout the world. The signs and symptoms of lead poisoning include but are not limited to nausea, vomiting, anorexia, hallucination, altered state of consciousness, behavior problems in children, fatigue, apathy, clumsiness, bizarre behavior, constipation, coma, cramps, crankiness, fatigue, hair loss, lethargy, joint pain, loss of appetite, loss of muscular coordination, seizures, peripheral neuropathy, cognitive dysfunction, sleep disorders, stomachaches, and increase in urinary coproporphyrin.[4,30–32] The health effects of lead on children include behavioral problems, learning disabilities, seizures, and death. Infants and young children are at high risk because their bodies are growing quickly. Exposure to high concentrations of lead causes severe damage to the brain and kidneys of adults and children, and miscarriage in pregnant women. There are several health effects of level of blood lead (see Tables 5.1 and 5.2).

Manganese (CAS no. 7439-96-5)

Molecular formula: Mn

Use and exposure: Manganese is a naturally occurring metal that is found in many types of rocks. Pure manganese is silver colored, but does not occur naturally. The metal is gray-white, resembling iron, but is harder and very brittle. The metal is reactive chemically and decomposes slowly. It is an important component of steel. In steel, manganese improves the rolling and forging qualities, strength, toughness, stiffness, wear resistance, and hardness. The common organic manganese compounds include pesticides such as Maneb or Mancozeb. Metallic manganese is used in the manufacturing

TABLE 5.1
Blood Lead Levels and Human Health Effects

Blood Lead Levels (μg/dl)	Effects
10–20	Initial biochemical changes, decreased metabolism of vitamin D
20–30	Hearing impairment, CNS damage
40–50	Slowing of red blood cell production, lower sperm production
50–100	Anemia, colic, seizure, brain damage, decreased longevity
Over 100	Convulsions, permanent brain damage, death

Sources: Published reports; Dikshith, T. S. S., and Diwan, P. V. 2003. *Industrial Guide to Chemical and Drug Safety.* Hoboken, NJ: John Wiley & Sons, Inc.

TABLE 5.2
Concentration of Lead and Health Disorders in Humans

System	Effect	Concentration (μg/dl)
Nervous system	Encephalopathy	80–100
Subclinical	Encephalopathy	
	IQ deficit	<30
In utero effects		<15
Peripheral	Neuropathy	40
Renal system	Acute nephropathy	80–100
Chronic	Neuropathy	60 (children)
	Vitamin D metabolism	<30
	Blood pressure	30 (children)
	Blood anemia	80–100
	U-aminolevulinic acid	40
	B-EPP	15
	Aminolevulinic acid inhibition	10
	Py-5-N-inhibition	<10

Sources: U.S. EPA. 1986. Air quality criteria for lead, EPA 600/8-83/02aF, Washington, D.C.; Dikshith, T. S. S., and Diwan, P. V. 2003. *Industrial Guide to Chemical and Drug Safety.* Hoboken, NJ: John Wiley & Sons, Inc.

of steel, carbon steel, stainless steel, cast iron, and super alloys to increase hardness, stiffness, and strength. Manganese chloride is used in dyeing, disinfecting, and batteries, and as a paint drier and dietary supplement. Manganese oxide (MnO) is used in textile printing, ceramics, paints, colored glass, and fertilizers, and as a food additive. Manganese dioxide is used in batteries and may also be generated from the welding of manganese alloys.[1–4,33]

Toxicity and health effects: Prolonged periods of exposure to high concentrations of manganese dust (mines) and fumes (welding) as it happens in industrial workplaces have health effects. Manganese toxicity—"manganism"—injures the part of the brain that helps to control body movements and affects motor skills such as holding one's hand steady. Workers exposed to manganese dust develop a neurological disorder called "manganese madness" or "locura manganica" that closely resembles Parkinson's disease in later stages. The symptoms of manganese poisoning include but are not limited to headache, insomnia, disorientation, speech disturbances, memory loss, languor, weakness, emotional disturbances, spastic gait, recurring leg cramps, and paralysis. Continuation of exposure to manganese causes disturbance to motor function, tremors, unsteady walking, and exaggerated reflexes similar to Parkinsonism. A high incidence of pneumonia and other upper respiratory infections has been found in workers exposed to dust or fumes of manganese compounds. More information can be found in the literature.[33–36]

Manganese and cancer: There are no reports indicating that manganese causes cancer in humans. The U.S. EPA has included manganese in group D, meaning not classifiable as a human carcinogen.[33]

Manganese tetroxide (as Mn): Occupational exposure to manganese tetroxide causes neurological disorders, Parkinson's gait disturbances, clumsiness, tremor, speech disturbances, mask-like facial expression, psychological disturbances, asthenia, insomnia, mental confusion, hypersomnia, anorexia, metal fume fever, pneumonitis, dry throat, cough, chest tightness, dyspnea, rales, flu-like fever, lower back pain, vomiting, malaise, weakness, exhaustion, kidney damage, and bronchitis. Occupational exposure to manganese tetroxide also causes damage to the central nervous system (CNS), lungs, and kidneys.[36,37]

Mercury (CAS no. 7439-97-6)

Molecular formula: Hg

Mercury is a naturally occurring metal that has several forms. Also known as quicksilver because it is a silver-colored liquid at room temperature, mercury is an element that does not break down. It occurs naturally and is found in very small amounts in oceans, rocks, and soils. It becomes airborne when rocks erode, volcanoes erupt, and soil decomposes. Mercury combines with carbon to make organic mercury compounds (methyl mercury).[38,38a]

Use and exposure: Mercury has been associated with human society over centuries. Alkali and metal processing, incineration of coal and medical and other waste, and mining of gold and mercury contribute greatly to mercury concentrations. Metallic mercury is a shiny, silver-white, odorless liquid. If heated, it is a colorless, odorless gas. Mercury combines with other elements, such as chlorine, sulfur, or oxygen, to form inorganic mercury compounds or "salts," which are usually white powders or crystals. Mercury also combines with carbon to make organic mercury compounds. The most common one is methyl mercury. Large quantities of metallic mercury are employed as electrodes in the electrolytic production of chlorine and sodium hydroxide from saline. Metallic mercury is used to produce chlorine gas and caustic soda, and in thermometers, dental fillings, and batteries.[1–4,38–41]

Toxicity and health effects: The toxic effects of mercury depend on its chemical form and the route of exposure. Methyl mercury (CH_3Hg) is the most toxic form. It affects the immune system, alters genetic and enzyme systems, and damages the nervous system, including coordination and the senses of touch, taste, and sight. Methyl mercury is particularly damaging to developing embryos, which are 5–10 times more sensitive than adults. Exposure to methyl mercury is usually by ingestion, and it is absorbed more readily and excreted more slowly than other forms of mercury. The episode of Minamata Bay, Japan, in the 1950s and 1960s and the health hazard there are still memorable. The CNS is the critical organ for the toxic effects of inhaled elemental mercury. Broken thermometers and the inhalation of vapors cause tremors, gingivitis, and excitability. The symptoms of mercury poisoning include but are not restricted to impairment of the peripheral

vision, disturbances in sensations ("pins and needles" feeling), and numbness. Mercury poisoning also causes lack of coordination of movements while writing; impairment of speech, hearing, and walking; muscle weakness; skin rashes; mood swings; memory loss; and mental disturbance.[38–41] Prolonged periods of exposure to high concentrations of mercury cause tremors, gingivitis, insomnia, shyness, memory loss, emotional instability, depression, anorexia, vasomotor disturbance, uncontrolled perspiration and blushing, headaches, polyneuropathy as seen in parasthesias, stocking glove sensory loss, hyperactive tendon reflexes, slowed sensory and motor conduction, cognitive defects with performance problem tests, renal failure, dementia and acrodynia, desquamating rash, hair loss, pruritus, diaphoresis, tachycardia, hypertension, and neuromuscular changes such as weakness, muscle atrophy, and muscle twitching. All forms of mercury are toxic to the fetus, and methyl mercury most readily passes through the placenta.

Methyl mercury and Minamata: The dumping of mercury-polluted wastewater into Minamata Bay brought the dangers of methyl mercury poisoning into international focus. The disasters in Minamata, Japan, in the 1950s and in Iraq in 1971 and 1972 clearly demonstrated neurological effects associated with ingestion of methyl mercury both in adults and in infants exposed in utero. The effects were convincingly associated with methyl mercury. Methyl mercury readily crosses the placenta; delayed for months following exposure, toxicity increases, leading to paresthesias (abnormal sensations such as numbness and tingling of toes, fingers, mouth, and lips) to ataxia (stumbling or clumsy gait) and generalized weakness to decreased vision and hearing, tremor, coma, and death.

Mercury and cancer: Mercuric chloride has caused several types of tumors in rats and mice and methyl mercury has caused kidney tumors in male mice, but information about human cancer is inadequate. The U.S. EPA has reported that mercuric chloride and methyl mercury are group C (meaning that they are possible human carcinogens) and elemental mercury as group D (not classifiable as to human carcinogenic potential). The IARC has classified metallic mercury and inorganic mercury compounds as group 3, meaning that they are not classifiable as human carcinogens and methyl mercury compounds as group 2B, possibly carcinogenic to humans. Similarly, the IARC reported that there is inadequate evidence in humans and animals for the carcinogenicity of mercury and mercury compounds. In its overall evaluation, the IARC included the metallic mercury and inorganic mercury compounds as group 3 are not classifiable as human carcinogens and methyl mercury compounds as group 2B are possibly carcinogenic to humans).[38–41]

Nickel (CAS no.7440-02-0)

Molecular formula: Ni

Use and exposure: Nickel is a silvery-white metallic element. It is tough, harder than iron, and highly resistant to rusting and corrosion. A large number of people are allergic to nickel and it causes more cases of allergic

contact dermatitis than all other metals combined. Many cases of allergic contact dermatitis occur from exposure to the nickel content of jewelry. Nickel has many uses in industry and in the manufacture of consumer products such as stainless steel, magnets, coinage, and special alloys. Human exposure to these nickel compounds in jewelry, soaps, fats, and oils is known. Nickel sulfate is used in electroplating, as a mordant in dyeing, in preparation of other nickel compounds, and in paints, varnishes, and ceramics. The nickel oxides are used in ceramic glazes, in glass manufacture, in the preparation of alloys, and in the Edison battery.[1–4,42]

Toxicity and health effects: Prolonged exposure to high concentrations of nickel and nickel compounds causes poisoning and health disorders in humans. These include but are not limited to headache, dizziness, nausea, vomiting, epigastric pain, substernal pain, eye and respiratory irritation, cough, shortness of breath (hyperpnea), cyanosis, pulmonary edema (may be delayed), weakness, leukocytosis, pneumonitis, pulmonary fibrosis, cerebral edema, delirium, convulsions, contact dermatitis, and skin and lung sensitization. Nickel-induced contact dermatitis is well documented for humans and is the most prevalent effect of nickel exposure in humans. Exposure to nickel dust, primarily nickel subsulfate in workplaces, causes increased incidences of pulmonary and nasal cancer and adverse effects to the lungs, upper respiratory tract, kidneys, cardiovascular system, immune system, and blood.[1–4,42–44] Acute inhalation exposure to nickel carbonyl results in initial headache, nausea, vomiting, decreased sense of smell, coughing, leucocytosis, pneumonitis, delirium, convulsions, chest pain progressing to hyperpnea, cyanosis, respiratory failure, and death if the exposure is severe. Nickel fumes cause an increase in airway and eye irritations, headaches, and tiredness. Most chronic inhalation exposure involves occupational exposure to nickel dust or nickel vapors resulting from welding nickel alloys. Generally, chronic inhalation of nickel dusts and aerosols contributes to respiratory disorders such as asthma, bronchitis, rhinitis, sinusitis, and pneumoconiosis.[1–3,42–44]

Nickel and cancer: Nickel and nickel compounds are known to be human carcinogens based on sufficient evidence of carcinogenicity from studies in humans, including epidemiological and mechanistic information, which indicates a causal relationship between exposure to nickel compounds and human cancer. The findings of increased risk of cancer in exposed workers are supported by evidence from experimental animals that shows that exposure to an assortment of nickel compounds by multiple routes causes malignant tumors. Nickel sulfide fumes and dust are believed to be carcinogenic, and various other nickel compounds may be as well. Chronic exposure to nickel and nickel compounds has been implicated in carcinogenic, nickel-induced contact dermatitis. It is well documented for humans and is the most prevalent effect of nickel in humans. Reports have also shown an excess of lung and nasal cancer among nickel refinery workers. Studies have indicated that nickel compounds—for instance, nickel subsulfide—is

carcinogenic to humans (group 1) and nickel carbonyl (group 2B) is a probable human carcinogen.[42–45]

Osmium (CAS no. 7440-04-2)
Molecular formula: Os
Use and exposure: Osmium is a bluish white, shiny metal, and osmium tetroxide is a colorless to pale yellow crystalline solid with an odor that has been described as pungent or chlorine-like. Osmium is dissolved by acids or by *aqua regia* only after long periods of exposure to the liquids. On heating, osmium metal combines with oxygen to form osmium tetroxide (OsO_4), which is very toxic and the only important commercial compound of osmium. Osmium tetroxide is used as a tissue fixative for electron microscopy, and as a catalyst for research purposes. Students and workers must take precautions in the use of osmium tetroxide.[46–48]
Toxicity and health effects: Human poisoning and symptoms of osmium tetroxide exposure are modulated by the route of exposure. In fact, osmium tetroxide causes adverse health effects very rapidly at very low concentrations. Osmium tetroxide is corrosive and causes severe chemical burns to the skin, blisters, and discoloration. Health disorders caused by prolonged exposure to osmium tetroxide include but are not limited to irritation and pain to the eyes and respiratory tract, burning sensations, tearing, cough, headache, wheezing, shortness of breath, digestive disturbance, distress to the pharynx and larynx, pulmonary edema, insomnia, and death. It also causes skin redness or rash, visual disturbances, severe conjunctivitis, and, in severe cases, a permanent loss of vision. Accidental ingestion causes abdominal cramps, burning sensations, vomiting, and collapse.[46–48]
Precautions: Osmium is very dangerous to use. It is shipped in small glass containers called ampules. Because osmium reacts violently, the ampules carry no labels and are not marked with ink. Great care is needed during use and handling of an ampule containing osmium tetroxide.
Osmium and compounds: Osmium tetroxide is a colorless to pale yellow crystalline solid with an odor that has been described as pungent or chlorine-like. Students and workers must take precautions in the use of osmium tetroxide. Prolonged periods of inhalation exposure to osmium tetroxide cause insomnia, digestive disturbance, and distress to the pharynx and larynx.[46–48]

Selenium compounds (as Se)
Molecular formula: Se
Use and exposure: Selenium is an essential trace element for human health. However, acute and prolonged periods of exposure to high concentrations of selenium compounds cause adverse health effects in humans. The symptoms include garlicky breath; irritation of eyes, skin, nose, and throat; visual disturbances; headache; nausea; vomiting; chills; fever; weakness; violent cough; bitter metallic taste in the mouth; nose bleeds; dyspnea; bronchial spasms; bronchitis; pulmonary edema; gastrointestinal tract disturbance;

dermatitis; eye and skin lesions; skin burns; lowered hemoglobin levels; tachycardia; and tremors. Exposure to selenium dioxide or selenium oxychloride is also known to cause skin burns, bronchospasm, and irritation of the upper respiratory passages.[49–52]

Toxicity and health effects: Selenium causes hair and nail loss, discoloration and decay of the teeth, and CNS disturbances, including pain and anesthesia of the extremities. Inhalation of hydrogen selenide causes pulmonary edema. The dusts of selenium produce respiratory tract irritation, while the fumes of selenium dioxide produce metal fume fever. Dermal exposure and ingestion of selenium oxychloride cause skin burns, corrosive injury to the gastrointestinal tract, stupor, respiratory depression, and refractory hypotension. Ingestion of selenious acid causes corrosive injury to the gastrointestinal tract, stupor, respiratory depression, and refractory hypotension.[49–52]

Selenium and cancer: Inadequate human data and inadequate evidence of carcinogenicity in animals suggest that selenium cannot be classifiable as a human carcinogen. However, with sufficient evidence, selenium sulfide is grouped as B2, meaning that it is a probable human carcinogen.[49]

Silver (CAS no. 7440-22-4)

Molecular formula: Ag

Use and exposure: Silver is a very ductile and malleable precious metal. A major use of silver is as jewelry and silverware made from sterling silver and standard silver for traditional purposes. Silver also is used in photography and to make solder and brazing alloys, electrical contacts, and high-capacity silver–zinc and silver–cadmium batteries. Silver has the highest electrical conductivity of all metals—even higher than copper.[53]

Toxicity and health effects: Silver and silver compounds in all three routes of exposure—namely, by ingestion, inhalation, or dermal absorption—cause a condition known as argyria, the most common indicator of long-term exposure. The symptoms of poisoning include blue-gray eyes (argyrosis); skin (argyria); metal fume fever; irritation to eyes, skin, and throat; breathing problems; lung and throat irritation; perforation of nasal septum; and sensory disturbances to taste and smell.[53–56]

Silver compounds: Silver and silver compounds are used extensively in industries and the compounds include: silver carbonate (Ag_2CO_3), silver chloride (AgCl), silver fulminate (Ag ONC), silver iodide (AgI), silver nitrate ($AgNO_3$), silver sulfide, and silver oxide.

Silver iodide (Ag I) (CAS no. 7783-96-2)

A pale yellow, odorless, tasteless powder that darkens when exposed to light and is used as an antiseptic.

Silver nitrate ($AgNO_3$) (CAS no. 7761-88-8)

Exposure to silver nitrate by inhalation cause deleterious effects to tissues of the mucous membranes and upper respiratory tract. The symptoms of poisoning include but are not restricted to burning sensations, coughing,

wheezing, laryngitis, shortness of breath, headache, nausea, and vomiting. By ingestion, silver nitrate cause severe burns of the mouth, throat, and stomach; blackening of the skin; mucous membranes, throat, and abdomen; salivation; vomiting of black material; diarrhea; collapse; shock; coma; and death.[53–56]

Tin (CAS no. 7440-31-5) and tin oxide (as Sn) (total dust)
Molecular formula: Sn
Use and exposure: Tin is a soft, pliable, silvery-white metal. Tin is not easily oxidized and resists corrosion because it is protected by an oxide film. Tin resists corrosion from distilled sea and soft tap water and can be attacked by strong acids, alkalis, and acid salts. Tin foil was once a common wrapping material for foods and drugs, now replaced by the use of aluminum foil.[57] Tin is used to coat cans of fruits and vegetables, processed foods, and industrial waste.[1–3,57]
Toxicity and health effects: The organic tin bonds are the most dangerous forms of tin for humans. Despite the danger, they are applied in a great number of industries, such as the paint and the plastics industries, and in agriculture through pesticides. The number of applications of organic tin substances is still increasing, despite the fact that the consequences of tin poisoning are known. The effects of organic tin substances differ and depend upon the kind of substance that is present and the organism that is exposed to it. Triethyltin is the most dangerous organic tin substance for humans. It has relatively short hydrogen bonds. When hydrogen bonds grow longer, a tin substance will be less dangerous to human health. Humans can absorb tin bonds through food, breathing, and the skin. The uptake of tin bonds can cause acute effects as well as long-term effects. Prolonged exposure causes adverse health effects. These include but are not limited to eye and skin irritations, headaches, stomachaches, dizziness, profuse sweating, abdominal cramping, abdominal bloating, nausea, fever, hyperglycemia, vision changes, liver pain, depression, liver damage, shortage of red blood cells, malfunctioning of immune systems, neurological disorders such as sleeping disorders, forgetfulness, stenosis (benign pneumoconiosis), cough, respiratory distress, and decreased pulmonary function. In fact, stenosis has been reported in men working in the smelter of a tin mine and working in tin recovery from scrap. Accumulation of tin causes adverse effects to the brain and liver.[57]

Vanadium (CAS no. 7440-62-2)
Molecular formula: V
Use and exposure: Vanadium is a soft and ductile, silver-gray metal. It has good resistance to corrosion by alkalis, sulfuric and hydrochloric acid, and salt water. Vanadium metal, sheet, strip, foil, bar, wire, and tubing have been used in industry. It is used in high-temperature service, in the production of

rust-resistant, high-speed tools, and in important carbide stabilizers in making steels. In fact, most vanadium is used as an additive to improve steels. Vanadium steel is especially strong and hard, with improved resistance to shock. Vanadium pentoxide (V_2O_5) is perhaps vanadium's most useful compound. It is used as a mordant, a material that permanently fixes dyes to fabrics. Vanadium pentoxide is used as a catalyst in chemical reactions and in the manufacture of ceramics. It can also be mixed with gallium to form superconductive magnets.[58]

Toxicity and health effects: Exposure to high levels of vanadium causes harmful health effects. The major effects from breathing high levels of vanadium are on the lungs, throat, and eyes. Workers who breathed it for short and long periods sometimes had lung irritation, coughing, wheezing, chest pain, runny nose, and sore throat. Prolonged periods of exposure to dusts and fumes of vanadium have caused potential symptoms of toxicity among industrial workers. The symptoms of poisoning include but are not limited to irritation of eyes and throat, green tongue, metallic taste, sore throat, cough, drowsiness, wheezing, bronchitis, abdominal cramps, nausea, vomiting, diarrhea, respiratory distress, pulmonary edema, bronchial damage, epistaxis (bloody nose), eczema, conjunctivitis, headache, dry mouth, dizziness, nervousness, insomnia, and tremor. Vanadium is a natural component of fuel oil, and workers have developed vanadium poisoning during cleaning operations on oil-fired furnaces.

Vanadium and cancer: The DHHS, IARC, and U.S. EPA have not classified vanadium as to its human carcinogenicity.[58]

Zinc (CAS no. 7440-66-6)

Molecular formula: Zn

Use and exposure: Zinc is available as a silver or bluish-white foil or powder. It is incompatible with amines, cadmium, sulfur, chlorinated solvents, strong acids, and strong bases. The important use of zinc is to coat iron or steel in a process called galvanization to prevent rust. Zinc powder is very flammable. Zinc is another essential micronutrient that is important in immunity and antioxidation. Zinc is an essential mineral that is found in almost every cell function. It stimulates the activity of approximately 100 enzymes, which are substances that promote biochemical reactions in the body. Zinc supports a healthy immune system that the body requires for wound healing. It helps to maintain a sense of taste and smell and is needed for DNA synthesis. Zinc supports normal growth and development during pregnancy, childhood, and adolescence.[59]

Toxicity and health effects: Exposure to high concentrations of fumes of zinc compounds such as zinc chloride and zinc oxide causes poisoning among industrial workers. The symptoms include but are not limited to headache, blurred vision, low back pain, vomiting, fever, chills, muscle ache, dry throat, cough, weakness, exhaustion, metallic taste in the mouth, chest tightness, respiratory distress, and decreased pulmonary function. The clinical

signs of zinc toxicosis include vomiting, diarrhea, red urine, icterus (yellow mucous membranes), liver failure, kidney failure, and anemia. High concentrations of fumes of zinc chloride cause irritation and redness in eyes; irritation to skin, nose, and throat; conjunctivitis; burning effect; cough with sputum; breathing problems; chest pain; pulmonary edema; pneumonitis; and pulmonary fibrosis.[59] While zinc is an essential trace metal, ingestion of excessive amounts by birds and pets causes toxicity somewhat similar to lead intoxication. Parrots are commonly housed in wire cages and repeated chewing of the galvanized steel wire cages causes zinc poisoning to the birds. Common signs of zinc intoxication in birds include excessive urine in the droppings and feather picking. Pet animals with zinc toxicity demonstrate three characteristics of poisoning: intravascular hemolytic anemia, gastrointestinal upset, and potential multi-organ failure.

Zinc oxide (CAS no. 1314-13-2)

Molecular formula: ZnO

Zinc oxide is an odorless, amorphous, white or yellowish-white powder. It is incompatible with chlorinated rubber, linseed oil, magnesium, hydrogen fluoride, aluminum + hexachloroethane, zinc chloride or phosphoric acid; water should be avoided. On decomposition, toxic fumes are released from zinc oxide.[60]

Toxicity and health effects: Exposure to zinc oxide causes adverse health effects to the lungs and the reproductive system in experimental animals. Inhalation of zinc oxide fumes by workers causes metal fume fever.[60–63]

Zinc sulfate heptahydrate (CAS no. 7446-20-0)

Molecular formula: $ZnSO_4 7H_2O$

Zinc sulfate heptahydrate is incompatible with strong oxidizing agents. It is hygroscopic and needs to be protected from moisture.

5.5 CONCLUSIONS

Minerals, metals, metallurgical processing, industrial progress, and the global economy are all closely related to human progress; that is, metals are essential and very important. In fact, several human activities and occupations closely involve extensive application of different metals and metal compounds. It is well known that metals are toxic and cause adverse health effects to humans. Inhalation of and skin contact with metal dust, fumes, or vapors in the workplace are known to cause severe health disorders among workers. Therefore, for purposes of human health and environmental safety, the user and industrial workers must know the elements of proper and judicious use of metals and metal compounds. This underlines the need for providing basic information and training to workers about the hazards and proper management of chemical substances.

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APPENDIX 5.1

Metals and Health Disorders in Humans

Prolonged exposure to high concentrations of metals and their accumulation in the soft tissues cause many kinds of health disorders:

Aluminum	Chronic fatigue syndrome (CFS), encephalopathy, weakness, malaise, neurofibrillary tangles, neuritis, retrobulbar neuritis, neuropathy, pulmonary fibrosis, pneumonia, laryngitis, pharyngitis, bronchitis, dementia, presenile and senile dementia, decreased locomotor activity, and speech disorders
Arsenic	Abdominal pain, stomach cramps, burning of the throat and mouth, gastroenteritis, blurred vision, sensitivity to light, colitis, encephalopathy, neuritis, retrobulbar neuritis, blood vessel damage, peripheral neuropathy, peripheral vascular disease, cardiovascular disease, vascular collapse, respiratory tract disorders, kidney disease, kidney failure, abnormal EEGs, numbness in the extremities, paresthesia, depression, mood swings, flat affect, impaired facial recognition, hearing loss, difficulty hearing, convulsions, and seizures
Copper	Autonomic disturbances, cirrhosis of the liver, hepatitis, depression, mood swings, flat affect, impaired facial recognition, convulsions, and seizures
Lead	Abdominal pain, stomach cramps, autonomic disturbances, burning of the throat and mouth, alterations in nerve conduction velocity, peripheral vascular disease, cardiovascular disease, vascular collapse, kidney disease, kidney failure, sleep difficulties/disturbances, abnormal EEGs, hearing loss, difficulty hearing, birth defects, premature births, spontaneous abortion, convulsions, and seizures
Mercury	Autonomic disturbances, blurred vision, sensitivity to light, gastroenteritis, colitis, peripheral neuropathy, sleep difficulties/disturbances, numbness in the extremities, paresthesia, abdominal pain, stomach cramps, burning of the throat and mouth, disturbances in menstrual cycle, menstrual pains, depression, mood swings, flat affect, impaired facial recognition, hearing loss, difficulty hearing, birth defects, premature births, spontaneous abortion, convulsions, and seizures
Thallium	Alterations in the spinal cord, autonomic disturbances, numbness in the extremities, paresthesia, abdominal pain, stomach cramps, hepatotoxicity, liver dysfunction, burning of the throat and mouth, encephalopathy, neuritis, retrobulbar neuritis, and alopecia (hair loss)

6 Pesticides

6.1 INTRODUCTION

Chemical pesticides have contributed to the control of crop pests and increased production of food grains. These chemicals still continue to play essential roles in agriculture and public health. Pesticides are required for the protection of plants, plant products, and stored grain and are used in agriculture, horticulture, forestry, and home gardens, as well as in the production of plentiful food and control of vector-borne diseases. The Federal Fungicide, Insecticide, and Rodenticide Act (FIFRA) defines a pesticide as "any instrument or contrivance (other than a firearm) which is intended for trapping, destroying, repelling, or mitigating any pest or any other form of plant or animal life." In fact, the term pesticide includes a range of chemical substances and products that are used for the control of a variety of pests. Never before has the public had access to such a variety of pesticides; however, they have potential adverse effects on health and the environment, which can be aggravated by the conditions of use in many countries.

During the early 1940s use of pesticides was limited to several arsenicals, petroleum oils, nicotine, pyrethrum, rotenone, sulfur, and hydrogen cyanide gas. Prior to the 1960s, DDT was the "wonder pesticide" that saved the lives of millions of people. During wartime, it protected soldiers from insect-carried diseases, which previously had taken more lives than battle itself. At that time, people did not complain about the possible dangers of DDT, as long as it was used to control human diseases. DDT is still one of the most important and well known pesticides in the world. While it is no longer used in the United States, its use continues in many other parts of the world. In fact, DDT usage in the world today is roughly the same as it was prior to the ban by most Western countries. DDT is still in use in India, China, South America, Africa, and Malaysia.

The sound management of pesticides, focusing on risk reduction, is important for protection of human and environmental health, and support of sustainable agricultural development. International treaties have called for stronger measures to eliminate certain persistent pesticides and to recognize the importance of training and capacity building. Many adverse effects of pesticides can be prevented if trained personnel use correct and appropriate techniques and sound management and take steps to limit the general public's easy access to pesticides. However, this cannot replace the impact of elementary knowledge about the proper use of pesticides, and it is necessary to educate all users who handle different kinds of pesticides in fields or residential areas or around children.

A science-based tool, the information collected in the following pages is very essential to educate persons involved at all levels of pesticide regulation, distribution,

transportation, use, storage, and disposal. The important purpose of this compilation on the safe use of chemical substances is to offer information about the widespread need for elementary knowledge and training in the sound management of chemicals. Everyone who uses pesticides has a responsibility to ensure that they use them correctly and effectively. Industrial workers, trainees, and field workers who need to be aware of the toxicity of pesticides and the possible health hazards and human safety issues are the right people to receive education and training. Management of proper use of chemicals, whether they are pesticides, industrial solvents, or other chemical substances, demands basic knowledge and correct scientific information.

These pages attempt to provide insight into the sound management of pesticides and other chemical substances used to respond to societal needs and to improve quality of life by addressing hunger and diseases. Everyone who uses pesticides has the responsibility to ensure that they are used properly, judiciously, and effectively, with proper knowledge.

6.2 GLOBAL DEVELOPMENT OF PESTICIDES

Pesticides are chemical substances used for preventing, controlling, or lessening the damage caused by pests. Although pesticides have been in use over the centuries for the control and eradication of crop pests, their global impact became evident with the entry of DDT and organophosphate pesicides[1–7] (Appendix 6.1). A pesticide may be a chemical substance or a biological agent like a virus or bacteria used against pests. The kinds of pests dealt with include but are not limited to insects, plant pathogens, weeds, mollusks, birds, fish, worms, and microbes, which all compete with humans for food, destroy property, and spread disease.

6.3 CLASSIFICATIONS OF PESTICIDES

Based on their chemical properties, pesticides are classified as:

organochlorine pesticides (OCPs);
organophosphate pesticides (OPPs);
carbamate pesticides;
synthetic pyrethoids; and
nicotinoids.

Pesticides are also grouped as synthetic pesticides or biological pesticides. The classification of pesticides according to the manner of use can be listed as (Table 6.1):

acaricides;
algicides;
antifouling agents;
antimicrobials;
attractants;
avicides;

bactericides;
biocides;
defoliants (cause leaves or other foliage to drop from a plant);
desiccants (promote drying of living tissues);
fungicides;
fumigants;
herbicides;
insecticides;
insect growth regulators (disrupt the molting, maturity from pupal stage);
miticides/acaricides;
microbial pesticides;
molluscicides;
nematicides;
ovicides;
plant growth regulators (alter the expected growth, flowering, or reproduction rate of plants);
repellents; and
rodenticides.

TABLE 6.1
Groups of Pesticides

Pesticide	Uses
Algicide	Control algae in lakes, canals, swimming pools, water tanks, and other sites
Antifouling agent	Kill or repel organisms that attach to underwater surfaces, such as boat bottoms
Antimicrobial	Kill microorganisms (such as bacteria and viruses)
Attractant	To attract pests—for instance, to lure an insect or a rodent to a trap
Avicide	Control of unwanted birds
Bactericide	Pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals
Biocide	Kill microorganisms
Fumigant	Produce gas or vapor intended to destroy pests in buildings or soil
Fungicide	Kill fungi, blights, mildews, molds, fungal diseases, and rusts
Herbicide	Kill weeds and other plants that grow where they are not wanted
Insecticide	Kill insects and other arthropods
Microbial pesticide	Microorganisms that kill, inhibit, or outcompete pests, including insects or other microorganisms
Miticide/acaricide	Kill mites that feed on plants and animals
Molluscicide	Kill snails and slugs
Nematicide	Kill nematodes (microscopic, worm-like organisms that feed on plant roots) and eelworms
Ovicide	Kill eggs of insects and mites
Pheromones	Biochemicals used to disrupt the mating behavior of insects
Piscicide	Control of fish
Repellent	Repel pests, including insects (such as mosquitoes) and birds
Rodenticide	Control mice and other rodents

Herbicides share common signs and symptoms. In general, herbicides cause irritation to the skin, eyes, and respiratory tract. However, they are also known to impart low levels of systemic toxicity to animals and humans. Herbicides prevent or eliminate weeds and thus replace or reduce manual and mechanical weeding. Because they reduce the need for cultivation, they can also prevent soil erosion and water loss. Herbicides can be divided into two categories: selective herbicides, which can be applied directly on specific crops without damaging them, and nonselective herbicides, which destroy or eliminate all plants. Weeds are undesirable plants growing within a crop that compete for resources such as nutrients, water, and light. It is well known that without weed control, crop yields suffer a significant loss. The discovery of selective herbicides in the twentieth century offered a boon for the control and elimination of weeds. These products contributed to substantial increases in yield and consistency of crop production.

Bipyridyl herbicides include alachlor, amitrole, atrazine, bromacil, bromoxynil, butylate, cyanazine, dalapon, dicamba, diuron, linuron, fluometuron, hexazinone, molinate, metolachlor, oryzalin, pendimethalin pronamide, propanil, propazine, simazine, terbacil, triallate, and triclopyr. In addition to these herbicides, the most common bipyridyls are diquat and paraquat. Paraquat is more toxic than diquat and produces chronic abnormal cell growth in the lungs, cornea and lens of the eye, nasal mucosa, skin, and fingernails. Diquat affects the eye lens and intestinal tract lining, but does not usually produce the frequently fatal lung changes characteristic of paraquat.

Ingesting diquat or paraquat causes severe irritation to the mucous membranes of the mouth, esophagus, and stomach. Repeated vomiting generally follows. Large doses of diquat also produce restlessness and reduced sensitivity to stimulation. Dermal exposure to paraquat and diquat concentrates may cause severe skin irritation and burning. Contact with dilute liquids and diquat dusts may cause slight to moderate irritation. Dermal absorption of paraquat apparently is slight, but diquat is absorbed and after repeated contact will produce symptoms similar to those following ingestion. Exposure to paraquat and diquat spray mist may produce skin irritations, nasal bleeding, irritation and inflammation of the mouth and upper respiratory tract, coughing, and chest pain. Exposure to paraquat concentrates may cause blackening of the nails and abnormal nail growth.

Chlorophenoxy herbicides include 2,4-D and MCPA. Human exposure to these chemical substances causes moderate irritation to skin and mucous membranes. Inhalation may cause burning sensations in the nose, sinuses, and chest; and coughing. Prolonged inhalation leads to dizziness. Further, irritation of the stomach usually leads to vomiting soon after ingestion, pain in the chest and abdomen, diarrhea, headache, mental confusion, and bizarre behavior—early signs and symptoms of severe poisoning leading to unconsciousness.

Arsenical herbicides such as Ansar and Montar cause very rapid, acute poisoning. The symptoms include inflammation of the mouth and esophagus, burning abdominal pain, thirst, vomiting, “rice water” or bloody diarrhea, headache, dizziness, muscle weakness and spasms, low body temperature, sluggishness, delirium, coma, and convulsions. The arsenical herbicides also cause liver damage, yellowness

of the skin, reduction in red and white blood cells and blood platelets, circulatory failure, and death. In contrast, chronic arsenic poisoning causes prominent dermal manifestations. These include overgrowth of the cornea or epidermis; scaling off of dead skin; excessive fluids under the skin of the face, eyelids, and ankles; white streaks across the nails; loss of nails or hair; and brick-red coloration of visible mucus membranes. For more information on herbicides, refer to the literature.[1–6]

Rodenticides include coumarins, zinc phosphide, and strychnine.

Synthetic pyrethroids are synthetic compounds that mimic the structure of naturally occurring pyrethrins. The systemic toxicity by inhalation or dermal absorption is low. There have been very few systemic poisonings of humans by pyrethroids. Dermal contact may result in skin irritation such as stinging, burning, itching, and tingling progressing to numbness. The group of synthetic pyrethroids includes allethrin, cyfluthrin, cypermethrin, esfenvalerate, fenvalerate, flucythrinate, fluvalinate, permethrin, resmethrin, tetramethrin, and tralomethrin.

Fungicides are extensively used in industry, agriculture, the home, and the garden. They vary enormously in their potential for causing adverse effects in humans. Most fungicides currently in use are unlikely to cause frequent or severe poisonings. Apart from poisonings that affect the body generally, fungicides have probably caused disproportionate numbers of irritant injuries to skin and mucous membranes, as well as some dermal sensitization. The fungicides cover a great variety of chemical compounds differing widely in their toxicity. Highly toxic compounds are used as fumigants of foods and in warehouses and for seed dressing and soil disinfection. Cases of poisoning have been described with organomercurials, hexachlorobenzene, and pentachlorobenzene, as well as with the slightly toxic dithiocarbamates. More information can be found in the literature.[1–5a]

6.4 USES OF PESTICIDES

The significant role of pesticides in increased production of food grains and food supply to combat hunger around the world needs no emphasis. Pesticides also help to control vectors of human and livestock diseases. Proper use of pesticides has increased countries' economies through production of quality food grains, fruits, and vegetables and protected farm lands, forests, and lawns. It is well known that pesticides are very poisonous, and can cause serious injury or death if used improperly and or because of negligence during use. The persistent property of OCPs has the added advantages for the control of different pests because the OCPs remain effective against target pests for long periods of time. They have been used on a large scale for the control of pests of crops and livestock and to protect buildings and households from the damaging effects of insects. DDT came into use in the 1940s and was widely introduced into Australia and New Zealand agriculture in the 1950s. DDT was the first highly effective broad-spectrum insecticide that gave an extremely high level of control over many important insect pests. It has low acute toxicity to humans and, as such, was widely acclaimed as a wonder chemical. It was also used in large quantities in the control of mosquitoes, which caused malaria in tropical countries. There has been a total ban on the use of DDT in Australia since 1987.

TABLE 6.2
Toxicity Classification

Route/LD_{50}	Extreme	High	Moderate	Low
Oral LD_{50}	<50 mg/kg	50–500 mg/kg	500–5000 mg/kg	>5000 mg/kg
Dermal LD_{50}	<200 mg/kg	200–2000 mg/kg	2000–20,000 mg/kg	>20,000 mg/kg
Inhalation LD_{50}	<200 mg/m^3	200–2000 mg/m^3	2000–20,000 mg/m^3	>20,000 mg/m^3

Source: U.S. Environmental Protection Agency, Office of Pesticide Programs. Registration and classification procedures, part II. *Federal Register* 40: 28279.

6.5 TOXICITY OF PESTICIDES

Pesticides are toxic chemicals that cause poisoning to animals and humans. Depending upon the chemical, dose, duration and route of exposure, pesticide poisoning can be mild, moderate, severe, or extremely severe (Appendices 6.2 and 6.7). Pesticides cause deleterious effects to different parts of the body (Appendix 6.3) and behavioral and nonbehavioral changes (Appendix 6.4). The possible nature of the mammalian toxicity of different pesticides and the symptoms suggest the intrinsic nature of the candidate chemicals (Appendix 6.5). Prolonged periods of exposure to pesticides also cause disturbances in some of the endocrine systems (Appendix 6.6). A wealth of information about the toxicity profile of an array of different pesticides belonging to different groups, such as the organochlorinate, organophosphate, and carbamate insecticides; triazines; dithiocarbamates; nitro compounds; phenoxy compounds; urea compounds; herbicides; fungicides; and rodenticides, is available in the literature.[1–7] The following pages therefore discuss selected aspects of pesticide toxicity with reference to proper and safe use and health disorders.

The World Health Organization (WHO) and U.S. Environmental Protection Agency (U.S. EPA) have designated classifications of extremely toxic, highly toxic, moderately toxic, and slightly toxic pesticides. Generally, the toxicity of a pesticide or any chemical substance is determined in relation to the manner of entry of the test material into the body, such as oral (digestive system), dermal (skin absorption), and inhalation (respiratory system). It is important for students and workers to know the general classification of toxicity of chemical substances (Tables 6.2 and 6.3) and the acute oral and dermal toxicity (LD_{50}) values (Table 6.4) for purposes of safety management of chemicals and, more importantly, pesticides.

6.6 SIGNS AND SYMPTOMS OF TOXICITY

In laboratory studies, species of animals exposed to different pesticides have been poisoned. The signs and symptoms of poisoning caused by different pesticides (Table 6.5), fungicides (Table 6.6), herbicides (Table 6.7), and insecticides (Table 6.8) provide suggestions for proper use of these chemical substances by students and workers. The U.S. EPA has dealt at length with the regulation of pesticides and the globally harmonized system (GHS). It provides more direction for the classification and labeling of hazardous chemicals as an initiative to promote common, consistent

TABLE 6.3
WHO Classification of Pesticide Hazards

	Oral Route		Dermal Route	
Class	**Solid**	**Liquid**	**Solid**	**Liquid**
I. Extremely hazardous	≤4	≤20	≤10	≤40
I. Highly hazardous	5–50	20–200	10–100	40–400
II. Moderately hazardous	50–00	200–2000	100–1000	400–4000
III. Slightly hazardous	>500	>2000	>1000	>4000

Notes: LD_{50} for the rat (mg/kg of body weight). Terms "solid" and "liquid" denote the physical state of the product/formulation.

TABLE 6.4
Acute Toxicity of Pesticides

	Oral LD_{50}		Dermal LD_{50}	
Class	**Solid**	**Liquid**	**Solid**	**Liquid**
Ia. Extremely hazardous	≤5	≤20	≤10	≤40
Ib. Highly hazardous	5–50	20–200	10–100	40–400
II. Moderately hazardous	50–00	200–2000	100–1000	400–4000
III. Slightly hazardous	>500	>2000	>1000	>4000

Notes: LD_{50} for the rat (mg/kg of body weight). Terms "solid" and "liquid" denote the physical state of the active ingredient.

Source: Classification of pesticides by hazard and guidelines to classification, 2000–2002, WHO.[5b]

criteria for classifying chemicals according to their health, physical, and environmental hazards, and to develop compatible labeling, safety data sheets for workers, and other information based on the resulting classifications.

6.7 PESTICIDE MANAGEMENT

It has now been well documented that the annual use pattern and consumption of different pesticides involves hundreds of millions of pounds of chemicals. With huge tonnage, pesticides have reached farmlands, roadsides, forests, and homes. The alarming part of the extensive use and global spreading of the organochlorine pesticides is that they need proper management. Research findings over the past two decades have demonstrated that several OCPs cause severe health effects, such as cancer, sterility, birth defects, and damage to the central nervous system (CNS) in animals and humans. It has been found that OCPs are very persistent, resist undergoing degradation, and accumulate in biological tissues; that is, they build up in the fatty tissues of plants, animals, and humans.

TABLE 6.5
Signs and Symptoms of Pesticide Poisoning

Pesticide	Symptoms
Acephate (OP)	Headache, excessive salivation and tearing, muscle twitching, nausea, diarrhea, respiratory depression, seizures, loss of consciousness, pinpoint pupils, inhibition of cholinesterase enzyme (ChE) activity
Aldicarb (C)	Weakness, blurred vision, headache, nausea, tearing, sweating, tremors, malaise, muscle weakness, dizziness, salivation, vomiting, abdominal pain, diarrhea, CNS depression, inhibition of ChE activity, pulmonary edema in serious cases
Carbaryl (C)	Headache, salivation, nausea, vomiting, abdominal pain, diarrhea, sweating, blurred vision, muscle weakness, poor coordination, convulsions, CNS depression, pulmonary edema
Chlorpyrifos (OP)	Headache, excessive salivation and tearing, muscle twitching, nausea, diarrhea, respiratory depression, seizures, loss of consciousness, pinpoint pupils, inhibition of ChE activity
Endosulfan (OC)	Headache, skin itching, burning, dizziness, nausea, vomiting, lack of coordination, tremor, confusion, seizures, respiratory depression, coma
Malathion (OP)	Headache, excessive salivation and tearing, muscle twitching, nausea, diarrhea, respiratory depression, seizures, loss of consciousness, pinpoint pupils, inhibition of ChE activity
Methyl parathion (OP)	Headache, excessive salivation and tearing, muscle twitching, nausea, diarrhea, respiratory depression, seizures, loss of consciousness, pinpoint pupils, inhibition of ChE activity
Phosmet (OP)	Headache, excessive salivation, tearing, muscle twitching, nausea, diarrhea, respiratory depression, loss of consciousness, pinpoint pupils, inhibition of ChE activity
Pyrethrin (NPY)	Sneezing, asthmatic breathing, loss of appetite, vomiting, irritation of skin and upper respiratory tract, diarrhea, disorientation, hyperactivity, seizures, tremors, depression, contact dermatitis, allergic reactions, asthma
Cypermethrin (SPY)	Abnormal facial sensation, nausea, repeated vomiting, stomach pain, dizziness, salivation, headache, fatigue, diarrhea, convulsions, coma
Resmethrin (SPY)	Coughing; wheezing; shortness of breath; runny or stuffy nose; chest pain; difficulty breathing; skin contact causes rash, itching, or blisters; local numbness; burning and tingling sensations near the site of exposure

Notes: C = carbamate; OC = organochlorine pesticides; OP = organophosphate pesticide; NPY = natural pyrethrin; SPY = synthetic pyrethroid.

Pesticide management must aim at and address the reduction of health hazards associated with the improper use of different pesticides. The hazards and risks of pesticides are multifaceted and there is no single effective approach to the problem. To find effective solutions, it is important that activities be considered in the context of an overall program of crop protection and government policy with respect to pesticide use. The International Code of Conduct of Food and Agriculture Organizations is the worldwide guide on the distribution and use of pesticides. It provides guidance on sound pesticide management practices, in particular for government authorities and the pesticide industry.

TABLE 6.6
Signs and Symptoms of Fungicide Poisonings (Active Ingredients)

Fungicide	Symptoms
Azoxystrobin	Irritating to skin, eyes, respiratory tract
Captan	Irritating to skin, eyes, respiratory tract
Chlorothalonil	Irritation to skin, mucous membranes of the eye, respiratory tract; allergic contact dermatitis
Copper compounds	Irritating to skin, eyes, respiratory tract
Copper sulfate salts	Corrosive to mucous membranes and cornea; metallic taste, nausea, vomiting, intestinal pain
Mancozeb	Irritating to skin, eyes, respiratory tract
Maneb	Irritating to skin, eyes, respiratory tract; skin disease in occupationally exposed individuals
Pentachloronitrobenzene	Allergic reactions
Sulfur	Irritating to skin, eyes, respiratory tract; breath odor of rotten eggs, diarrhea; irritant dermatitis in occupationally exposed individuals
Thiram	Irritating to skin, eyes, respiratory mucous membranes
Ziram	Irritating to skin, eyes, respiratory tract; prolonged inhalation causes neural and visual disturbances

TABLE 6.7
Signs and Symptoms of Herbicide Poisonings (Active Ingredients)

Herbicide	Symptoms
2,4-Dichlorophenoxyacetic acid (2,4-D)	Irritating to skin and mucous membranes, diarrhea, vomiting, headache, confusion, bizarre or aggressive behavior, muscle weakness
Acetochlor	Irritating to skin, eyes, respiratory tract
Atrazine	Irritating to skin, eyes, respiratory tract, mucous membranes; abdominal pain; diarrhea; vomiting; eye irritation; skin reactions
Dicamba	Irritating to skin and respiratory tract, loss of appetite (anorexia), vomiting, muscle weakness, slowed heart rate, shortness of breath, CNS effects
Glyphosate	Irritating to skin, eyes, respiratory tract
Mecoprop	Irritating to skin and mucous membranes, vomiting, headache, diarrhea, confusion, bizarre or aggressive behavior, muscle weakness
Metolachlor	Irritating to skin and eyes
Paraquat	Burning in mouth, throat, chest, and upper abdomen; diarrhea; giddiness; headache; fever; lethargy; dry, cracked hands; skin ulceration
Pendimethalin	Irritating to skin, eyes, respiratory tract
Propanil	Irritating to skin, eyes, respiratory tract

Pesticide management is an activity carried out within the overall framework of the plant protection service of the Food and Agricultural Organization (FAO). It is designed to work together with member countries as a partner to introduce

TABLE 6.8
Signs[a] or Symptoms[b] of Insecticide Poisoning

Organ System	Signs or Symptoms
CNS, somatomotor	Twitch, tremor, ataxia, convulsion, rigidity, flaccidity, restlessness, general motor activity, reaction to stimuli, headache, dreams, poor sleep, nervousness, dizziness
Autonomic	Miosis, mydriasis, salivation, lacrimation
Respiratory	Discharge, rhinorrhea, bradypnea, dyspnea, yawning, constriction of chest, cough, wheezing
Ocular	Ptosis, exophthalmos, dimness, lacrimation, conjunctival redness
Gastrointestinal	Diarrhea, vomiting
General side effects	Temperature, skin texture and color, cyanosis

[a] Signs in animals.
[b] Symptoms in man.

sustainable and environmentally sound agricultural practices that reduce health and environmental risks associated with the use of pesticides. It is of particular importance that countries and industrial workers associated with the management of a variety of pesticides should also be aware of living and working conditions, and the risks of improper use of pesticides.

There is, therefore, an urgent need to educate industrial workers and different strata of management about proper use, storage, and waste disposal, as well as about use of adequate personal protection, particularly during pesticide formulation activities by the workers in factories and in fields and the risks of improper use. This has become very necessary for the protection of human health and the environment and to have the benefit of sustainable agricultural development. In fact, it has been reported that in many countries around the world, huge amounts of obsolete pesticides, often stored outdoors in leaking containers, regularly enter nearby water bodies and soil systems. Therefore, essential and basic information about pesticides, as well as education and training of students, workers, and management, helps in the protection and safety of humans and the living environment.

It is very important to remember that pesticides need to be used as tools to control and combat crop pests and unwanted weeds. With proper use and safety precautions during handling, storage, and disposal, pesticides provide benefits to the user and to the living environment.

6.8 SYMPTOMS OF PESTICIDE POISONING

Pesticide poisoning has become common among farm workers, pesticide applicators, mixers, loaders, and handlers. This has been traced to the users' ignorance, carelessness, and lack of elementary knowledge about taking the proper precautions before handling toxic chemicals. The symptoms of pesticide poisoning are not common to all the products, but vary with each product and its formulation. Some of the symptoms include headache, nausea, muscle aches, irritation of eyes and nasal and

pharyngeal passages, pulmonary edema, lassitude, mental disorientation, convulsions, hemolysis, cyanosis, and coma.

The OCPs cause poisonings in animals and humans and are usually targeted at the CNS as stimulants or cause convulsions. In general, the symptoms of OCP poisoning include myoclonic jerking, neuronal irritability, convulsions, myocardial and cardiac arrhythmias, sensory disturbances, hyperesthesia, paresthesia of face and extremity, headache, dizziness, nausea, vomiting, poor coordination, tremor, mental confusion, myoclonic jerking, and tonic-clonic convulsions. The other early symptoms of poisoning include but are not limited to apprehension, excitability, dizziness, headache, disorientation, weakness, a tingling or pricking sensation on the skin, and muscle twitching. Subsequently, the poisoned worker shows loss of coordination, convulsions similar to epileptic seizures, and unconsciousness. In cases of dermal absorption of OCPs in high concentrations, the worker soon demonstrates apprehension, twitching, tremors, confusion, and convulsions[1–7] (Tables 6.3–6.6) (Appendices 6.2–6.6)

The OPPs cause very rapid symptoms of poisoning. These include anxiety, restlessness, tremor, vomiting, dizziness, stomach cramps, diarrhea, salivation, tearing, blurred vision, slow heartbeat, muscle twitching, chest discomfort and tightness, wheezing, productive cough, tachycardia, hypertension, sinus arrest, toxic psychosis, confusion, bizarre behavior, unconsciousness, incontinence, convulsions, and death. All OPPs cause inhibition of cholinesterase. The cholinergic junctions produce muscarinic effects on smooth muscles and gland cells, causing muscle contractions and secretions. The nicotinic effects produce excitatory effects on skeletal muscles and autonomic ganglia that can cause twitching, sensory and behavioral changes, poor coordination and depressed motor function[1,2] (Tables 6.3–6.6) (Appendices 6.2–6.6).

Carbamate pesticides, unlike the OPPs, dissociate more readily with the inhibition of AChE activity. They do not cause the accumulation of acetylcholine and thus the duration of poisoning is limited. The early symptoms of poisoning include malaise, muscle weakness, dizziness, and sweating. Prolonged exposure to carbamate pesticides causes poisoning, with symptoms such as headache, salivation, nausea, vomiting, abdominal pain, diarrhea, miosis, poor coordination, slurred speech, dyspnea, bronchospasm, chest tightness, pulmonary edema, blurred vision, dark vision, muscle twitching, seizures, and incontinence. In severe cases the poisoned worker shows symptoms of seizures, incontinence, respiratory depression, and cardiac complications.

It is very important to remember that some of the symptoms of pesticide poisoning are mistaken for symptoms of other illnesses such as the flu or heat exhaustion. It is also very important that, in all cases of pesticide poisoning in factories, in fields, or at home, a sound medical judgment must prevail readily and quickly. Compare the following:

symptoms of heat exhaustion: sweating, headache, fatigue, dryness in the mouth, nausea, dilated pupils, CNS depression, loss of coordination, confusion, fainting, and easy recovery

symptoms of pesticide poisoning: sweating, headache, fatigue, salivation, slow pulse, nausea, diarrhea, pinpoint pupils, CNS depression, loss of coordination, confusion, and coma

For more information on pesticides and poisoning, refer to other pages of this book and to the literature.[1–7a]

6.9 APPROACHES TO REDUCE INTENTIONAL AND SUICIDAL POISONINGS

Suicide deaths and impulsive acts of self-harm associated with pesticides have caused increasing global concern. It has been reported that deliberate ingestion associated with pesticides has resulted in 2–3 million hospital admissions and about 220,000 deaths each year.[8,9] In recent years, pesticides have been used in a spate of suicides in some parts of India (Andhra Pradesh). Pest resistance and resurgence (mainly on cotton crops) and abuse of pesticides because of lack of strict market regulation of toxic chemicals like pesticides have been found to be the causative factors of human poisonings.

Pesticide poisoning among agricultural crop workers (especially cotton growers), as documented in the report of the Center for Sustainable Agriculture (CSA), Secunderabad and Modern Architects for Rural India (MARI), India, during 2004 and 2005 is very alarming. The cause of human fatalities has been attributed to ignorance of, negligence in following, improper management of, and completely ignoring safety measures, such as wearing gloves, shoes, face masks, and other protective clothing by the users.

The easy availability of common pesticides helps to facilitate suicide and self-harm by children and others. It has been reported that in China about 65% of pesticide suicides use items stored in the home and close to household materials.[10] The importance of broad-based commitment from industry, nongovernmental organizations (NGOs), and national and international health and regulatory organizations is highlighted.

Some elementary practices have been suggested to reduce pesticide poisoning, if it is not possible to completely stop such chemical hazards, among farm workers:

Restrict the availability of pesticides (especially class 1 and class 2 pesticides) to users unless qualified, trained, and certified operators supervise the pest control operations.
Store supplies of pesticides in a proper security facility.
Improve and impart public education specifically on the dangers of pesticide poisoning and the importance of safe storage and proper labeling of containers and packages.
Encourage pesticide manufacturers to improve product safety.
Educate workers about proper use and handling of pesticides. Let them be aware of the fact that pesticides are poisonous chemical substances.
Workers should not be negligent when working with pesticides.

6.10 THE INSECTICIDE ACT (1968)

The indiscriminate, improper, and careless use and management of pesticides have caused untold health hazards to animals and humans and to the living environment

over the decades. More than four decades ago, people in India witnessed a major pesticide disaster involving the general public. A large number of people suffered poisoning and died in Kerela and Tamil Nadu (then, Madras). This was later traced to the consumption of imported wheat contaminated by the pesticide parathion. It was reported that the ship carried the food grains and the pesticide together and the accidental contamination and consumption of these imported grains ended in large-scale human fatalities. This led to the introduction of legislation for the safe use of pesticides in India. The government of India constituted an expert committee and the Insecticides Act of 1968 became operative in India. In principle, this act deals with the regulation, import, manufacture, sale, transport, distribution and use of insecticides with a view to prevent risks to human beings and animals. Subsequently, in 1970, the enforcement of the Insecticide Act was transferred to the Ministry of Agriculture by the Ministry of Health and Family Planning. The Department of Agriculture of this ministry took immediate steps to frame the rules and constituted the Central Insecticides Board (CIB) and Registration Committee. All pesticides, both technical and formulations, must be registered first with the CIB before introduction to the market. For the effective enforcement of the Insecticide Act, several committees have been constituted at the central level over the years.

The registration of pesticides to be used in India as well as imported into the country is based on the good points and regulations of the United Kingdom and the U.S. EPA systems in the management of pesticides. The CIB has given due consideration while framing regulations in the management of pesticides based on the guidelines of the FAO, the WHO, and the U.S. EPA to meet national requirements. In accordance with the CIB regulations and recommendations of the subcommittee on pesticide toxicology (of which the author was a member for many years), the toxicology data are to be generated under local conditions.[1a]

6.11 REGULATIONS

Huge tonnage of pesticides has been in use in different countries for the control and management of pests that cause damage to agricultural crops, household materials, vegetables, food grains, fruits, flowers, and lawns, and serve as vectors of human and livestock diseases. Over the decades, regulatory agencies and bodies of different governments around the world have made systematic efforts for proper use and good management of these toxic substances to be followed by the concerned users. Regulatory agencies have passed strict enactments regarding the proper use, application, storage, transportation, safety and protective measures, and waste disposal of different pesticides. However, because of improper use, negligence, and, more than all, lack of elementary knowledge and education, pesticides have caused human fatalities and chemical disasters. This has caused global concern. In fact, many problems with pesticides are caused by uninformed consumers who do not read labels and follow precautions. For this reason, trained and licensed pest management professionals should be consulted.

There is a need, therefore, to educate workers at workplaces in fields or factories about the consequences of the misuse of pesticides and the important precautions

that each worker must follow for his or her own protection and for the safety of the living environment.

6.12 PESTICIDES AND CARCINOGENICITY

Carcinogenicity of pesticides provides information about the production of malignant tumors in animals and humans exposed to pesticides. The general terms tumor, cancer, and neoplasm are all used to describe the phenomenon of uncontrolled progressive growth of cells eventually leading to serious health disorders. The global regulatory authorities have made it mandatory to evaluate the carcinogenic potential of all pesticides. Accordingly, FIFRA in the United States and the Insecticide Act in India require testing to determine the carcinogenic potential of pesticides. In fact, the evaluation of pesticides for carcinogenicity in animal bioassay studies began in the late 1960s.[11–11b] These tests are required to determine oncogenic potential, which is the ability to cause benign and/or malignant tumors; a substance causing malignant tumors would be considered carcinogenic.

According to the regulations of the U.S. EPA, European Commission, and the IARC (WHO), any pesticide or any chemical substance is classified within one of six possible groups:

group A: human carcinogen;
groups B1 and B2: probable human carcinogen;
group C: possible human carcinogen;
group D: not classifiable; and
group E: noncarcinogenic.

The U.S. EPA considers that all pesticides fall into groups B2 and C.

Studies conducted by several workers and the epidemiologic findings with specific pesticides have caused concern. For instance, lung cancer has been associated with blood levels of DDT among residents of South Carolina,[7a] and the pancreatic cancer risk was excessive among workers employed in the manufacture of DDT[12] in the United States. Reports have indicated that breast cancer among humans has been associated with concentrations of DDT and its metabolites in blood and adipose tissue[13–15] and ovarian cancer among Italian women engaged in agricultural activities.[16] Breast cancer in rodents[17] has been linked with the use of triazine herbicides.[16–18] A study of manufacturers and workers associated with phenoxyacetic acid herbicides and exposed to dioxin showed excesses of several cancers, including lung cancer and soft-tissue sarcoma[19] (Appendices 6.8 and 6.9).

6.13 CONCLUSION

A variety of pesticides have been in use for many decades for the control of insect pests of agricultural crops and storehouses and as vectors of communicable diseases. Human exposure to pesticides during mixing, spraying, transportation, and waste disposal has become common. Prevention of inhalation and dermal absorption of

pesticides requires proper training and education to achieve safety to the worker and to the environment. Also, studies have shown an association between occupational pesticide poisoning and incidence of prostate, kidney, brain, and lung cancers. All these observations suggest proper use and management of pesticides at workplaces, at home, or in the field are very necessary for human health, safety, and protection of the living environment.

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APPENDIX 6.1

Global Development of Pesticides

Period/ Era	Chemicals and Location
	Era of Natural Products (900–1690)
900	Arsenites (China)
1690	Tobacco (Europe)
	Era of Modern Synthetic Insecticides (1800–1920)
1800	Pyrethroids (Caucasus)
1848	Derris root (Malaya)
	Era of Fumigants, Inorganics, Petroleum Products
1854	Carbon disulfide (France)
1867	Paris green (United States)
1892	Lead arsenate (United States)
1918	Chloropicrin (France)
1932	Methyl bromide (France)
1939	DDT (Germany)
1941	BHC (France)
	Chlorinated Cyclodienes (1945–1955)
1945	Aldrin (United States)
1947	Dimetan (Switzerland)
	Cholinesterase Inhibitors, Organophosphate Compounds, Carbamates (1945–1970)
1944	Parathion (Germany)
1958	Sevin (United States)

APPENDIX 6.1 (continued)

Global Development of Pesticides

Period/ Era	Chemicals and Location
	Era of Hormone Mimics and Pheromones; Rebirth of Botanical Insecticide
1967	First juvenile hormone analog (United States)
1970–1985	Synthetic pyrethroids, avermectins, juvenile hormone mimics, biological pesticides
1985–	Genetically engineered organisms

Source: Stephenson, G. A., and Solomon, K. R. 1993. Pesticides and the Environment. Guelph, Ontario, Canada: Department of Environmental Biology.

APPENDIX 6.2

Pesticide Poisoning—Mild, Moderate, and Severe

Users can suffer from pesticide poisoning after a brief or short exposure (acute poisoning) or after a prolonged period of exposure (chronic poisoning). The degree of poisoning is broadly graded as mild, moderate, or severe, although certain symptoms are common in all.

Mild poisoning: headache, dizziness, weakness, fatigue, nervousness, loss of appetite, thirst, nausea, irritation of throat and nose, eye irritation, constriction of pupils, blurred vision, skin irritation, changes in mood, loss of body weight

Moderate poisoning: symptoms of mild poisoning along with abdominal cramps, vomiting, diarrhea, excessive salivation, constriction in throat and chest, abdominal cramps, rapid or slow pulse, excessive perspiration, trembling, poor muscle coordination, mental confusion

Severe poisoning: symptoms of mild or moderate poisoning along with inability to breathe, respiratory distress, loss of reflexes, uncontrollable muscle twitching, headache, dizziness, sweating, rashes, reddening of skin, pinpoint pupils, blurred vision, excessive tearing, salivation, tightness in chest, elevated blood pressure, rapid heartbeat, vomiting, cramps, diarrhea, tremors, muscle weakness, convulsions, coma

APPENDIX 6.3

Pesticide Components, Signs of Toxicity, and Parts of the Body Affected

Component	Toxic Signs	Site Affected
Parasympathetic	Lacrimation, increased salivation, miosis, blurred vision, "bloody tears"	Exocrine glands (muscarinic)
	Nausea, vomiting, diarrhea	GI tract
	Bronchial secretions, rhinorrhea, dyspnea	Respiratory tract
	Tachycardia, decreased blood pressure	Cardiovascular
	Urinary incontinence	Bladder
Parasympathetic and sympathetic (nicotinic)	Tachycardia, increased blood pressure	Cardiovascular
Somatic motor (nicotinic)	Fasciculations, ataxia, paralysis	Skeletal muscles
Brain (AChe receptors)	Lethargy, tremors, convulsions, dyspnea, depression of respiratory center, cyanosis	CNS

APPENDIX 6.4

Behavioral and Nonbehavioral Changes Caused by Pesticide Exposure

Behavioral	Nonbehavioral
Anxiety and irritability	Tremor
Depression	Ataxia
Memory deficit	Paralysis
Reduced concentration	Paraesthesia
Insomnia	Polyneuritis
Linguistic disturbance	

APPENDIX 6.5

Pesticides and Mammalian Toxicity

Groups and Names of Pesticides	Nature and Symptoms of Toxicity
	A. Organochlorine Pesticides
Aldrin	General malaise, anxiety, irritability, vomiting, convulsions
Benzene hexachloride	Hyperexcitability, neurological disorders, myoclonic jerks, aplastic anemia, heptatotoxicity, neurotoxicity, cerebral seizures
Chlordane	Generalized convulsions, reproductive toxicity, birth defects, loss of consciousness, change in EEG pattern, hepatic disorders, neurological disturbances, mutagenicity, carcinogenicity

APPENDIX 6.5 (continued)

Pesticides and Mammalian Toxicity

Groups and Names of Pesticides	Nature and Symptoms of Toxicity
DDT	Loss of weight, anorexia, tremors, parathesia, hepatotoxicity, reproductive toxicity, cancer
DDD	Ataxia, confusion, abnormal walk, mild anemia
Dicofol	Nausea, vomiting, muscular weakness
Dieldrin	Violent headache, muscular pain, reproductive toxicity, birth defects, cancer
Dimethoate	Cancer, mutagenicity, reproductive toxicity, birth defects
Endrin	Nausea, dizziness, headache, hyperexcitability, abdominal discomfort
Endosulfan	Agitation, diarrhea, foaming, vomiting, hyperplexia, muscle twitching, cyanosis, chronic toxicity
Heptachlor	Myoclonic jerking, psychological disorders, irritability, anxiety, carcinogenicity
Isodrin	Motor hyperexcitability, intermittent muscle twitching
Lindane gamma H C H	Neurotoxicity, hepatotoxicity
Methoxychlor	Neurotoxicity, hepatotoxicity
Telodrin	Nausea, vomiting, hyperexcitability
Toxaphenre	Loss of consciousness, epileptiform
	B. Organophosphate Pesticides[a]
Azinphos-methy	Convulsions, carcinogenicity, neurotoxicity, depression, slurred speech
Bromophos ethyl	Neurotoxicity, depression, slurred speech
Chlorpyrifos	Neurotoxicity, depression, slurred speech
Crotoxyphos	Neurotoxicity, depression, slurred speech
Demeton	Mutagenicity, birth defects
Diazinon	Neurotoxic, neurobehavioral
Dichlorvos	Neurotoxicity, depression, slurred speech
Dimethoate	Muscle weakness, respiratory distress
Ediphenphos	Dizziness, vomiting, nausea
Ethion	Discomfort, vomiting, muscular twitching, nausea, nervousness, convulsions
Fenitrothion	Tremors, fatigue, memory loss, lethargy
Fensulfothion	Vomiting, diarrhea, muscular twitching, pulmonary edema, convulsions, coma
Fenthion	Muscle weakness, respiratory distress, neurotoxicity
Methamidophos	Muscle weakness, respiratory distress
Mevinphos	Mutagenicity
Monocrotophos	Muscle weakness, respiratory distress
Parathion (ethyl)	Headache, miosis, nervousness, salivation, diarrhea, respiratory distress, convulsions, coma, cancer, mutagenicity
Parathion (methyl)	Diarrhea, salivation, nervousness, respiratory distress, convulsions, chronic toxicity, mutagenicity
Phosmet	Cancer, mutagenicity

(continued on next page)

APPENDIX 6.5 (continued)

Pesticides and Mammalian Toxicity

Groups and Names of Pesticides	Nature and Symptoms of Toxicity
Phosphamidon	Respiratory distress, nervousness, diarrhea, convulsions, salivation, paralysis, coma
Quinalphos	Respiratory distress, nervousness, diarrhea, convulsions, salivation, paralysis, coma
	C. Carbamate Pesticides
Aldicarb (Temik)	Extremely toxic even in very small concentrations
Aminocarb (Metacil)	Abdominal cramps, diarrhea, nausea, vomiting
Bendiocarb	Carcinogenicity, reproductive and developmental toxicity, neurotoxicity
Carbaryl (Sevin)	Mutagenicity, nephrotoxicity
Carbofuran (Furadan)	Carcinogenicity, reproductive and developmental toxicity, neurotoxicity
Chlorpropham	Mutagenicity
Fenvalerate	Cancer
Isoprocarb (Etrofolan)	Acute toxicity, carcinogenicity, reproductive and developmental toxicity, neurotoxicity
Methomyl	Acute toxicity, chronic toxicity, mutagenicity
Pirimicarb	Carcinogenicity, reproductive and developmental toxicity, neurotoxicity
Propoxur (Baygon)	Carcinogenicity, reproductive and developmental toxicity, neurotoxicity
	D. Chlorophenoxy Compounds
2,4-Dichlorophenoxyacetic acid (2, 4-D)	Nausea, dizziness, vomiting
2,4,5-Trichlorophenoxyacetic acid (2,4,5-T)	Nausea, dizziness, vomiting
	E. Synthetic Pyrethroids
Cypermethrin	Burrowing and sinuous writhing
Deltamethrin	Clonic seizures
Fenpropanthrin	Dermal tingling
Fenvalerate	Burrowing, sinuous writhing
Permethrin	Prostration
Phenorthrin	Whole body tremor
Resmethrin	Enhanced startle response
Tetramethrin	Aggressiveness

[a] Organophosphate pesticides (OPPs) are potent neurotoxins and extremely toxic to animals and humans. They function by inhibiting the action of acetylcholinesterase (AChE) in nerve cells. The OPPs are known as the most common causes of poisoning worldwide.

Source: Costa, L. G. 2006. *Clinica Chimica Acta* 366(1–2): 1–13.

APPENDIX 6.6

Pesticides and Hormone Disturbances in Mammals

Organochlorine compounds	Alachlor, benzene hexachloride, cycloodines, aldrin, chlordane, dieldrin, endrin, endosulfan, heptachlor, isodrin, telodrin and toxaphene, DDT and metabolites, dicofol, dimethoate, lindane, methoxychlor, mirex, pentachlorophenol, perthane
Organophosphate compounds	Azinphosmethyl, bromophos ethyl, chlorpyrifos, crotoxyphos, demeton, diazinon, dichlorvos, ethion, fenitrothion, fensulfothin, fenthion, flusulfothin, methamidophos, mevinphos monocrotophos and dichrotophos, oxamyl, phorate, parathion (ethyl), parathion (methyl), phosphomidon, quinolphos temephos
Carbamate compounds	Aldicarb, benomyl, carbaryl, chlorpropham, fenvalerate, methomyl
Chlorophenoxy compounds	2,4-D; 2,4,5-T

APPENDIX 6.7

Classification of Pesticide[a] Toxicity

Acephate III	Dicrotophos Ib	Famphur Ib	Oxydemeton methyl Ib
Anilofos II	Dimethoate II	Fenamiphos Ib	Parathion Ia
Azamethiphos III	Dimethylvinphos	Fenitrothion II	Parathion methyl Ia
Azinphos ethyl Ib	Disulfoton Ia	Fenthion II	Phenthoate II
Azinphos methyl Ib	Edifenphos Ib	Fosamine U	Phorate Ia
Butamifos II	EPN Ia	Fosthiazate	Phosalone II
Cadusafos Ib	Ethion II	Heptenophos Ib	Phosmet II
Chlorethoxyfos Ia	Phosphamidon Ia	Isoxathion Ib	Sulfotep Ia
Chlorfenvinphos Ib	Phoxim II	Malathion III	Tebupirimfos Ia
Chlormephos Ia	Piperophos II	Mecarbam Ib	Tebupirimfos Ia
Chlorpyrifos II	Pirimiphos methyl III	Methacrifos II	Temephos U
Chlorpyrifos methyl II	Profenofos II	Methamidophos Ib	Terbufos Ia
Coumaphos Ib	Propetamphos Ib	Methidathion Ib	Tetrachlorvinphos U
Cyanophos II	Prothiofos II	Mevinphos Ia	Thiometon Ib
Cythioate	Pyraclofos II	Monocrotophos Ib	Triazophos Ib
Demeton-*s*-methyl Ib	Pyridaphenthion III	Naled II	Trichlorfon II
Diazinon II	Quinalphos II	Omethoate Ib	Vamidothion Ib
Dichlorvos Ib	Ethoprophos Ia		

[a] Indicates active ingredient.

Notes: Ia = extremely hazardous; Ib = highly hazardous; II = moderately hazardous; III = slightly hazardous.

Source: WHO Recommended Classification of Pesticide by Hazard, 2004 (updated 2005).

APPENDIX 6.8

Organochlorinate Pesticides and Carcinogenicity

Pesticide	IARC	NTP	U.S. EPA	Types of Changes
Aldrin	3	—	B2	Mouse liver tumors
Chlordane heptochlor	3	—	B2	Mouse liver tumors
Kepone (chlordecone)	2B	e	—	Rat, mouse liver tumors
DDT	2B	e	B2	Mouse liver, lung tumors, lymphomas; rat liver tumors; no tumors in three hamster studies
Dieldrin	3	e	B2	Mouse liver tumors
Endrin	3	—	—	No evidence of tumor
Lindane	—	e	B2/C	Mouse liver tumors
Mirex	2B	e	B2	Mouse, rat liver tumors; thyroid tumors
Toxaphene	2B	e	B2	Mouse, rat liver tumors

Notes: B2 = probable human carcinogen (no human evidence); 2B = possibly carcinogenic to humans; C = possible human carcinogen; 3 = not classifiable as to carcinogenicity in humans; e = reasonably anticipated to be carcinogenic to humans.

APPENDIX 6.9

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
Acephate	C		
Acetaldehyde[a]	B2	3	2B
Acetamide[a]	C	3	2B
Acetochlor	2	—	—
Acifluorfen, sodium	2, 4	—	—
Acrolein	C	—	3
Acrylamide[a]	B2	2	2A
Acrylonitrile	B1	2	2B
Alachlor	L2	3	—
Aldicarb	3	—	—
Aldrin	B2	3	3
Amitraz	C	—	—
Amitrole	B2	3	3
Aniline[a]	B2	3	—
Aramite	B2	—	2B
Asulam	C	—	—
Atrazine	—	—	3

APPENDIX 6.9 (continued)

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
Azobenzene	B2	2	3
Benfluralin	3	—	—
Benomyl	C	—	—
Benzyl-4-chlorophenol, 2-C	—	—	
Bifenthrin	C	—	—
Bioallethrin	3	—	—
Bis(chloroethyl)ether (BCEE)[a]	B2	—	—
Bromacil	C	—	—
Bromoxynil	C	—	—
Buprofezin	3	—	—
Butachlor	L1	—	—
Cacodylic acid	B2	—	—
Cadmium[a]	B1	—	—
Captafol	B2	2	2A
Captan	B2	3	3
Carbaryl	2	3	3
Carbendazim	C	—	—
Carbon tetrachloride	B2	3	2B
Chlordane	B2	3	2B
Chlordecone	—	3	2B
Chlordimeform	B2	3	—
Chlorfenapyr	3	—	—
Chloroaniline, p-a	B2	—	—
Chloroform	B2	3	2B
Chloropropham	—	—	3
Chlorothalonil	B2	3	2B
Chlozolinate	—	3	—
Clodinafop-propargyl	L1	—	—
Clofencet (MON 21200)	C	—	—
Clofentezine	C	—	—
Cocamide diethanolamine	2	—	—
Coumarin	3	—	—
Creosote	B1	2	2A
Cyanazine	C	—	—
Cypermethrin (and zeta cypermethrin)	C	—	—
Cyproconazole	B2	—	—
Dacthal (DCPA)	C	—	—
Daminozide	B2	3	—
DDD	B2	—	—

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APPENDIX 6.9 (continued)

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
DDT	B2	3	2B
Deltamethrin	—	—	3
Di(2-ethylhexyl) phthalatea	B2	—	3
Dibromochloropropane (DBCP)	B2	2	2B
Dibromoethane1,2-	B2	2	—
Dichlobenil	C	—	—
Dichloromethane	B2	3	2B
Dichloropropene, 1,3- Telone II	B2	—	2B
Dichlorvos	3	—	2B
Diclofop-methyl	L1	—	—
Dicofol	C	—	3
Dicrotophos	3	—	—
Dieldrin	B2	3	3
Difenoconazole	C	—	—
Dimethenamid	C	—	—
Dimethoxane	3	—	—
Dimethipin	C	—	—
Dimethoate	C	—	—
Dinoseb	C	—	—
Diuron	Known	3	—
Endrin	—	3	—
Epichlorohydrin	B2	—	—
Epoxiconazole	2	3	—
Esbiothrin	3	—	—
Ethalfluralin	C	—	—
Ethofenprox	C	—	—
Ethoprop	L1	—	—
Ethyline dichloride	—	2	—
Etridiazole	—	3	—
Fenbuconazole	C	—	—
Fenoxycarb	L1	—	—
Fentin acetate	—	3	—
Fentin hydroxide	—	3	—
Fenvalerate	—	—	3
Ferbam	—	—	3
Fipronil	C	—	—
Fluazinam	3	—	—
Fluometuron	C	—	3
Flusilazole	—	3	—

APPENDIX 6.9 (continued)

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
Fluthiacet-methyl	L1	—	—
Folpet	B2	3	—
Fomesafen	C	—	—
Formaldehyde	B1	3	1
Furilazole	L1	—	—
Furmecyclox	B2	3	—
Haloxyfop-methyl	B2	—	—
Heptachlor	B2	3	2B
Hexachlorobenzene	B2	2	2B
Hexachlorocyclohexane	B2	—	2B
Hexaconazole	C	—	—
Hexythiazox	C	—	—
Hydramethylnon	C	—	—
Hydrogen cyanamide	C	—	—
Imazalil	L1	—	—
Iprodione	L1	3	—
Iprovalicarb	2	—	—
Isophoronea	C	3	—
Isoproturon	—	3	—
Isoxaben	C	—	—
Kresoxim-methyl	L1	3	—
Lactofen	2, 4	—	—
Lindane (hexachloro cyclohexane)	3	—	2B
Linuron	C	3	—
Malathion	3	—	3
Maleic hydrazide	3	—	—
Mancozeb	B2	—	—
Maneb	B2	—	3
Mecroprop-p	3	—	—
Mercaptobenzothiazole, 2-	C	—	—
Metam sodium and its dihydrate	B2	—	—
Methidathion	C	—	—
Methoxychlor	—	—	3
Methyl bromide	—	—	3
Methyl isothiocyanate	B2	—	—
Methylene bis(thiocyanate)	B2	—	—
Methylphenol, 3-	C	—	—
Metiram	B2	—	—
Metolachlor	C	—	—

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APPENDIX 6.9 (continued)

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
MGK Repellent 326	B2	—	—
Mirex	—	3	2B
Molinate	3	3	—
MON 4660a	L1	—	—
Monuron	—	3	3
Monuron-TCA	—	3	—
Naphthalene	—	2	2B
Nitrapyrin	2	—	—
Nitrofen	—	2	2B
Norflurazon	C	—	—
Orthophenylphenol and sodium salt	—	B2	—
Oryzalin	2	—	—
Oxadiazon	C	—	—
Oxadixyl	C	—	—
Oxyfluorfen	C	—	—
Oxythioquinox	B2	—	—
Paradichlorobenzene	C	—	—
Parathion ethyl	C	—	3
Parathion methyl	—	—	3
Pendimethalin	C	—	—
Pentachloronitrobenzene	C	—	—
Pentachlorophenol	B2	3	—
Permethrin	3	—	3
Phosmet	3	—	—
Phosphamidon	C	—	—
Picloram	—	—	3
Piperonyl butoxide	C	—	3
Poly(hexamethylenebiguanide)	3	—	—
Prochloraz	C	—	—
Procymidone	B2	—	—
Prodiamine	C	—	—
Pronamide (propyzamide)	B2	3	—
Propachlor	L1	—	—
Propanil	3	—	—
Propargite	B2	3	—
Propazine	C	3	—
Propham	—	—	3
Propiconazole	C	—	—
Propoxur	B2	—	—
Propylene oxide	B2	2	—

APPENDIX 6.9 (continued)

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
Propyzamide	—	3	—
Pymetrozine	L1	—	—
Pyraflufen-ethyl	2	—	—
Pyrimethanil	C	—	—
Pyrithiobac-sodium	C	—	—
Quintozene	—	—	3
Simazine	C	3	3
Sulfallate	—	2	2B
Sulfosulfuron	L1	—	—
TCMTB (Busan 72)	C	—	—
Tebuconazole	C	—	—
Tebufenpyrad	3	—	—
Terbutryn	C	—	—
Terrazole	B2	—	—
Tetrachloroethane, 1,1,2,2-	C	—	3
Tetrachlorvinphos	2	—	3
Tetraconazole	2	—	—
Tetramethrin	C	—	—
Thiacloprid	2	—	—
Thiamethoxam	2	—	—
Thiazopyr	C	—	—
Thiodicarb	B2	—	—
Thiopanate-methyl	2	—	—
Thiram	—	—	3
Tolylfluanid	2	—	—
Toxaphene	B2	—	2B
Tralkoxydim	2, 3	—	—
Triadimefon	C	—	—
Triadimenol	C	—	—
Triallate	C	—	—
Tribenuron methyl	C	—	—
Tribufos (Tribuphos/DEF)	L2	—	—
Trichlorfon	L2	—	3
Trichlorophenol, 2,4,6-	B2	3	—
Tridiphane	C	—	—
Trifluralin	C	—	3
Triforine	2, 3	—	—
Triflusulfuron-methyl	C	—	—
Triphenyltin hydroxide	B2	3	—

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APPENDIX 6.9 (continued)

The Classificatin of Chemicals Including Pesticides and Carcinogenicity (U.S. EPA, EU, IARC)

	Group		
Pesticide	**U.S. EPA**	**EU**	**IARC**
Uniconazole	C	—	—
Vinclozolin	C	3	—
Zineb	3	—	—
Ziram	2, 3	—	3

Notes: Group 1: carcinogenic to humans; group 2A: probably carcinogenic to humans; group 2B: possibly carcinogenic to humans; group 3: unclassifiable as to carcinogenicity in humans; group 4: probably not carcinogenic to humans; group B2: probable human carcinogens.

[a] Chemical other than a pesticide.

Source: IARC. 2004. Evaluations of Carcinogenicity to Humans, IARC Monographs Vols. 1–88.

APPENDIX 6.10

Pesticides Listed in India[a] as Carcinogens

There is no readily available list of carcinogenic chemical substances in India, so the compilation is from the U.S. EPA's evaluation of chemicals evaluated in the United States, possibly depending on the registration there. This does not mean that there are no other registered pesticides in India that can be classified into the preceding categories. In 1986, the following classification of chemical substances as carcinogens was first introduced and was in use until 1996. Subsequently, modifications were added to the classification of carcinogens as found here:

Group A (human carcinogen) is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer.

Group B (probable human carcinogen) includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is limited; this also includes agents for which the weight of evidence of carcinogenicity based on animal studies is sufficient. The group is divided into two subgroups:

Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiologic studies.

Group B2 is used for agents for which there is sufficient evidence from animal studies and for which there is inadequate evidence or no data from epidemiologic studies.

Group C (possible human carcinogen) is used for agents with limited evidence of carcinogenicity in animals in the absence of human data.

Group D (not classifiable as to human carcinogenicity) is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available.

Group E (evidence of noncarcinogenicity for humans) is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in adequate epidemiologic and animal studies.

Pesticides Registered in India and Carcinogenicity Index[a]

Pesticide	Classification
Acephate	C (possible human carcinogen)
Alachlor	Likely to be carcinogenic
Benomyl	C (possible human carcinogen)
Bifenthrin	C (possible human carcinogen)
Buprofezin	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Butachlor	Likely to be carcinogenic
Captan	B2 (probable human carcinogen)
Carbaryl	Likely to be carcinogenic
Chlorfenapyr	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Chlorothalonil	B2 (probable human carcinogen)
Cypermethrin	C (possible human carcinogen)
DDT	B2 (probable human carcinogen)
Diclorvos (DDVP)	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Diclofop-methyl	Likely to be carcinogenic
Dicofol	C (possible human carcinogen)n
Difenocenazole	C (possible human carcinogen)
Dimethoate	C (possible human carcinogen)
Diuron	Known or likely to be carcinogen
Et(h)ofenprox	C (possible human carcinogen)
Fipronil	C (possible human carcinogen)
Glycophene	Likely to be carcinogenic
Hexaconazole	C (possible human carcinogen)
Hydrogen cyanamid	C (possible human carcinogen)
Isoproturon	EU category 3
Lindane	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Linuron	C (possible human carcinogen)
Mancozeb	B2 (probable human carcinogen)

Pesticide	Classification
Malathion	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Metolachlor	C (possible human carcinogen)
Oxadiazon	C (possible human carcinogen)
Oxyflourfen	C (possible human carcinogen)
Paradichlorobenzene	C (possible human carcinogen)
Permethrin	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Phosphamidon	C (possible human carcinogen)
Primiphos-methyl	Not known; more studies required
Propanil	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Propergite	B2 (probable human carcinogen)
Propiconazole	C (possible human carcinogen)
Propoxur	B2 (probable human carcinogen)
Pyrethrins	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen
Simazine	C (possible human carcinogen)
Sulfosulfuron	Likely to be carcinogenic
Simazine	C (possible human carcinogen)
Sulfosulfuron	Likely to be a carcinogen
Tebuconazole	C (possible human carcinogen)
Temephos	Not known; more studies required
Thiodicarb	B2 (probable human carcinogen)
Thiophanate-methyl	Likely to be a carcinogen
Triadimefon	C (possible human carcinogen)
Triallate	C (possible human carcinogen)
Trichlorofon	Likely to be a carcinogen in high doses
Trifluralin	C (possible human carcinogen)
Ziram	Suggestive evidence of carcinogenicity, but not sufficient to assess as a human carcinogen

[a] Based on U.S. EPA classification.

Source: Data compiled by Center for Sustainable Agriculture from U.S. EPA's "Chemicals Evaluated for Carcinogenic Potential," July 2004, and from "Insecticides Registered under Section 9(3) of the Insecticides Act 1968 of India," June 2005.

7 Air Pollutants and Toxic Gases

7.1 INTRODUCTION

Air pollutants and industrial gases cause adverse health effects in industrial workers and the general public, depending upon the manner of exposure and the concentration of the candidate or mixture of pollutants. Air pollutants are toxic and hazardous to human health. It is important to know the differences between toxicity and hazard. In fact, toxicity and hazard are not synonymous terms. The word toxicity identifies the capacity of a chemical substance to cause injury or harm to a living organism, while the word hazard identifies the possibility that exposure to a chemical substance will cause an injury to the living organism when a specific quantity or concentration is used under a certain condition. Further, the characterization of a hazard takes toxicity into account, along with several other factors, to arrive at risk determination.

7.2 SOURCES OF POLLUTANTS AND HEALTH EFFECTS

Combustion of fuels produces and releases pollutants such as hydrocarbons, carbon monoxide, oxides of nitrogen, particulate matter, sulfur dioxide, and greenhouse gases such as carbon dioxide and nitrous oxide. Air pollutants are also released by some household products—for instance, paints, paint strippers, solvents, wood preservatives, aerosol sprays, cleansers and disinfectants, moth repellents, stored fuels, and automotive products.

Air pollutants cause mild to severe health effects in the exposed individual and involve sensitive organ systems. These include the eyes, nose, and throat; irritation, headaches, loss of coordination, nausea, and damage to liver, kidney, and central nervous system (CNS) can occur. Some organic pollutants cause cancer in animals, while some are suspected of causing cancer in humans. The signs and symptoms of poisoning caused by the volatile organic chemicals include conjunctival irritation, nose and throat discomfort, headache, allergic skin reaction, dyspnea, declines in serum cholinesterase levels, nausea, emesis, epistaxis, fatigue, and dizziness. As reported by the World Health Organization, indoor and outdoor air pollution caused very large-scale deaths in different countries of the world during 2002 (Table 7.1).

7.2.1 Air Pollutants

There are many air pollutants, and the composition and level depend on several factors. Air pollutants cause a range of adverse health and environmental effects. These pollutants include ammonia, carbon dioxide, carbon disulfide, carbon monoxide, chlorine, cyanide and cyanide compounds, cyanogen, diborane, fluorine and flourine

TABLE 7.1
Global Air Pollution and Human Mortality

Country	Indoor Air Pollution	Outdoor Air Pollution
China		275,600[a]
India	407,100	120,600
Japan	—	23,800
Mexico	2,400	7,200
Nigeria	79,000	14,700
Pakistan	70,700	28,700
Philippines	6,900	3,900
Vietnam	10,600	6,300
United States	—	41,200
Global mortality	1,497,000	865,000

[a] Figures indicate number of deaths during 2002.

Source: Dikshith, T. S. S. and Diwan, P. V., 2003. *Industrial Guide to Chemical and Drug Safety*. Hoboken, NJ: John Wiley & Sons, Inc.

compounds, formaldehyde, hydrogen bromide, hydrogen chloride, hydrogen sulfide, methyl bromide, methyl chloride, nickel carbonyl, nitrogen oxides, nitric oxide, nitrogen dioxide, ozone, phosgene, phosphine, sulfur dioxide, vinyl chloride, and volatile organic compounds (VOCs).

The air pollutants also include high global-warming-potential gases—perfluorocarbons, sulfur hexafluoride, hydrofluorocarbons, nitrogen trifluoride, hydrofluoroethers, and ozone-depleting substances. Sources of air pollution also emit quantities of other substances, which are often referred to collectively as toxic or "hazardous" air pollutants (HAPs). These pollutants can have more serious health impacts than some of the general pollutants, depending on the level of exposure. In many cases, toxic pollutants constitute a small fraction of the total hydrocarbons and or particulate matter emissions.[1] The following pages discuss in brief a few of the selected air pollutants and toxic gases and the health disorders they cause in humans.

Ammonia (CAS no. 7664-41-7)

Molecular formula: NH_3

Synonyms and trade names: ammonia gas, ammonia, anhydrous, Nitro-Sil, liquid ammonia

Use and exposure: Ammonia is a colorless gas with a sharp, penetrating, and irritating odor. It is very soluble in water and is also soluble in ethanol, diethyl ether, other organic solvents, and mineral acids. It is incompatible with oxidizing agents like perchlorates, chlorates, hydrogen peroxide, chromic trioxide, nitrogen oxides, and nitric acid, and with heavy metals and their salts. The primary use of ammonia gas is in the fertilizer industry, as a direct-application fertilizer and as a building block for the manufacture of nitrogen fertilizers, such as urea, ammonium nitrate, ammonium sulfate,

and ammonium phosphate, and nitrogen fertilizer solutions. It is also used in production of nitric acid and in the fibers and plastics industries for the production of caprolactam and acrylonitrile.[2,3]

Toxicity and health effects: Ammonia gas is a severe respiratory tract irritant. High levels of airborne ammonia gas dissolve in moisture on the skin, forming corrosive ammonium hydroxide. Ammonia does not accumulate in the body. Exposure to high levels of ammonia causes irritation to the skin, eyes, throat, and lungs, as well as coughing and burns. Direct exposure to liquid ammonia causes frostbite, corrosive burns, and permanent scarring among industrial workers. Symptoms of poisoning include mild frostbite, numbness, prickling and itching in the affected area, a burning sensation, and stiffness of the affected area. In severe cases, the skin color turns to waxy white or yellow, blisters, and tissue death and gangrene follow. Corrosive burns of the skin have resulted from direct contact with a jet of liquefied ammonia. Direct contact with the liquefied ammonia gas causes corrosive injury to the eye, permanent eye damage, or blindness.[2,3]

Ammonia gas and cancer: There are no reports indicating that ammonia gas causes cancer in animals and humans. The Department of Health and Human Services (DHHS), the U.S. Environmental Protection Agency (EPA), and the International Agency for Research on Cancer (IARC) have not classified ammonia for carcinogenicity.[2]

Exposure limits: The Occupational Safety and Health Administration (OSHA) has set 50 ppm as the permissible exposure limit (PEL) for an 8-hour work period (time weight average [TWA]), and a short-term exposure limit (STEL; 15 minutes) as 35 ppm. OSHA and the National Institute of Occupational Safety and Health (NIOSH) have set a limit of 500 ppm as immediately dangerous to life and health.[2]

Precautions: Ammonia gas is very toxic and poses an explosion hazard, particularly in improper storage conditions. Unprotected industrial workers should avoid all contact with ammonia gas and use of contaminated equipment. Ammonia gas should be stored in a cool, dry, well-ventilated area, out of direct sunlight, away from heat and ignition sources, and away from flammable material. Always use chemical safety goggles, a face shield for skin protection, chemical protective gloves, coveralls, boots, and/or other chemical protective clothing.

Carbon disulfide (CAS no. 75-15-0)

Molecular formula: CS_2

Synonym: carbon bisulfide

Use and exposure: Pure carbon disulfide is a colorless liquid with a sweet odor similar to that of chloroform, while impure carbon disulfide is a yellowish liquid with an unpleasant odor like that of rotting radishes. Exposure to carbon disulfide occurs in industrial workplaces. Industries associated with coal gasification plants release carbon disulfide, carbonyl sulfide, and hydrogen sulfide. Carbon disulfide is used in large quantities as an industrial chemical for the production of viscose rayon fibers. In fact, the major

source of environmental indoor and outdoor pollution by carbon disulfide is caused by emission released into the air from viscose plants.[4–6]

Toxicity and health effects: Laboratory animals exposed to carbon disulfide experienced deleterious health effects—for instance, developmental effects, skeletal and visceral malformations, embryotoxicity, and functional and behavioral disturbances. Studies of animals exposed to carbon disulfide indicate destruction of the myelin sheath and axonal changes in both central and peripheral neurons along with changes in the cortex, basal ganglia, thalamus, brain stem, and spinal cord. Neuropathy and myelopathy were studied extensively in rats and rabbits. In the muscle fibers, atrophy of the denervation type occurred secondary to the polyneuropathy. Studies have also shown that carbon disulfide causes vascular changes in various organs of animals as well as myocardial lesions.[4–6] Industrial workers exposed to carbon disulfide showed symptoms of irritability, anger, mood changes, manic delirium and hallucinations, paranoic ideas, loss of appetite, gastrointestinal disturbances, and reproductive disorders.[4–6] The slowing down of nerve conduction velocity in the sciatic nerves preceded clinical symptoms. Studies have indicated that carbon disulfide can affect the normal functions of the brain, liver, and heart. Workers exposed to high concentrations of carbon disulfide have suffered with skin burns when the chemical accidentally touched them (Table 7.2).[5a]

Carbon disulfide and cancer: The U.S. EPA and IARC have not classified carbon disulfide as a human carcinogen.[4,5]

TABLE 7.2
Symptoms of Carbon Disulfide Poisoning

Concentration (mg/m^3)	Exposure Period (years)	Symptoms and Signs
500–2500	0.5	Polyneuritis, myopathy, acute psychosis
450–1000	<0.5	Polyneuritis, encephalopathy
200–500	1–9	Increased ophthalmic pressure
60–175	5	Eye burning, abnormal papillary light reactions
31–137	10	Psychomotor and psychological disturbances
29–118	15	Polyneuropathy, abnormal EEG, conduction velocity slowed, psychological changes
29–118	10	Increase in coronary mortality, angina pectoris, slightly higher systolic and diastolic blood pressure
40–80	2	Asthenospermia, hypospermia, teratospermia
22–44	>10	Arteriosclerotic changes and hypertension
30–50	>10	Decreased immunological reactions
30	3	Increase in spontaneous abortions and premature births
20–25	<5	Functional disturbances of the CNS
10	10–15	Sensory polyneuritis, increased pain threshold

Source: Dikshith and Diwan, 2003.[5a]

Exposure limits: OSHA has set a limit of 20 ppm of carbon disulfide for an 8-hour workday (TWA), while the NIOSH has set a limit of 1 ppm in workroom air.[4,5]

Carbon monoxide (CAS no. 630-08-0)
Molecular formula: CO
Synonyms and trade names: carbonic oxide, flue gas, CO, carbon oxide
Use and exposure: Carbon monoxide is a colorless, odorless, tasteless gas that is extremely hazardous. It can be formed from incomplete burning of gasoline, wood, kerosene, or other fuels. Carbon monoxide is also found in cigarette smoke and vehicle exhaust. In homes, carbon monoxide can build up from a poorly vented or malfunctioning heater, furnace, range, or any appliance that runs on natural gas or oil. Presence of carbon monoxide is very common inside and outside the workplace. It can be found around heaters, in improper use of gas- or kerosene-fired heaters or gas-fired central heating equipment combined with improper venting or poorly functioning chimney due to blocked heating flues, improper flue vent connectors, or hood installation, inadequate combustion air, from car exhaust, and gas-fired water heaters.[7–9]
Toxicity and health effects: Carbon monoxide is a highly toxic gas that is often called a chemical asphyxiant. When inhaled, it combines with hemoglobin more readily than does oxygen, displacing oxygen from hemoglobin and thereby interfering with oxygen transport by the blood. The early symptoms of CO poisoning include headaches, nausea, and fatigue, which are often mistaken for the flu because CO is not detected in a home. Prolonged exposure to CO causes deleterious health effects, brain damage, and eventually death. The symptoms of CO poisoning include but are not restricted to drowsiness, nausea, tiredness, vomiting, headaches, dizziness, visual changes, abdominal pain, chest pains, memory and walking problems, brain damage, and, in severe cases, death. Exposure to high concentrations of CO causes severe headache, weakness, dizziness, irregular heartbeat, seizures, coma, respiratory failure, and unconsciousness.[7–11a] Carbon monoxide poisoning can happen to anyone, anytime, almost anywhere. Depending upon the period of exposure and concentration of CO, poisoning may be severe, moderate, or mild:

- Extreme exposure causes confusion, drowsiness, rapid breathing or pulse rate, vision problems, chest pain, convulsions, seizures, loss of consciousness, cardiorespiratory failure, and death.
- Moderate exposure causes severe throbbing headache, drowsiness, confusion, vomiting, and fast heart rate.
- Mild exposure causes slight headache, nausea, and fatigue.

The toxicity of CO results from its very tight binding to hemoglobin, the species that carries oxygen from the lungs to bodily tissues. For hemoglobin to work, it cannot bind oxygen very tightly (otherwise, it could not release it at its destination). Unfortunately, CO binds to hemoglobin 200 times more tightly than oxygen. Carboxyhemoglobin (the molecule

TABLE 7.3
Symptoms of Carbon Monoxide Poisoning

Concentration (ppm)	Symptoms/Effects
12,800	Immediate effects: unconsciousness, danger of death in 1–3 minutes
6,400	Headache and dizziness in 1–2 minutes; unconsciousness, danger of death in 10–15 minutes
3,200	Headache, dizziness in 5–10 minutes; unconsciousness, danger of death in 30 minutes
1,600	Headache, dizziness, and nausea in 20 minutes; collapse and death in 1 hour
800	Headache, dizziness, and nausea in 45 minutes; collapse and possible death in 2 hours
400	Frontal headache, nausea after 1–2 hours, occipital after 2.5–3.5 hours
200	Possible mild frontal headache in 2–3 hours
50	Permissible exposure level for 8 hours

Sources: American Industrial Hygiene Association; adapted from Gilman, A. G. 2002. *Goodman and Gilman's the Pharmacological Basis of Therapeutics,* 10th ed., 1881. New York: McGraw–Hill.

formed when CO binds to hemoglobin) does not perform oxygen transport, and it rapidly builds up. In essence, victims are slowly suffocated because their hemoglobin is consumed. The fatal concentration of CO depends on the length of the air exposure and exertion. Carbon monoxide also causes a decrease in heart oxygen supply and induces myocardial hypoxia. Levels above 300 ppm for more than 1–2 hours can lead to death, and exposure to 800 ppm (0.08%) can be fatal after an hour (Table 7.3). It is alarming to note that each year more than 500 Americans die from unintentional carbon-monoxide poisoning and more than 2000 commit suicide by intentionally poisoning themselves with carbon monoxide.[7–11]

Exposure limits: OSHA has set the PEL for carbon monoxide as 50 ppm for an 8-hour period (TWA) and NIOSH has set a standard of 35 ppm.[7,8]

Preventing CO poisoning:

- Install a carbon monoxide alarm on each level of a home.
- Inspect home heating systems; chimneys and flues must be inspected and cleaned by a qualified technician every year. Keep chimneys clear of bird and squirrel nests, leaves, and residue to ensure proper ventilation.
- Make sure that the furnace and other appliances, such as gas ovens, ranges, and cooktops, are inspected for adequate ventilation.
- Do not burn charcoal inside the house, even in the fireplace.
- Do not operate gasoline-powered engines in confined areas such as garages or basements. Do not leave a car, mower, or other vehicle running in an attached garage, even with the door open.
- Do not block or seal or close exhaust flues or ducts for appliances such as water heaters, ranges, and clothes dryers.

Chlorine (CAS no. 7782-50-5)

Periodic table designation: Cl

Use and exposure: Chlorine is a yellow-green gas that is heavier than air and has a strong, irritating odor. Chlorine is extensively used in the production of paper products, dyestuffs, textiles, petroleum products, medicines, antiseptics, insecticides, food, solvents, paints, plastics, and many other consumer products. It is mainly used as a bleach in the manufacture of paper and cloth and to make a wide variety of products. Most of the chlorine produced is used in the manufacture of chlorinated compounds for sanitation, pulp bleaching, disinfectants, and textile processing. Further use is in the manufacture of chlorates, chloroform, carbon tetrachloride, and in the extraction of bromine. Organic chemistry demands much from chlorine, both as an oxidizing agent and in substitution. In fact, chlorine was used as a war gas in 1915 as a choking (pulmonary) agent. Chlorine itself is not flammable, but it can react explosively or form explosive compounds with other chemicals such as turpentine and ammonia.[12,13] Chlorine is slightly soluble in water. It reacts with water to form hypochlorous acid and hydrochloric acid. The hypochlorous acid breaks down rapidly. Chlorine gas is used to synthesize other chemicals and to make bleaches and disinfectants. Chlorine is a powerful disinfectant, and in small quantities ensures clean drinking water. It is used in swimming pool water to kill harmful bacteria. Chlorine has a huge variety of uses—for instance, as a disinfectant and purifier; in plastics and polymers, solvents, agrochemicals, and pharmaceuticals; and as an intermediate in manufacturing other substances where it is not contained in the final product. Also, a very large percentage of pharmaceuticals contain and are manufactured using chlorine. Thus, chlorine is essential in the manufacture of medicines to treat illnesses such as allergies, arthritis, and diabetes.[12,13]

Toxicity and health effects: Chlorine is a respiratory irritant. It causes irritation to the mucus membranes and the liquid burns the skin. The poisoning caused by chlorine depends on the amount a person is exposed to and the length of exposure time. Prolonged exposure to high concentrations of chlorine causes poisoning with symptoms that include but are not limited to coughing; burning sensation in the nose, throat, and eyes; blurred vision; nausea; vomiting; pain, redness, and blisters on the skin; chest tightness; and pulmonary edema.[12,13]

Chlorine and cancer: There are no reports indicating that chlorine causes cancer in animals and humans. The DHHS, IARC, and U.S EPA have not classified chlorine as a human carcinogen.[12,13]

Exposure limits: OSHA has set a PEL of 1 ppm for chlorine for an 8-hour workday (TWA), while the American Conference of Governmental Industrial Hygienists (ACGIH) has set a limit of 0.5 ppm as the TLV for an 8-hour day (TWA) and an STEL of 1 ppm of chlorine.[12,13]

Chlorofluorocarbons (CFCs)

Chlorofluorocarbons are the most important ozone-destroying chemicals. These have been used in many ways since they were first synthesized in

1928. They are stable, nonflammable, low in toxicity, and inexpensive to produce. Over time, CFCs found uses as refrigerants, solvents, foam-blowing agents, and aerosols, as well as in other smaller applications. When released into the air, CFCs rise into the stratosphere. In the stratosphere, they react with other chemicals and reduce the stratospheric ozone layer, which protects the Earth's surface from the sun. Reducing CFC emissions and eliminating the production and use of ozone-destroying chemicals is very important to protecting the Earth's stratosphere.

Use and exposure: Chlorofluorocarbons are a family of organic compounds containing chlorine, fluorine, and carbon and are also called Freon. CFCs entered the industrial scene in the late 1920s and early 1930s as safer alternatives to the sulfur dioxide and ammonia refrigerants used at the time. The CFCs are inert and volatile compounds with extensive uses as refrigerants and blowing agents for cleaning agents, in the production of plastic foams, as solvents to clean electronic components and propellants in air conditioners and aerosol sprays. These compounds are low in toxicity, nonflammable, noncorrosive, and nonreactive with other chemical species, and have desirable thermal-conductivity and boiling-point characteristics. The primary chlorine-containing products on the market are denoted by industry nomenclature such as CFC-11, CFC-12, CFC-113, CFC-114, CFC-115, and the hydrochlorofluorocarbon HCFC-22. Chlorofluorocarbons are marketed under many different trade names—for instance, Algcon, Algofrene, Arcton, Eskimon, Flugene, Forane, Freon, Frigen, Genetron, Isceon, and Osotron.[14]

Toxicity and health effects: The commercial chlorofluorocarbons are persistent in the environment because of their chemical stability. The prolonged period of accumulation and presence of inert CFCs in the atmosphere leads to depletion of the ozone layer and increased intensity of sunlight. This in turn is known to cause health complications such as skin cancer and eye cataracts, as well as ecological disasters. At high concentrations, CFCs cause neurological disorders such as tingling sensation, humming in the ears, apprehension, EEG changes, slurred speech, and decreased performance in psychological tests.[14]

Cyanide (CAS no. 57-12-5) and cyanide compounds

Molecular formula: CN

Use and exposure: The most common cyanide is hydrogen cyanide (HCN) and its salts—sodium cyanide (NaCN), and potassium cyanide (KCN). Cyanides are ubiquitous in nature, arising from both natural and man-made sources. They are found in several plant species as cyanogenic glycosides and are produced by certain bacteria, fungi, and algae. In very small amounts, cyanide is a necessary requirement in the human diet. Cyanide is released to the environment from numerous sources. Metal finishing and organic chemical industries as well as iron and steel production are major sources of cyanide releases to the aquatic environment. More than 90% of emissions to the air are attributed to releases in automobile exhaust. Workers in a wide variety of occupations may be exposed to cyanides. The general

population may be exposed to cyanides by inhalation of contaminated air, ingestion of contaminated drinking water, and/or consumption of a variety of foods.[15,16]

Toxicity and health effects: In tropical regions of Africa, a high incidence of ataxic neuropathy, goiter, amblyopia, and other health disorders has been associated with chronic ingestion of cassava, one of the dietary staples containing cyanogenic glycosides that release hydrogen cyanide when metabolized in vivo.[15,16] Cyanides are readily absorbed by inhalation, oral, and dermal routes of exposure. Hydrogen cyanide and its simple soluble salts are among the most rapidly acting poisons. The CNS is the primary target organ for cyanide toxicity. Neurotoxicity has been observed in humans and animals following ingestion and inhalation of cyanides. Cardiac and respiratory effects, possibly CNS mediated, have also been reported.

Exposure limits: The U.S. EPA has set a limit of 0.2 ppm for cyanide in drinking water. OSHA has set a limit of 10 ppm for hydrogen cyanide and most other cyanide salts in the workplace.[15]

Cyanide compounds

Calcium cyanide (CAS no. 592-01-8); molecular formula: $Ca(CN)_2$
Copper cyanide (CAS no. 54-92-3); molecular formula: CuCN
Cyanogen (CAS no. 460-19-5); molecular formula: NCCN
Cyanogen chloride (CAS no. 506-77-4); molecular formula: CNCl
Potassium cyanide (CAS no. 151-50-8); molecular formula: KCN
Sodium cyanide (CAS no. 143-33-9); molecular formula: NaCN
Hydrogen cyanide (CAS no. 74-90-8); molecular formula: HCN

Synonyms and trade names: Formonitrile, hydrocyanic acid, prussic acid

Use and exposure: Hydrogen cyanide is a colorless to a pale blue liquid or gas. It has a distinct odor resembling bitter almonds. Exposure to cyanide occurs in workplaces such as the electroplating, metallurgical, firefighting, steel manufacturing, and metal-cleaning industries. Human exposure to cyanide also occur from wastewater discharges of industrial organic chemicals, iron and steel works, and wastewater treatment facilities.

Toxicity and health effects: Hydrogen cyanide is particularly dangerous because of its toxic/asphyxiating effects on all life requiring oxygen to survive. HCN combines with the enzymes in tissue associated with cellular oxidation. When oxygen becomes unavailable to the tissues, it leads to asphyxia and causes death. Inhalation of hydrogen cyanide results in the most rapid onset of poisoning, producing almost immediate collapse, respiratory arrest, and death within minutes (Table 7.4).

Hydrogen cyanide and cancer: Information on the carcinogenicity of hydrogen cyanide in humans or animals for oral exposure is unavailable. Similarly, there are no reports that cyanide can cause cancer in animals and humans. The U.S. EPA has classified cyanide as a group D, meaning that it is not classifiable as to human carcinogenicity.[15,16]

Exposure limits: OSHA has set a limit of 10 ppm for hydrogen cyanide and most cyanide salts in the workplace.[15]

TABLE 7.4
Signs and Symptoms of Hydrogen Cyanide Poisoning

Concentration (ppm)	Symptoms/Effects
100–200	Death from exposure in 30–60 minutes
0–100	Feeling of suffocation; nausea
10–50	Headache, dizziness, unsteadiness
10	Headache, dizziness, unsteadiness

Source: Lewis, S. 2004. *Sax's Dangerous Properties of Industrial Materials*, 11th ed. New York: Wiley Interscience.

Cyanogen (CAS no. 460-19-5)
Molecular formula: C_2N_2
Synonyms and trade names: carbon nitride, Dicyan, Dicyanogen, Ethanedinitrile; Nitriloacetonitrile, Oxalonitrile, Oxalic Acid Dinitrile, oxalyl cyanide
Use and exposure: Cyanogen is a colorless, flammable, pungent, highly poisonous gas. It is used as a rocket propellant, an insecticide, and a chemical weapon. Cyanogen is typically generated from cyanide compounds in the laboratory. Cyanogen gas is very toxic and undergoes reduction to cyanide. It is an irritant to the eyes and respiratory system. Cyanogen produces the hottest known natural flame, with a temperature of over 4525°C (8180°F) when it burns in oxygen.[17]
Toxicity and health effects: Prolonged periods of exposure to high concentrations of cyanogens in workplaces cause symptoms of toxicity that include but are not limited to irritation of eyes, nose, and throat; lacrimation; respiratory distress; headache; dizziness; rapid pulse; tachypnea; hyperpnea; bradycardia; vomiting; loss of consciousness; convulsions; and death.[17]

Diborane (CAS no. 19287-45-7)
Molecular formula: B_2H_6
Synonyms and trade names: boroethane, boron hydride, diboron hexahydride
Use and exposure: Diborane is a colorless gas at room temperature with a repulsive, sweet odor. It mixes well with air and easily forms explosive mixtures. Diborane will ignite spontaneously in moist air at room temperature and can cause explosions. Diborane is used in rocket propellants and as a reducing agent, a rubber vulcanizer, a catalyst for hydrocarbon polymerization, a flame-speed accelerator, and a doping agent. Diborane is a very toxic and flammable gas used by chemists to make other compounds. It is also used in electronics to impart electrical properties in pure crystals. Industrial workers are exposed to diborane by breathing in its vapors in work areas.[18,19]
Toxicity and health effects: Diborane is a poisonous gas. Industrial workers exposed to diborane show sensations of tightness of the chest, diaphragmatic pain, shortness of breath, cough, and wheezing. These signs and

symptoms can occur immediately or be delayed for up to 24 hours and can be seen for 3–5 days after an exposure. Skin and eye irritation can also occur. Prolonged periods of exposure, even to low concentrations of diborane, have caused respiratory irritation, seizures, fatigue, drowsiness, confusion, and occasional transient tremors among workers. Eighteen laboratory animals exposed to diborane demonstrated damage to kidney, pulmonary edema, and hemorrhage. Children are more vulnerable to diborane and require prompt attention.[18,19]

Diborane and cancer: There are no studies of carcinogenicity of diborane in humans or in animals. The DHHS, IARC, and U.S. EPA have not classified diborane as to its carcinogenicity.[18,19]

Exposure limits: OSHA has set a limit of 0.1 ppm for diborane in workplace air for an 8-hour workday (TWA). The revised immediately dangerous to life or health (IDLH) concentrations for diborane are set at 15 ppm.[18,19]

Precautions: Diborane is a highly toxic, flammable, and reactive gas. It is spontaneously combustible in moist air and may burn or explode upon contact with halogenated compounds. It explodes on contact with fluorine, chlorine, halogenated hydrocarbons, fuming nitric acid, and nitrogen trifluoride. It is a very dangerous gas and must be handled and used only in chemical laboratories by experienced and trained professional workers.[18,19]

Flourine (CAS no. 7782-41-4): flourine compounds: hydrogen fluoride (CAS no. 7664-39-3); sodium fluoride (CAS no. 7681-49-4)

Molecular formula: F_2

Use and exposure: Fluorine was discovered in 1886 as a member of the halogen group. Fluorine is a naturally occurring, univalent, poisonous, colorless to pale yellow-green colored gas with a sharp odor. It is chemically reactive and combines with metals as a salt to make fluorides such as sodium fluoride and calcium fluoride. It is very reactive and burns glass, metals, and even water with a bright flame in a jet of fluorine gas. It reacts with water to form corrosive acids. Hydrogen fluoride in water is called hydrofluoric acid. Ordinary substances like wood and rubber burst into flame when held into a stream of fluorine gas.[20] Fluorine is used for plasma etching in semiconductor manufacturing, flat panel display production, and main electronics module fabrication. Fluorine is indirectly used in the production of low friction plastics such as teflon and in halons such as Freon in the production of uranium. Fluorides are often added to toothpaste and, somewhat controversially, to municipal water supplies to prevent dental cavities.[20] Fluorine is an extremely strong oxidant that may react violently with combustible materials, plastics, reducing agents, and organic material. In vapor phase, hydrogen fluoride is used for etching glass. Hydrofluoric acid must be handled with great care because skin contact produces lesions that heal very slowly. Hydrofluoric acid can be stored in polyethylene containers. Sodium fluoride (NaF) is used as an insecticide. Application of fluorochlorohydrocarbons in air conditioning and in refrigeration is very common.[20,21]

Toxicity and health effects: Fluorine gas is very toxic and causes severe burns. It causes serious damage to the eyes, skin, and respiratory system. Accidental inhalation is fatal. At low concentrations, it causes eye and nose irritation. Humans are exposed to fluorine through food and drinking water and by breathing it in the air. Fluorine can be found in any kind of food in relatively small quantities. Large quantities of fluorine can be found in tea and shellfish.[20,21] Inhalation exposure to fluorine or hydrogen fluoride causes respiratory, nasal, and ocular irritation; kidney and liver necrosis have also been observed in animals. However, information on prolonged exposure to fluorine is very sketchy. Both fluorine and hydrogen fluoride can cause lethal pulmonary edema.[20,21]

Fluorine and cancer: The IARC has determined that the carcinogenicity of fluoride to humans is not classifiable.[20]

Exposure limits: The U.S. EPA has set a maximum allowable amount of fluoride in drinking water as 4.0 mg/L of water. OSHA has set the limits for fluorine as 0.2 mg/m^3, hydrogen fluoride as 2.0 mg/m^3, and fluoride in workplace air as 2.5 mg/m^3 for an 8-hour workday (TWA).[20]

Formaldehyde (CAS no. 50-00-0)

Molecular formulation: HCHO

Synonyms and trade names: formaldehyde 37%, Formalin, morbicid acid, methylene oxide, methyl aldehyde

Use and exposure: Formaldehyde is a flammable, colorless gas with a pungent, suffocating odor. It is highly soluble in water, acetone, benzene, chloroform, diethyl ether and ethanol, alcohols, ketones, chlorinated and aromatic hydrocarbons, and other organic solvents; it is slightly soluble in pentane and petroleum ether. Formaldehyde gas is stable in the absence of water, but it is incompatible with oxidizers, alkalis, acids, phenols, and urea. It reacts with peroxide, nitrogen oxide, and performic acid and causes explosions.[22–24] Formaldehyde has been in extensive use in many industries (e.g., in the production of urea-formaldehyde resins, phenolic resins, acetylenic chemicals, polyacetal resins, methylene diisocyanate, pentaerythritol, melamine resins, nitroparaffin derivatives, and textile treatings and as an intermediate in the synthesis of many other chemicals). Commercial formaldehyde is produced and sold as an aqueous solution containing 37–50% formaldehyde by weight. It is also used in association with other chemicals as an adhesive in the manufacture of particle board, fiberboard, and plywood, and for molding, paper treating, surface coating, and foams for insulations, building materials, carpets, paints, and varnishes.[22–24] Important sources of exposure to formaldehyde include manufacture of resins and plastics, permanent-press fabrics, plywood and particle board, disinfectant, tissue preservative, embalming fluid, laboratory reagent, tanning operations, urea-formaldehyde insulation, tobacco smoke, pentaerythritol production, and seed and bulb treatment (Table 7.5).

Toxicity and health effects: Exposure to high concentrations of formaldehyde is known to cause irritation to the eyes, nose, and throat; fatigue; headache;

TABLE 7.5
Important Sources of Exposure to Formaldehyde

Manufacture
Resins and plastics
Permanent-press fabrics
Plywood and particle board
Disinfectant
Tissue preservative
Embalming fluid, laboratory reagent
Tanning operations
Urea-formaldehyde insulation
Tobacco smoke
Pentaerythritol production
Seed and bulb treatment
Paint preservative

nausea; upper airway irritation and increased nasal airway resistance; chronic pulmonary obstruction; pulmonary edema; inflammation; choking; dyspnea; chest tightness; pneumonia; skin rash; and severe allergic reactions. There is evidence that some people can develop a sensitivity to formaldehyde and, in severe cases, death can result.[22–24]

Formaldehyde gas and cancer: Laboratory animal studies have indicated that inhalation exposure to formaldehyde causes increased incidence of nasal squamous cell carcinomas. The U.S. EPA indicates that formaldehyde is a probable human carcinogen and ranks it as group B1. Formaldehyde (gas) is reasonably anticipated to be a human carcinogen based on limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals.[22–24] The IARC reported sufficient evidence in experimental animals for the carcinogenicity of formaldehyde, but the evidence in humans is limited. Formaldehyde is classified by the IARC as group 2A, meaning that it is probably carcinogenic to humans. However, the working group of the IARC concluded that formaldehyde is carcinogenic to humans.[22–24]

Exposure limits: OSHA has set a PEL for formaldehyde as 0.75 ppm for an 8-hour workday (TWA), and NIOSH has set a limit of 0.016 ppm.[22–24]

Hydrogen bromide (CAS no. 10035-10-6)

Molecular formula: HBr

Synonyms and trade names: anhydrous hydrobromic acid, anhydrous hydrogen bromide, hydrobromic acid

Use and exposure: Hydrogen bromide is a colorless or faintly yellow-colored, corrosive gas; it is highly toxic, with a sharp, unpleasant, irritating odor. It can also be found as a liquid, either as hydrobromic acid (hydrogen bromide dissolved in water) or as a compressed gas under pressure (anhydrous

hydrogen bromide). It is an extremely dangerous substance and must be handled with caution. It is incompatible with fluorine gas, ammonia, ozone, ferric oxide, alkalis, metal, water, and strong oxidizing agents, reacting violently and forming a flammable, explosive gas. It is heavier than air and can travel to low-lying or confined areas. Containers of hydrogen bromide may explode when heated. It reacts instantaneously with ozone to cause an explosion.[25]

Toxicity and health effects: Human exposure to hydrogen bromide causes redness, pain, frostbite, and severe burns and blisters on the skin. Eye contact with the liquid causes redness, pain, severe burns, and possible permanent eye damage. It causes nose and throat irritation, watery eyes, bloody nose, nausea, vomiting, chest pain and/or light-headedness, coughing, shortness of breath, fluid in the lungs or pulmonary edema, unconsciousness, low blood pressure, rapid heartbeat, kidney failure, coma, and death.[25]

Exposure limits: OSHA has set a PEL for hydrogen bromide as 3 ppm in an 8-hour period (TWA). Similarly, NIOSH has set a recommended exposure limit (REL) for hydrogen bromide of 3 ppm in working exposure. The ACGIH has set a ceiling of 3 ppm for hydrogen bromide as the working exposure.[25]

Precautions and storage: Keep stored containers of hydrogen bromide tightly closed in a cool, dry, ventilated area away from sources of heat or ignition. Exposure to hydrogen bromide is very dangerous. The liquid and mist of hydrogen bromide cause severe burns to all body tissues. Vapors cause irritation to eyes and lungs; prolonged inhalation or accidental ingestion is fatal.[25]

Hydrogen chloride (CAS no. 7647-01-0)

Molecular formulation: HCl

Synonyms and trade names: anhydrous hydrochloric acid, hydrochloride, muriatic acid, spirits of salt, hydrochloric acid, chlorohydric acid

Use and exposure: Hydrogen chloride is a corrosive, colorless to slightly yellow, nonflammable gas. It is heavier than air and has a strong, irritating odor. On exposure to air, hydrogen chloride forms dense white corrosive vapors. It is formed during the burning of many plastics, and volcanoes also release hydrogen chloride to the atmosphere. Uses of hydrogen chloride are many and include but are not limited to cleaning, pickling, electroplating metals, tanning leather, and refining and producing a wide variety of products. On contact with water, hydrogen chloride becomes hydrochloric acid. Workers are often exposed to hydrogen chloride in different industrial occupations, such as metal pickling, ore refining, food processing, manufacture of fertilizers and dyes, and rubber and textile industries. Soldering materials cause exposure to hydrogen chloride.[26,27]

Toxicity and health effects: Exposure to hydrogen chloride causes irritation and corrosive effects to the tissue on contact. Acute exposure to low concentrations of hydrogen chloride causes throat irritation, and prolonged exposure

to high concentrations causes rapid breathing, narrowing of the bronchioles, blue coloring of the skin, accumulation of fluid in the lungs, swelling and spasm of the throat, and suffocation. In certain cases, the exposed worker develops an inflammatory reaction to hydrogen chloride, resulting in reactive airways dysfunction syndrome, also called RADS. When swallowed accidentally, concentrated hydrochloric acid causes severe corrosive injury to the lips, mouth, throat, esophagus, and stomach.[26,27]

Hydrogen chloride and cancer: The DHHS, IARC, and U.S. EPA have not classified hydrogen chloride as a human carcinogen.[26,27]

Precautions and storage: Hydrogen chloride should be stored in a cool, dry, well-ventilated area in tightly sealed containers and with a proper label. Containers of hydrogen chloride should be protected from physical damage and should be stored separately from hydroxides, amines, alkalis, or metals, such as copper, brass, zinc, potassium, and sodium.[27]

Exposure limits: OSHA has set a ceiling limit of 5 ppm for hydrogen chloride in the workplace air.[26,27]

Hydrogen fluoride (CAS no. 7664-39-3)

Molecular formula: HF

Synonyms and trade names: hydrofluoric acid

Use and exposure: Hydrogen fluoride is a colorless gas or a fuming liquid made up of a hydrogen atom and a fluorine atom. It creates strong fumes and readily dissolves in water. Hydrogen fluoride, in both the liquid and gas form, causes severe burns upon contact. The liquid form is called hydrofluoric acid. Commercially, hydrogen fluoride is used in the production of aluminum and chlorofluorocarbons, and in the glass-etching and chemical industries. Other fluoride compounds are used in making steel, chemicals, ceramics, lubricants, dyes, plastics, and pesticides. Fluorides are often added to drinking water supplies and to a variety of dental products, including toothpaste and mouth rinses, to prevent dental cavities.[20,21]

Toxicity and health effects: Hydrofluoric acid is dangerous to humans. Acute inhalation of gaseous hydrogen fluoride causes severe poisoning, with symptoms that include but are not restricted to irritation of the eyes, nose, and upper and lower respiratory tract; lacrimation; sore throat; cough; chest tightness; wheezing; respiratory damage; and pulmonary edema. The initial exposure to hydrofluoric acid may not look like a typical acid burn. Skin may only appear red and may not be painful at first. Damage to skin may happen over several hours or days, and deep, painful wounds may develop. When not treated properly, serious skin damage and tissue loss can occur. Breathing large amounts of hydrogen fluoride causes damage to the lungs and heart. Exposure to hydrogen fluoride or fluoride-containing dust for several years through breathing causes changes in bones called skeletal fluorosis.[20,21]

Fluorides and hydrogen fluoride and cancer: The IARC and U.S. EPA have not classified hydrogen fluoride as a human carcinogen.[20,21]

Exposure limits: OSHA has set limits of 0.2 mg/m^3 for fluorine, 2.0 mg/m^3 for hydrogen fluoride, and 2.5 mg/m^3 for fluoride in workroom air during an 8-hour period (TWA).[20,21]

Precautions

- Hydrogen fluoride, whether in gaseous, liquid, or solution form, is a dangerous chemical and must be handled with caution by trained, qualified professionals.
- Any work with hydrofluoric acid in the laboratory or elsewhere must never be attempted by an untrained person.
- Work using hydrofluoric acid must never be attempted out of normal working hours and it is strongly advised that procedures are restricted over the lunch period when personnel trained in first aid may not be available.
- Work using hydrofluoric acid must never be attempted by someone working alone; for larger scale operations, workers should operate in pairs.
- All work with hydrofluoric acid must be carried out in a fume hood.
- Appropriate personal protective equipment (PPE: safety glasses, preferably a face shield, PVC or Neoprene gloves, chemical-proof apron) must be worn during work.
- Washing hands and gloves frequently with water is wise when working with even dilute HF.

Methyl bromide (CAS no. 74-83-9)

Molecular formula: CH_3Br

Synonyms and trade names: bromomethane, monobromomethane, isobrome, methyl fume

Use and exposure: Methyl bromide is a colorless gas at room temperature and with a musty or fruity odor. It is water soluble and flammable in the presence of ignition. Methyl bromide is three times heavier than air and can accumulate in poorly ventilated or low-lying areas. It reacts with strong oxidizers, magnesium, aluminum, tin, zinc, and alloys. It attacks aluminum to form aluminum trimethyl, which is spontaneously flammable. Methyl bromide gas easily penetrates most protective clothing. The primary use of methyl bromide is as a fumigant in soil to control fungi, nematodes, and weeds; in space fumigation of food grains; and in storage facilities, warehouses, ships, and freight cars. It is also used as a solvent in aniline dye manufacture and as an oil extractant in chemical syntheses.[1a,28]

Toxicity and health effects: Methyl bromide is a neurotoxic gas. Industrial workers exposed to methyl bromide show symptoms of poisoning such as convulsions, coma, and long-term neuromuscular and cognitive deficits. Exposure to high concentrations of pure methyl bromide may cause inflammation of the bronchi or lungs, an accumulation of fluid in the lungs, and irritation of the eyes and nose. Tearing agents added to methyl bromide to provide warning of its presence can also cause these symptoms, even at very low concentrations. Skin contact with high vapor concentrations or with liquid methyl bromide can cause systemic toxicity and may cause stinging pain and blisters.[1a,28]

Exposure limits: OSHA has set a ceiling limit of 20 ppm (skin) and NIOSH has set the IDLH as 250 ppm.[1a,28]

Nitrogen oxides:

(1) nitric oxide (CAS no. 10102-43-9); molecular formula: NO; synonyms and trade names: mononitrogen monoxide, nitrogen monoxide
(2) nitrogen dioxide (CAS no. 10102-44-0); molecular formula: NO_2; synonyms and trade names: dinitrogen tetroxide, nitrogen peroxide, nitrogen tetroxide, NTO

Use and exposure: Nitrogen oxides are a mixture of gases designated by the formula NOx. The mixture includes nitric oxide (NO), nitrogen dioxide (NO_2), nitrogen trioxide (N_2O_3), nitrogen tetroxide (N_2O_4), and nitrogen pentoxide (N_2O_5). Nitrogen oxides are released to the air from the exhaust of motor vehicles; the burning of coal, oil, or natural gas; and during processes such as arc welding, electroplating, engraving, and dynamite blasting. They are also produced commercially by reacting nitric acid with metals or cellulose. Nitrogen oxides are used in the production of nitric acid, lacquers, dyes, and other chemicals. Nitrogen oxides form naturally during the oxidation of nitrogen-containing compounds such as coal, diesel fuel, and silage. Nitrogen oxides are also formed as components of rocket fuel, and nitration reactions such as in the production of nitro-explosives, including gun-cotton, dynamite, and TNT. Nitrogen dioxide is a yellow-brown liquid or red-brown gas, with an irritating, sharp odor. Nitrogen dioxide and nitric acid react with combustible materials, carbon disulfide, and ammonia. They also react violently with cyclohexane, fluorine, formaldehyde, alcohol, nitrobenzene, petroleum, and toluene.[29,30]

Toxicity and health effects: Nitrogen oxides (namely, NO_2, N_2O_4, N_2O_3, and N_2O_5) are irritating to the upper respiratory tract and lungs even at low concentrations. Brief and prolonged periods of exposure to nitrogen oxides cause cough, hyperpnea, and dyspnea. The deleterious effects to the pulmonary system include pulmonary edema, pneumonitis, bronchitis, bronchiolitis, emphysema, and possibly methemoglobinemia. Nitrogen oxides also cause chest congestion and circulatory collapse. The liquid nitrogen oxides cause severe eye burns after brief contact. High concentrations of the gas cause irritation and, after prolonged exposure, may cause clouding of the eye surface and blindness.[29,30] Low levels of nitrogen oxides in the air causes irritation to the eyes, nose, throat, and lungs, possibly causing cough, shortness of breath, fatigue, and nausea. Exposure to low levels can also result in fluid buildup in the lungs 1 or 2 days after exposure. Breathing high levels of nitrogen oxides can cause rapid burning, spasms, swelling of tissues in the throat and upper respiratory tract, reduced oxygenation of body tissues, buildup of fluid in the lungs, and death.

Nitrogen oxides and cancer: The DHHS, IARC, and U.S. EPA have not classified nitrogen oxides as a potential human carcinogen.[29,30]

Exposure limits: The U.S. EPA has set a limit of 0.053 ppm of nitrogen dioxide in ambient air, while OSHA has set a limit of 25 ppm of nitric oxide

in workplace air during an 8-hour workday (TWA). The IDLH level set by NIOSH for nitric oxide is 100 ppm and for nitrogen dioxide is 20 ppm.[29,30]

Ozone

Molecular formula: O_3

Use and exposure: Ozone is a pale blue gas composed of three atoms of oxygen that exists in the stratosphere of our atmosphere (6-30 miles above the Earth's surface) as the ozone layer. Ozone is an unstable molecule. High-energy radiation from the sun not only creates it, but also breaks it down again. It is formed from atmospheric oxygen by the absorption of ultraviolet (UV) radiation of the right energy. The sun emits radiations of varying wavelengths known as the electromagnetic spectrum. Ultraviolet radiation is one form of radiant energy coming from the sun. Ozone is harmless when it is in low concentrations; it acts as a shield to protect the Earth's surface by absorbing harmful ultraviolet radiation. If this ozone becomes depleted, then more UV rays will reach the Earth. Exposure to higher amounts of UV radiation could have serious impacts on human beings, animals, and plants. Near ground level, ozone is formed when pollutants emitted by cars, power plants, industrial boilers, refineries, chemical plants, and other sources react chemically in the presence of sunlight. Ozone pollution is a concern during the summer months when the weather conditions needed to form ground-level ozone—lots of sun and hot temperatures—normally occur. The protective ozone layer is damaged when the CFCs release chlorine or bromine when they break down.

The gas itself is a respiratory irritant. It penetrates into small airways and the lung and causes pulmonary edema at high concentrations. Other illnesses include lung fibrosis and reduction of lung function. It precipitates asthma attacks. It is constantly created and destroyed. The presence of chlorofluorocarbons generates reactive chlorine radicals that constantly destroy ozone. Ozone can be good or bad for human health depending on its location in the atmosphere. Ozone at ground level is a harmful air pollutant. Extensive use of man-made chemicals often referred to as ozone-depleting substances (ODSs)—for instance, chlorofluorocarbons (CFCs), hydrochlorofluorocarbons (HCFCs), halons, methyl bromide, carbon tetrachloride, and methyl chloroform—have affected the protective ozone layer. Reports have indicated that ozone depletion has caused increased amounts of UV radiation to reach the Earth, leading to more and more human health disorders—for instance, skin cancer (melanoma), cataracts, and impaired immune systems. Since 1990, the risk of developing melanoma has more than doubled.[31]

Toxicity and health effects: The thinning of the ozone layer may lead to an increase of skin cancer and eye cataracts. Ozone interferes with and reduces the lung function in humans. Breathing ozone can trigger a variety of health problems, including chest pain, coughing, throat irritation, and congestion. It can worsen bronchitis, emphysema, and asthma. "Bad" ozone also can reduce lung function and inflame the linings of the lungs. Repeated

exposure may permanently scar lung tissue. Also, individuals with asthmatic problems are more severely affected by the reduced lung function and irritation that ozone causes in the respiratory system. Prolonged exposure to ozone causes chronic lung diseases like emphysema and bronchitis, and the immune system becomes too weak to fight off bacterial infections in the respiratory system.[31]

Particulate matter (PM)

Particulate matter includes fine solids suspended in the air in the form of smoke, dust, and vapors, which can remain suspended for extended periods. In addition to reducing visibility and soiling clothing, microscopic particles from the air can be breathed in and lodged in lung tissue, causing increased respiratory disease and lung damage. Particulates are also the main source of haze, which reduces visibility. Particulates are produced by many sources, including cars, trucks, and buses burning diesel fuels and other fossil fuels; the preparation and application of fertilizers and pesticides; road construction; industrial processes such as steel making; mining; agricultural burning; and the operation of fireplaces and wood stoves.

Phosphine (CAS no. 7803-51-2)

Molecular formula: PH_3

Synonyms and trade names: Celphos, Delicia, Detia, hydrogen phosphide, phosphoretted hydrogen, phosphorus trihydride

Use and exposure: Phosphine is a colorless, flammable, highly toxic gas with a fishy or garlic-like odor. It is slightly heavier than air. Pure phosphine is odorless, extremely flammable, and highly reactive with air, copper, and copper-containing alloys. Phosphine is largely used as a fumigant during the storage of agricultural products such as nuts, seeds, grains, coffee, and tobacco. Workers employed as fumigators, pest-control operators, transport workers, and others involved in the production or use of phosphine and metal phosphides (welding, metallurgy, semiconductors) may be exposed to higher levels of phosphine. Phosphine spontaneously ignites in air or even explodes when mixed with oxygen, oxidizers, halogenated hydrocarbons, or aluminum and copper. It is for this reason that extreme care must be taken whenever working with or around phosphine[32,32a] (Table 7.6).

Toxicity and health effects: Phosphine acts on the CNS and lungs, leading to pulmonary edema. Symptoms of phosphine poisoning are nonspecific and include but are not limited to irritation of the respiratory tract, headaches, dizziness, faintness, abdominal pain, nausea, vomiting, and tightness in the chest. Severe phosphine poisoning can cause convulsions; damage to the lungs, heart, liver, and kidney, and death. Long-lasting effects of single-dose exposure are unlikely; most symptoms clear within a month. Long-term exposure to phosphine, although unlikely to occur, can cause bronchitis; gastrointestinal, visual, speech, and motor problems; toothache; swelling of the jaw; anemia; and spontaneous fractures.[32,32a,32b]

TABLE 7.6
Toxicity and Health Effects of Phosphine

Concentration (ppm)	Symptoms/Effects
2000	Lethal effect after 1–3 minutes
500	Fatal
35	Diarrhea, nausea, respiratory disorders
1	Short-term exposure limit (OSHA)
0.3	Permissible exposure limit (OSHA)

Source: Agency for Toxic Substances and Disease Registry (ATSDR). 2007.

Sulfur dioxide (CAS no. 7446-09-5)

Molecular formula: SO_2

Use and exposure: Sulfur dioxide is a colorless gas with a pungent odor. It is a liquid when under pressure, and it dissolves in water very easily. It results from burning of coal and oil at power plants or from copper smelting. Volcanic eruptions are the major sources of sulfur dioxide release in the living environment. Industrial workers and the general public become exposed to sulfur dioxide while working in the manufacture of sulfuric acid, paper, food preservatives, or fertilizers or living near heavily industrialized activities where sulfur dioxide occurs. Prolonged exposure to sulfur dioxide causes a burning sensation to the nose and throat, breathing difficulties, and severe airway obstructions.[33]

Toxicity and health effects: Laboratory animals exposed to high concentrations of sulfur dioxide showed decreased respiration, inflammation of the airways, and destruction of areas of the lung. It aggravates heart and lung disease symptoms, obstructs breathing—especially in combination with other pollutants—and increases incidence of acute respiratory diseases, including coughs and colds, asthma, bronchitis, and emphysema. In workers, lung function changes were seen when they were exposed to low levels of sulfur dioxide for 20 years or more. Asthmatics are found to be more sensitive to the respiratory effects of low concentrations of sulfur dioxide.[33]

Sulfur dioxide and cancer: There is no literature about the carcinogenicity of sulfur dioxide in humans. The IARC has classified sulfur dioxide as group 3—not classifiable as to human carcinogenicity.[33]

Exposure limits: The U.S. EPA has set a limit of 0.03 ppm for sulfur dioxide for long-term exposure. OSHA has set a limit of 2 ppm over an 8-hour workday (TWA).[33]

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8 Chemical Substances and Carcinogenicity

8.1 INTRODUCTION

Progress in a global economy is now primarily based on improved technology and its distribution to extensive human activities. The global market and production, with its easy movement and transportation, a less expensive workforce, and less stringent regulations, have been found to be closely interrelated activities. With these kinds of situations, human exposure to hazardous chemical substances becomes more evident. Uncontrolled, irrational transboundary movement of hazardous chemical substances and waste disposal have caused health hazards in communities. Occupational and environmental exposure to many chemical substances, industrial solvents, metals, plastics, and asbestos, such as in mining; shipwrecks, and production and use of pesticides in agriculture and horticulture, and many others, is known to have effects on health. To contain any kind of untoward incident at the workplace or in the community, proper management of hazardous chemical substances is a must. To achieve this, workers, managers, regulatory agencies and the public at large require ready information about the good and bad aspects of chemical substances so that they have proper knowledge.

The following pages provide, in brief, lists of known carcinogens, suspected carcinogens, and probable carcinogens. Proper use and careful management of chemical substances protect human health and safety and the living environment.

8.2 CARCINOGENS AND CARCINOGENESIS

Workers come in contact with a large number of chemical substances in work areas, as does the general public. The commonly found chemical carcinogens are grouped under (1) polycyclic aromatic hydrocarbons (PAHs), (2) nitroso compounds, (3) halogenated hydrocarbons (solvents; e.g., carbon tetrachloride, chloroform, trichloroethylene, and methylene chloride), (4) inorganic metals and minerals (beryllium, cadmium, nickel, cobalt, chromium, asbestos and arsenic), and (5) naturally occurring chemical substances (aflatoxins).

Halogenated hydrocarbons. Several of these compounds are commonly used as solvents. Examples include carbon tetrachloride, chloroform, trichloroethylene, and methylene chloride.

Inorganic metals and minerals. Several carcinogens are known among metals or their salts. Examples of these include beryllium, cadmium, nickel,

cobalt, and chromium. Only two minerals are known to cause cancer: asbestos and arsenic.

Naturally occurring. Several naturally occurring carcinogens are known. Among these is aflatoxin, probably the most potent of all carcinogens. Aflatoxins are produced by molds that grow on peanuts and corn. Other naturally occurring carcinogens are present in sassafras and chili peppers.

Cancer, in fact, has afflicted humans around the world and throughout recorded history. The origin of the word *cancer* is credited to the Greek physician Hippocrates (460–370 BC), considered the "father of medicine." Hippocrates used the terms *carcinos* and *carcinoma* to describe non-ulcer-forming and ulcer-forming tumors. Bernardino Ramazzini, an Italian doctor, reported in 1713 the high incidence of breast cancer in nuns. Percival Pott of Saint Bartholomew's Hospital in London described in 1775 an occupational cancer in chimney sweeps, cancer of the scrotum, caused by soot collection under the scrotum of workers.

The chemical substances that cause cancer are called *carcinogens* and the process of cancer development is known as *carcinogenesis.* Cancer occurs when cells become abnormal and keep dividing and multiplying with more and more cells, without control or order. Over the years, several chemical substances in use have been categorized as carcinogens or cancer-producing chemical substances. It is heartening to know that, to date, most known occupational carcinogens are either banned or well regulated within the respective countries of the world.

Prolonged periods of occupational exposure to toxic chemical substances are known to increase the risk of developing cancer either by causing mutations in DNA or by various "epigenetic" mechanisms of promotion (those not involving damage to DNA), including increased cell proliferation. Most occupational carcinogens discovered to date are mutagens and therefore appear to be cancer initiators. It is important to learn from the experiences of industrialized countries and prevent the introduction of newer chemical substances and the production processes that have been found to be hazardous to human health.

It is important to remember always the statement of Paracelsus in the use and management of chemical substances: "All chemical substances are poisons and there is none which is not a poison and only the right dose differentiates a poison and a remedy." Carcinogens do not cause cancer in every case. Substances classified as carcinogens may have different levels of cancer-causing potential. Some may cause cancer only after prolonged, high levels of exposure. For any particular person, the risk of developing cancer depends on many factors, including the length and intensity of exposure to the carcinogen and the person's genetic makeup.[1–5]

8.3 CLASSIFICATION OF CARCINOGENS

The most widely used system for classifying chemical substances as carcinogens comes from the International Agency for Research on Cancer (IARC),[3] which is a part of the World Health Organization (WHO). During the past 30 years, the IARC has evaluated more than 900 chemical substances to identify their cancer-causing potential. The confirmed and suspected carcinogens have been categorized as

- group 1: carcinogenic to humans;
- group 2A: probably carcinogenic to humans;
- group 2B: possibly carcinogenic to humans;
- group 3: unclassifiable as to carcinogenicity in humans; and
- group 4: probably not carcinogenic to humans.

The complete list of agents and chemical substances evaluated by the IARC and their classifications is available in IARC *Monographs,* volumes 1–98.[3,4,6]

The National Toxicology Program (NTP) has listed chemical substances for carcinogenicity under two categories:

- *Known to be a human carcinogen.* There is sufficient evidence of carcinogenicity from studies in humans.
- *Reasonably anticipated to be a human carcinogen.* There is limited evidence of carcinogenicity from studies in humans, but sufficient evidence of carcinogenicity from studies in experimental animals.

A large number of chemical substances are included in group 1 as carcinogenic to humans. Similarly, the IARC has included many other chemical substances under group 2, meaning that they are probably carcinogenic to humans. More than 900 agents have been evaluated since 1971 and about 400 chemical substances have been identified as carcinogenic or potentially carcinogenic to humans. Over half of the agents classified by the IARC as known, probable, or possible human carcinogens are primarily occupational.

The types of cancers and the chemical substances closely associated with them are well known. For instance, exposure to asbestos, radon, inorganic arsenic, chromium, and *bis*-chloromethyl ether cause lung cancer; vinyl chloride causes liver cancer and benzene causes leukemia. Some of the occupations, although small in number, are closely associated with human cancer—for instance, increased risk of nasal cancer in wood workers, bladder cancer among dye manufacturers, and lung and nasal cancers among nickel refiners. Several types of mineral fibers, such as asbestos, are known to pose a carcinogenic hazard to humans. Also, industrial workers exposed to polycyclic aromatic hydrocarbons formed from the combustion of fossil fuels are prone to increased risk of lung, skin, and bladder cancer. These substances are relatively ubiquitous, but exposures are particularly high among workers in aluminum smelters, gas works, and coke ovens as well as in jobs involving use of tar and other coal derivatives.

Occupational carcinogens hold a special place among the different classes of human carcinogens. The occupational environment has been the most fruitful one for investigating the etiology and pathogenesis of human cancer. It is important to discover occupational carcinogens because most occupational exposures find their way into the general environment, sometimes at higher concentrations than in the workplace. Industrial workers are at excess risk of cancer, as well documented: scrotal cancer among chimney sweeps caused by polyaromatic hydrocarbons (PAHs) in soot,[3] and lung cancer among asbestos miners. In some instances, the group experienced excess risk but the causative agent was unknown or at least unproven, as in

TABLE 8.1
Cancer-Causing Chemical Substances and Occupation Affected

Arsenic compounds	Glass, metal, and pesticide manufacturing
Asbestos	Insulation and textiles industries
Benzene	Petroleum industry
Benzidine and cadmium dyes	Textile industry
Beryllium and compounds	Aerospace and metal industries
Chromium pigments	Paint and paint products industries
Fertilizers and pesticides	Agriculture, pest control
Organic solvents	Industries associated with rubber, textiles Paint, printing, and industrial cleaning
Metal compounds, cadmium, nickel, uranium, etc.	Metal and mining industries
Tobacco	Tobacco industry

Source: Modified from different sources.

the cases of lung cancer among painters and bladder cancer among workers in the aluminum industry. The strength of the evidence for an association can vary. There is not much data on human cancer, although hundreds of chemical substances have been shown to be carcinogenic in species of laboratory animals.

The overall evaluation of human carcinogenicity is based on the epidemiologic and animal evidence of carcinogenicity, plus any other relevant evidence on genotoxicity, mutagenicity, metabolism, or mechanisms. The epidemiologic evidence, wherever available, has been given greatest weight. Direct evidence from laboratory animal data is next in importance, with increasing attention paid to mechanistic evidence that can inform the relevance of the animal evidence for human risk assessment. Categories for the overall evaluation and how they are derived from human, animal, and other evidence are shown in Tables 8.1 and 8.2.

Generally, workplace exposures to chemical substances are considered to be at higher levels than for public exposures. Material safety data sheets (MSDSs) should always contain an indication of carcinogenic potential. The Report on Carcinogens (RoC) is an informational scientific and public health document first ordered by the U.S. Congress in 1978. This report has identified agents, substances, mixtures, or exposure circumstances that may pose a hazard to human health by virtue of their carcinogenicity.

8.4 CHEMICAL SUBSTANCES, OCCUPATIONS, AND CANCER

It has been reported recently that the existing systems of classification of carcinogens are a matter of worldwide discussion. However, there is agreement that any classification should distinguish between genotoxic and nongenotoxic chemical substances. For details refer to the literature.[7] The close association between prolonged use of

TABLE 8.2
Organs and the Carcinogens Suspected to be Associated with Them

Bladder cancer	Benzidine, tetrachloroethylene, cyclophosphamide, 4-aminodiphenyl, tobacco smoking, chloraphazine, tetrachloroethylene
Kidney cancer	Coke oven emissions, zinc chromate, tetrachloroethylene
Liver cancer	Vinyl chloride, aflatoxin, alcoholic drinks
Lung cancer	Arsenic, asbestos, benzo(*a*)pyrene, *bis*(chloromethyl)ether, chromium, nickel subsulfide, zinc chromate, tobacco, mustard gas, uranium, acrylonitrile, beryllium, cadmium, 1,2-dibromo-3-chloropropane, polyaromatic hydrocarbons (PAHs)
Mouth cancer	Alcoholic drinks, tobacco smoking
Pharynx, larynx, esophagus cancer	Chewing (mouth only), mustard gas
Prostate cancer	Cadmium
Skin cancer	Arsenic, benzo(*a*)pyrene, polyaromatic hydrocarbons, tetrachloroethylene

Sources: American Cancer Society. 2001. *Cancer Facts and Figures, 2001.* New York: American Cancer Society; American Cancer Society. 2006. *Known and Probable Carcinogens* New York: American Cancer Society; Waldron, A. 1983. A brief history of scrotal cancer, *British Journal of Industrial Medicine*, 40:390–401.

chemical substances in high concentrations in different occupations leading to cancer has become evident (Tables 8.1 and 8.2).

The toxicological effects of a variety of chemical substances vis-à-vis their carcinogenicity potentials to animals and humans have undergone progressive changes during the early years. The evidence is the classification and categorization of carcinogenicity in laboratory animals and humans (epidemiological studies). As has been stated, the U.S. Environmental Protection Agency (U.S. EPA) intends to revise the cancer guidelines when substantial changes become necessary; as more information about carcinogenesis develops, the need may also arise to make appropriate changes in risk assessment guidance. Thus, the terms of definitions have undergone modifications. One of the first classifications of carcinogenicity was made during 1986. After a decade the classification underwent a slight change in 1996. Further changes were made in the draft classification of 1999 followed by that in 2007. These updates of the guidelines over the years have become important for understanding the manner of behavior of chemical substances that cause cancer in humans.

The classification scheme for cancer was first introduced in 1986. The U.S. EPA issued updated guidance, which included a letter system (A–E) for designating degree of carcinogenic potential. In the guidelines, hazard identification and the weight-of-evidence process focused on finding tumors in animals and humans. The carcinogenic potential of agents to humans was characterized by a six-category alphanumeric classification system as A, B1, B2, C, D, and E.

The U.S. EPA has categorized chemical substances into six groups of confirmed or suspected carcinogens:

- ***Group A: human carcinogen.*** This group includes agents only with "sufficient evidence" from epidemiological studies to support a causal association between exposure to the agents and cancer (Appendix 8.1).
- ***Group B: probable human carcinogen.*** This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiological studies is limited as well as agents for which the weight of evidence of carcinogenicity based on animal studies is sufficient. The group is divided into two subgroups:

  Group B1 includes agents with limited evidence of carcinogenicity from epidemiological studies (Appendix 8.2).

  Group B2 includes agents with sufficient evidence from animal studies and inadequate evidence or no data from epidemiologic studies.
- ***Group C: possible human carcinogen.*** This group includes agents with limited evidence of carcinogenicity in animals and absence of data in humans.
- ***Group D: not classifiable as to human carcinogenicity.*** This group includes agents with inadequate human and animal evidence of carcinogenicity or no data available in animals and/or humans.
- ***Group E: evidence of noncarcinogenicity for humans.*** This group includes agents with no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiological and animal studies (Appendix 8.3).

Subsequently, in 1996 the U.S. EPA released "Proposed Guidelines for Carcinogen Risk Assessment," which used descriptive phrases rather than the alphanumeric classification to classify carcinogenic potential. In the 1996 classification structure, increased emphasis was placed on discussing characterization of hazard, dose–response, and exposure assessments. To reduce the uncertainty in describing the likelihood of harm, the hazard and weight-of-evidence process embraced an analysis of all relevant biological information and emphasized understanding the agent's mode of action in producing tumors.

Advanced studies and research on carcinogens and carcinogenicity have progressed significantly over the years. In 1999 the U.S. EPA issued draft guidelines with greater emphasis on risk characterization, discussions for hazard, dose–response assessment, exposure assessment, and the use of mode of action of the test chemical substance in the assessment of carcinogenic potential, besides guidelines to consider risks to children. Thus, in 2005 the U.S. EPA recommended the classification of the "Guidelines for Carcinogen Risk Assessment," keeping in view the weight-of-evidence narrative in the cancer risk assessment. These guidelines represent the culmination of a long development process, replacing the original cancer risk assessment guidelines of 1986 and 1999. The descriptor indicates a strong evidence of human carcinogenicity with different combinations of evidence. The descriptor becomes appropriate with convincing evidence of epidemiology and the causal association between human exposure and cancer. The conditions thus include:

- There is strong evidence of an association between human exposure and either cancer or the key precursor events of the agent's mode of action, but not enough for a causal association.
- There is extensive evidence of carcinogenicity in animals.
- The modes of carcinogenic action and associated key precursor events have been identified in animals.
- There is strong evidence that the key precursor events that precede the cancer response in animals are anticipated to occur in humans and progress to tumors, based on available biological information.

Multiple descriptors. More than one descriptor can be used when an agent's effects differ by dose or exposure route. For example, an agent or the chemical substance may be "carcinogenic to humans" by one exposure route, but "not likely to be carcinogenic" using a route by which it is not absorbed. Also, an agent or the chemical substance could be likely to be carcinogenic above a specified dose, but not likely to be carcinogenic below that dose because a key event in tumor formation does not occur below that dose. Thus, the route of exposure and the concentration of the candidate chemical substance modulate the induction of carcinogenesis.

8.5 CHILDREN AND PESTICIDE-INDUCED CANCER

Children are exposed to potential carcinogenic pesticides in various areas of activity, such as in schools, on playgrounds and lawns, through food and contaminated drinking water, and through parental exposure to pesticides during the child's gestation and the preconception stage. Case reports and case control studies have indicated that pesticides have caused malignancies that include but are not limited to leukemia, neuroblastoma, soft-tissue sarcoma, lymphoma, and cancers of the brain, colon and rectum, and testes. The studies suggest that children are more sensitive to the carcinogenic effects of pesticides than adults and, once again, demand the need for knowledge about the proper use of chemicals.

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APPENDIX 8.1

Known Human Carcinogens

Aflatoxins	Estrogens, steroidal
Alcoholic beverage consumption	Ethylene oxide
4-Aminobiphenyl	Hepatitis B virus
Analgesic mixtures containing phenacetin	Hepatitis C virus
Arsenic compounds, inorganic	Human papilloma viruses: some genital-mucosal types
Asbestos	Melphalan
Azathioprine	Methoxsalen with ultraviolet A therapy (PUVA)
Benzene	Mineral oils (untreated and mildly treated)
Benzidine	Mustard gas
Beryllium and beryllium compounds	2-Naphthylamine
1,3-Butadiene	Nickel compounds
1,4-Butanediol dimethylsulfonate (busulfan)	Oral tobacco products
Cadmium and cadmium compounds	Silica
Chlorambucil	Crystalline (respirable size)
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (MeCCNU)	Solar radiation
bis(Chloromethyl) ether and technical-grade chloromethyl methyl ether	Soots
Chromium hexavalent compounds	Strong inorganic acid mists containing sulfuric acid
Coal tar pitches	Tamoxifen
Coal tars	2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) "Dioxin"
Coke oven emissions	Thiotepa
Cyclophosphamide	Thorium dioxide
Cyclosporin A (ciclosporin)	Vinyl chloride
Diethylstilbestrol (DES)	Ultraviolet radiation
Dyes metabolized to benzidine	Broad spectrum UV radiation
Environmental tobacco smoke	Wood dust
Erionite	X-radiation and gamma radiation

Source: U.S. Department of Health and Human Services. 2005. Public Health Service, National Toxicology Program. *Report on Carcinogens,* 11th ed. (updated 2006).

APPENDIX 8.2

Group B2—Probable Human Carcinogens

Acetaldehyde	Dieldrin
Acetochlor	Epichlorohydrin
Acifluorfen, sodium	Ethylene thiourea (ETU)
Acrylamide	Folpet
Aldrin	Furmecyclox (Xyligen B)
Amitrole	Haloxyfop-methyl (Verdict)
Aniline	Heptachlor
Aramite	Heptachlor epoxide
Azobenzene	Hexachlorobenzene (HCB)
Propoxur	Hexachlorocyclohexane
bis(Chloroethyl)ether (BCEE)	Lactofen
Cacodylic acid	MGK Repellent 326
Captafol	Mancozeb
Captan	Maneb
Carbon tetrachloride	Metam sodium
Chlordane	Orthophenylphenol and Na salt
Chlordimeform	Oxythioquinox (Morestan)
Chloroaniline, p-	Pentachlorophenol
Chloroform	Polychlorinated biphenyls
Cyproconazole	Procymidone (Sumilex)
DDD	Pronamide (Kerb)
DDE	Propargite (Omite)
DDT	Propylene oxide
Daminozide (Alar)	Terrazole
Di(2-ethylhexyl)phthalate	Thiodicarb (Larvin)
Dibromochloropropane (DBCP)	Toxaphene (Campechlor)
Dibromoethane, 1,2-	Trichlorophenol, 2,4,6-
Dichloroethane, 1,2-	Triphenyltin hydroxide
Dichloromethane	UDMH
Dichloropropene	

Source: U.S. Environmental Protection Agency. 2007. *Pesticides: Health and Safety Evaluation of Pesticides for Carcinogenic Potential.* Washington, D.C.: U.S. EPA.

APPENDIX 8.3

Group E—Evidence of Noncarcinogenicity for Humans

Avermectin B1	Fonofos (Dyfonate)
Bardac 22	Formetanate hydrochloride
Bentazon (Basagran)	Glyphosate
Borax	Glyphosate trimesium
Boric acid	Imazapyr (Arsenal)
Boron	Imidacloprid
Bromuconazole	Maleic hydrazide
Bronopol	Mepiquat chloride
Butylate (Sutan)	Metalaxyl
Cadusafos	Methamidophos
Chlorpropham (CIPC)	Methomyl
Chlorpyrifos	Myclobutanil
Coumaphos	Naled (Dibrom)
Cyromazine	Nicosulfuron
Difenzoquat methyl sulfate	Oxamyl
Diflubenzuron	Paraquat dichloride
Dinocap (Karathane)	Phorate (Thimet)
Diquat dibromide	Phostebupirim
Disulfoton (Disyston)	Picloram (+ salts)
Dithiopyr	Profenofos
Esfenvalerate	Prometryn
Ethion	Pyridaben
Fenamiphos (Nemacur)	Pyriproxyfen
Fenarimol	Rimsulfuron
Fenbutatin oxide (Vendex)	Rotenone
Fenitrothion (Sumithion)	Sulfentrazone
Fenpropathrin	Sulfosate
Fenthion	Sulprofos
Fenvalerate (Pydrin)	Tebufenozide
Flumetsulam	Terbacil
Flumiclorac pentyl	Terbufos
Fluridone	Triasulfuron
Flutolanil	Triflumizole

APPENDIX 8.4

Classification of Benign and Malignant Tumors in Mammals

Tissue	Benign Tumor	Malignant Tumor
	Connective Tissue	
Adult fibrous	Fibroma	Fibrosarcoma
Bone	Osteoma	Osteosarcoma
Cartilage	Chondroma	Chondrosarcoma
Embryonic fibrous	Myxoma	Myxosarcoma
Fat	Lipoma	Liposarcoma
	Endothelium	
Blood vessels	Hemangioma	Hemangiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
	Epithelium	
Glandular	Adenoma	Adenocarcinoma
Squamous	Squamous cell papilloma	Squamous cell carcinoma
Transitional	Transitional cell papilloma	Transitional cell carcinoma
	Hematopoietic	
Bone marrow	Not recognized	Leukemia
	Lymphoreticular	
Lymph nodes	Not recognized	Lymphosarcoma
	Muscle	
Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
	Nervous System	
Glial cells	Glioma	Malignant glioma Glioblastoma
Nerve sheath	Neurilemmoma	Neurogenic sarcoma

9 Chemical Substances and Neurotoxicity

9.1 INTRODUCTION

Industrial development and use of different chemical substances are closely related with human activities. Obviously, large numbers of workers are associated with equally large numbers of industry around the world. Workers and the general public have been using, handling, and transporting many chemical substances over the decades. The list of industrial chemical substances is huge and linked with many implications to human health. Chemicals have become an indispensable part of human life—sustaining activities and development, preventing and controlling many diseases, and increasing agricultural productivity. Despite their benefits, chemicals may, especially when misused, cause adverse effects on human health. The nervous system has been shown to be particularly vulnerable to certain chemical exposures, and there is increasing global concern about the potential health effects from exposure to neurotoxic chemicals.

It has been well proved now that exposure to chemical substances causes adverse effects on the nervous system by inducing neurotoxicity. Prolonged exposure to chemical substances, as is common in workplaces, may lead to neurological disorders and damage the central nervous system (CNS). In fact, neurotoxicity disturbs the normal activity of the nervous system and eventually disrupts or even kills neurons, the key cells that are responsible for the transmittance of signals in the brain and other parts of the nervous system. The symptoms of neurotoxicity may appear immediately after an exposure to toxic chemical substances or may be delayed. The poisoned worker can show several symptoms that include but are not limited to fatigue; limb weakness; numbness; loss of memory and vision; headache; cognitive and behavioral problems such as confusion, irritability, behavioral changes, degenerative diseases of the brain, and encephalopathy; peripheral nervous system problems; paralysis; tingling in the limbs (paresthesia); loss of coordination; convulsion; and fatal injury. The toxicological data on the neurotoxic potential of a large number of chemical substances in daily use has not been adequately assessed. The need for a multidisciplinary approach to neurotoxicity risk assessment has been recognized by a number of international and scientific organizations and national governments.[1–3]

A large number of industrial chemicals are hindering children's development, lowering IQ scores, and triggering attention and behavior disorders. The National Institute of Occupational Safety and Health (NIOSH) studies have revealed a large number of chemical substances that cause damage to the human nervous system. The *Lancet* identified 201 chemicals with the ability to cause neurological effects in humans. Many chemical substances with neurotoxic potential have not been

thoroughly tested for adverse health effects. The causative factor for the induction of neurotoxicity may be a chemical, biological, or physical agent.[4–8] Neurotoxicity can occur any time during the life cycle of the individual, from conception to senescence. The manifestations of neurotoxicity also change with the age advancement and health conditions of the individual. With the knowledge and experience available in the literature about the developmental effects of neurotoxicants on infants and children, the societal responsibility to protect children from different neurological disorders becomes more important and urgent.[9]

9.2 NEUROTOXICITY

The term neurotoxicity refers to the capability of a chemical substance to cause adverse effects in the CNS, peripheral nerves, or sensory organs of animals and humans. A chemical substance is considered neurotoxic if it is capable of inducing a consistent pattern of neural dysfunction or change in the chemistry or structure of the nervous system. Short-term or low-dose exposure of animals and humans to a neurotoxic chemical substance may result in subjective symptoms such as headache and dizziness, but the effect usually is reversible. With increasing dose of a chemical substance, along with the duration, the neurological changes become severe and eventually result in irreversible morphological changes[10] (Table 9.1, Appendix 9.1).

Besides causing other adverse health effects, prolonged periods of exposure to high concentrations of different chemical substances are known to induce neurotoxicity among workers. The symptoms of neurotoxicity become visible with the

TABLE 9.1
Development of Neurotoxicity

Level	
6	Morphological changes include cell death and axonopathy as well as subcellular morphological changes
5	Neurological changes include abnormal findings in neurological examinations on single individuals
4	Physiological and behavioral changes include experimental findings on groups of animals or humans such as changes in evoked potentials and EEG, or changes in psychological and behavioral tests
3	Biochemical changes include evaluations and analysis of biochemical parameters (e.g., transmitter level, GFA-protein content [glial fibrillary acidic protein] or enzyme activities)
2	Subjective symptoms • Irreversible changes: no evidence of abnormality on neurological, psychological, or other medical examination • Reversible changes: no evidence of abnormality on neurological, psychological, or other medical examination

Sources: Arlin-Sorberg, P. 1992. *Solvent Neurotoxicity*. Boca Raton, FL: CRC Press; Simonsen, L., Midtgard, U., Lund, S. P., and Hass, U. 1995. *Occupational Neurotoxicity: Evaluation of Neurotoxicity Data for Selected Chemicals*. Copenhagen: Nordic Council of Ministers.

TABLE 9.2
Symptoms of Neurotoxicity

General effects	Appetite loss, headache, depression, drowsiness, thirst
Sensory effects	Disturbed vision, ringing in the ears, tinnitus, loss of equilibrium, dizziness, pain, tactile disorders, tingling, numbness, increased coldness
Motor effects	Weakness, convulsions, tremors, paresis, twitching, lack of coordination, gait change, reflex abnormalities
Cognitive effects	Fatigue, memory problems, confusion, learning and speech impairments, dullness, mental slowing, delirium, hallucinations
Personality effects	Sleep disturbances, depression, anxiety, excitability, tension, increased irritability, restlessness, delirium, nervousness

Sources: Anger, W. K. 1986. In *Neurobehavioral toxicology*, ed. Z. Ammau, 331–347. Baltimore, MD: Johns Hopkins University Press; Anger, W. K. 1984. *Neurobehavioral Toxicology and Teratology* 6: 147–153.

increased period of exposure[10,11] (Table 9.2). The neurotoxicant syndromes caused by a large number of chemical substances have adversely affected the nervous tissue and become one of the leading occupational disorders among workers. Neurotoxic chemical substances interfere with the normal function of the neurons and the nervous tissue and lead to irreversible cellular damage and cell death. Thus, the nervous system is delicate and vulnerable to chemical injuries. Since neurotoxic chemicals cross the blood–brain barrier with much ease and the architectural features of nerve cells, with their long processes, provide a vast surface area for chemical attack and chemical interference, the exposed worker suffers an irreparable neural damage with profound consequences.

The following pages discuss in brief these aspects so that workers can become fully aware of the dangers of neurotoxic chemicals and understand the importance of good chemical management in and around the workplace. The serious and adverse health effects observed among very large groups of workers and children in different countries of the world and the risks to brain development caused by neurotoxic substances have aroused national and international attention and increasing public concern has become very evident.

Neurotoxicity generally develops as a result of acute and prolonged exposure to toxic substances. The degree of severity of neurotoxicity depends on the nature of the chemical substance, the dose, the duration or period of exposure, and the possible behavior traits of the exposed worker. The neurotoxic chemicals and heavy and organic metals attack the immune system. They attack and destroy the CNS and the peripheral nervous system (PNS). The symptoms include but are not limited to problems with memory, dizziness, lightheadedness, concentration, emotion, personality changes, sleep disturbances, including sleep apnea and insomnia; extreme tiredness and chronic fatigue symptoms; headaches; pain and/or numbness in the arms, hands, legs, or feet; loss of learning ability, motivation, and interest in daily activities;

attentional complaints; impaired judgment; hearing problems, including hearing loss and tinnitus (in some cases); visual disturbances; abnormal neuropsychological testing; and often (but not always) findings of cortical atrophy as demonstrated by CAT scans. Reports have also indicated frequent nosebleeds for no apparent reason; difficulty recognizing familiar faces; breathing difficulties; pains in the chest; recurring pneumonia; head, arm, hand, and leg shaking; and many more.

Any kind of brief exposure to low concentrations of toxic chemical substances is known to result in the development of subjective symptoms—for instance, headache and dizziness—that usually return to normal and are reversible. In contrast, prolonged periods of exposure to high concentrations of neurotoxic chemical substances trigger irreversible neurological and morphological changes among workers.

9.3 INDUSTRIAL CHEMICALS AND NEUROTOXICITY

Chemical substances and their applications in industry are common and the exposure of workers to them is known. Several chemical substances have been suspected as neurotoxicants, but the information on many of them is still sketchy.[12–14] Neurotoxic pesticides and solvents are common sources of exposure in the workplace. The chemical substances include but are not limited to adhesives, agent orange, aspartame, ammonia, arsenic, benzene, carbonless copy paper, carbon monoxide, carpet cleaning agents, CCA (copper-chromium-arsenate), chlorine, combustion products, dioxin, drugs, formaldehyde, gamma butyrolactone, gasoline, glues, heavy metals, herbicides, indoor air pollution, lead, lithium, MDI (methyl diisocyanate), MEK (methyl-ethyl-ketone), manganese, carbon dioxide, hydrogen sulfide, cyanide, nitrous oxide, mercury, metals, methylene chloride, mixed toxic waste, municipal sludge, mycotoxins, naphthalene, *n*-hexane, oil- and gas-field emissions, opiates, organic metals, paint, paint remover, pentachlorophenol, pesticides, phenolic resins, polychlorinated biphenyl (PCB), drugs, radiation injuries, solvents, styrene, synthetic carpets, TDI (toluene diisocyanate), toluene, toxic waste, trichloroethane, trichloroethylene, welding fumes, wood preservatives, xylene, and many more. It is known that organic mercury compounds are potent neurotoxic substances and have caused a number of human poisonings, with symptoms and signs of vision, speech and coordination impairment.[15–17] Recent reports have documented the possible adverse effects of chemical substances on the nervous systems of animals and humans.[18–22]

Lead has been recognized as a poison for millennia and has been the focus of public health regulation in much of the developed world for the better part of the past century. Lead exposure continues to be a major public health problem, particularly in urban areas in the United States and in Third World nations.[23] The neurotoxicity of manganese has been well known since the last century. The adverse effect of "manganism" is characterized by extrapyramidal dysfunction and neuropsychiatric symptomatology. Since then this syndrome has been observed in hundreds of cases among miners and industrial workers throughout the world who were exposed to high levels of manganese.

Acute human poisoning from organophosphorous insecticides can cause muscle weakness, paralysis, disorientation, convulsions, and death. Of particular concern are the delayed neurotoxic effects of some of the organophosphorous insecticides. Some of these compounds cause degeneration of nerve processes in the limbs, leading to changes in sensation, muscular weakness, and lack of coordination.[24] Because of this property, the U.S. EPA requires that organophosphorous insecticides undergo special testing for delayed neurotoxicity.

9.4 MONOMERS

Monomers constitute a large, heterogeneous group of reactive chemicals with a wide range of industrial applications. These are used for chemical synthesis and production of polymers, resins, and plastics. Monomers comprise polyhalogenated aromatic compounds such as *p*-chlorobenzene and 1,2,4-trichlorbenzene; unsaturated organic solvents such as styrene and vinyltoluene, acrylamide, and related compounds; phenols; caprolactam; and aminobutyrolactam. Exposure to neurotoxic monomers may take place in industries manufacturing, transporting, and using chemical products and plastic products. Workers are exposed during handling of polymers containing rest monomers, in the manufacturing of molds for boat yards, and in dental clinics. The manner of exposure to monomers may be during inhalation of carbon disulfide and styrene, or by skin contact with acrylamide.

Exposure for prolonged periods to high concentrations of acrylamide, which is used for the production of polymers and tunneling and drilling operations, causes impaired axonal transport, polyneuropathy, dizziness, tremor, and ataxia among workers. The acrylonitrile used for polymer and rubber production chemical synthesis produces hyperexcitability, salivation, vomiting, cyanosis, ataxia, and breathing distress. Carbon disulfide, used in rubber and viscose rayon industries, causes impaired axonal transport, peripheral neuropathy, encephalopathy, headache, vertigo, and gastrointestinal disturbances among workers. Styrene use in the production of glass-reinforced plastics, monomer manufacture and transportation, and styrene-containing resins and coatings cause headache, CNS depression, polyneuropathy, encephalopathy, and hearing loss among workers. Vinyltoluene also produces polyneuropathy and reduced motor nerve conduction velocity.

A large number of organic chemical substances also cause neurological disturbances among workers after a prolonged period of exposure. For instance, chlorinated hydrocarbons; trichloroethylene, 1,1,1-trichloroethane; tetrachloroethylene; methylene chloride; methyl chloride; toluene; xylene; styrene; hexacarbons like hexane; methylbutylketone and methyl ethyl ketone used in leather, shoe, and graphics industries for gluing, printing, plastic coatings, painting, extraction, and in laboratories also cause neurological effects such as impairment of the axonal transport system, prenarcotic symptoms, polyneuropathy, and encephalopathy. Industrial chemical substances, such as phenol, cresol, and pyridiene, cause loss of appetite, fatigue, irritability, sleep disorders, double vision, loss of reflexes, weakness, tremors, sweating, coma, mental disturbance, ringing in the ears, mental depression, and polyneuropathy.

9.5 NEUROTOXICITY AND CHILDREN

It has been reported that about 12% of the 63 million children under the age of 18 in the United States suffer from one or more mental disorders, and exposure to toxic substances before or after birth has been identified as one of the several risk factors that appear to make certain children vulnerable to these disorders.[25] Reports have also indicated that fetuses and children are more vulnerable to the effects of certain neurotoxic substances than are adults. Children exposed to a mix of pesticides, including organophosphates, showed diminished short-term memory and disturbed hand–eye coordination and drawing ability, whereas unexposed children of the same tribe showed normal development. Preschool children from agricultural communities in the United States showed poorer performance on motor speed and latency than did those of urban communities.[26–28]

9.6 SYMPTOMS OF NEUROTOXICITY

Evaluation of neurotoxicity of a chemical substance is dependent on several parameters—for instance, changes in neurochemistry, anatomy, physiology, and or the behavior of the poisoned animal or human. Also, alterations in sensory processes such as paresthesia and visual, olfactory, and or auditory impairments have been often indicated as symptoms of neurotoxicity observed among workers exposed to different toxic substances in workplaces.[29–31]

Neurotoxicity is a general term that includes (1) neuropathy (i.e., dysfunction of motor and sensory peripheral nerve fibers), (2) encephalopathy (i.e., brain dysfunction due to generalized impairment of the brain), and (3) ataxia (i.e., impaired motor coordination). The acute and chronic effects caused by hydrogen sulfide (H_2S) include blocking oxidative metabolism, loss of consciousness, and encephalopathy. Similarly, the neurotoxic effects caused by cyanide (HCN) and nitrous oxide (N_2O) include blocking of respiratory enzymes, dyspnea, falling blood pressure, convulsions, loss of consciousness, encephalopathy, ataxia, neuropathy, and death. Symptoms sometimes start as flu-like symptoms. Neurotoxic chemicals and heavy metals attack the immune system. They attack and destroy the CNS and the PNS. Many target organs like the liver, brain, and kidneys. The symptoms caused by neurotoxic chemical substances among workers are many. For instance, heavily exposed workers show dizziness; light headedness; problems with concentration; emotion; personality changes; sleep disturbances; sleep apnea; insomnia; extreme tiredness and chronic fatigue; numbness in the arms, hands, legs, and feet; loss of learning ability, motivation, and hearing; visual disturbances; and abnormal neuropsychological behavior.

9.7 POLYNEUROPATHY

Some metals, industrial solvents, and pesticides, besides other chemical substances, cause polyneuropathy among workers. The exposed person suffers from the impairment of motor and sensory nerve function, weakness of the muscles, tingling or numbness in the fingers and toes, paresthesia (most pronounced peripherally in the

upper and lower extremities of hands and feet), difficulties in walking, and difficulty in the fine coordination of hands and fingers.

9.8 ENCEPHALOPATHY

Toxic substances such as industrial solvents, metals, industrial gases, and pesticides cause encephalopathy among exposed workers. After a prolonged period of exposure to high concentrations of these substances, alone and in combination, the workers demonstrate impairment of the brain; fatigue; impairment of learning, memory, and ability to concentrate; anxiety; depression; increased irritability; and emotional instability. These symptoms indicate early brain disorder as well as occupational chronic encephalopathy. The exposed worker often shows an increased frequency of headaches, dizziness, changes in sleep pattern, and reduced sexual activity. In severe cases of neurotoxicity, exposed workers demonstrate specific neurological symptoms, such as Parkinsonism with tremor, rigidity of the muscles and slowing of movements, and cerebellar dysfunctions like tremor and reduced coordination of hand movements and gait. Occupational exposure to manganese or MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), toluene, and mercury have been associated with these neurological disorders.

During metal work, mining, work in industrial plants, car repair, shipyard work, glass work, and work in ceramics, pottery, and plastic industries, workers are associated with and become heavily exposed to metals like lead, elemental mercury, calomel (Hg_2Cl_2), sublimate ($HgCl_2$), and manganese and suffer from neurological health effects. The workers indicate symptoms of impairment of oxidative metabolism of nerve cells and glia; possible changes in dopamine and catecholamine in basal ganglia in the center of the brain; dysphoria, inflammation of gums; appetite loss; impaired speech; encephalopathy, including tremor; irritability; abdominal pain; headache; lung inflammation; acute tubular and glomerular renal degeneration; seizures; polyneuropathy; and the symptoms of "drop hand."

The World Health Organization (WHO) Workshop and the International Solvent Workshop have categorized the symptoms of neurotoxic disorders in detail. Accordingly, symptoms have been classified as type 1, type 2A, type 2B, and type 3. The mildest type of neurotoxic disorder is the organic affective syndrome or the type 1 disorder. The symptoms of this disorder include fatigue, memory impairment, irritability, difficulty in concentrating, and mild mood disturbance. The second level of disorder is described as mild chronic toxic encephalopathy (WHO workshop), or the type 2 disorder is characterized with symptoms of neurotoxicity and abnormalities of performance on formal neuropsychological testing. Here again, the exposed worker demonstrates type 2A disorder with sustained personality or mood changes such as emotional instability and diminished impulse control and motivation, and the type 2B with symptoms of impairment in intellectual function manifested by diminished concentration, memory, and learning capacity. Type 3 includes the most pronounced level of neurological disorders—severe and chronic toxic encephalopathy. The condition is characterized by global deterioration in intellectual and memory functions (dementia) that may be irreversible or, at best, only poorly reversible.[32]

9.9 NEUROTOXICANTS AND NEONATES

Occupational exposure to neurotoxic chemicals before and after conception has been reported to produce a wide range of adverse effects on reproduction. Studies in the United States and Europe have shown increased risk of congenital malformations and reductions in birth weight among infants born to parents living near hazardous waste sites.[33–35]

Several substances have caused serious birth defects. For instance, mercury, lead, hair dye, PCBs, soldering, solvents, paints and paint stripping, benzene, carbon tetrachloride, toluene, tetrachloroethylene, thalidomide, tricloroethylene, pesticides, chloroform, trihalomethanes, hazardous wastes, methyl mercury, and some drugs have been associated with structural birth defects in epidemiological studies. The importance of the management of neurological conditions such as perinatal encephalopathy, neurological disorder, and intracranial hypertension and myotonic syndrome among children in different countries of the world has been discussed, which again underlines the need for proper education and training for the safe management of chemicals. Today, it has become very important to develop methods and validate and quantify the biomarkers associated with neurotoxicity and its biological expression, particularly with workers. A multidisciplinary approach is required—for instance, neurochemistry, molecular neurobiology, neuropathology, neurophysiology, and the specific behavior observed among workers suffering from neurotoxicity.

9.10 CONCLUSION

Prolonged periods of exposure to natural, synthetic, or man-made chemical substances cause neurotoxicity. The effects of neurotoxicity result in a variety of health disturbances. In simple terms, neurotoxic chemical substances change the normal activity of the nervous system, eventually leading to disruption of the network of neurons. Thus, the key cells of neural transmission and signal processing in the brain and other parts of the nervous system get damaged.

Neurotoxicity is the result of improper (careless) use, handling, and negligence in the management of chemical substances such as metals, food additives, pesticides, industrial solvents, cosmetics, radiation treatment, and drug therapies. Depending upon route and dose of exposure, the symptoms of neurotoxicity appear immediately after exposure or are delayed. The symptoms include limb weakness or numbness; loss of memory, vision, and/or intellect; headache; cognitive and behavioral problems; and sexual dysfunction. Children and workers with certain existing health disorders are more vulnerable to the adverse effects of neurotoxic chemicals.

Neurotoxicity caused by chemical substances requires careful interpretation based on well confirmed data on experimental animals and surveys of workers and the general population. Neurotoxicity is one of several noncancer end-points that share common default assumptions and principles. The interpretation of data as indicative of a potential neurotoxic effect involves the evaluation of the validity of the database. Attention should be given to the existing gaps—for instance, (1) identification of the specific toxic substance, (2) knowing the observed effects and significance in terms of neurotoxicity, and (3) whether the conclusions made agree

with the data of behavioral, morphological, neurochemical, and physiological studies. Perhaps answers to these help to arrive at a satisfactory, meaningful, and good management of chemical substances. Imparting basic knowledge to workers about chemical substances, avoidance of negligence during the use, and proper management of chemical substances comprise the first steps to contain neurotoxicity.

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APPENDIX 9.1

Chemical Substances and Neurotoxicity

Neurotoxic chemicals and motor neuropathy: Chlorpyrifos, dichlorvos (DDVP), EPN, *n*-hexane, 2-hexanone, lead, lead chromate, lead II thiocyanate, leptophos, methamidophos, mipafox, omethoate, parathion, trichlorfon, trichloronate, triorthocresyl phosphate

Neurotoxic chemicals and sensorimotor neuropathy: acrylamide, allyl chloride, arsenic and compounds, arsenic trichloride, calcium arsenate, carbon disulfide, dichloroacetylene, ethylene oxide, gallium arsenide, lead arsenate, mercuric chloride, mercuric nitrate, mercurous nitrate, mercury, nitrous oxide, phenyl arsine oxide, thallium and soluble compounds, thallous nitrate

10 Chemical Substances and Nephrotoxicity

10.1 INTRODUCTION

Nephrotoxicity is a renal health disorder due to direct or indirect effects of chemical substances. One of the most common kidney problems, nephrotoxicity has been traced to exposures to drugs and toxic chemical substances. The disorder eventually causes kidney damage and disturbs the body functions and elimination of urine and wastes. Reports have indicated that prolonged periods of exposure to metals causes neurotoxicity among workers. Also, cadmium, other environmental heavy metals and the organometallic compounds used as therapeutic agents, anticancer drugs, cyclosporin, analgesic abuse, and antibiotics have been implicated in kidney disorder diseases.

The kidney is the filtration mechanism for the blood. As is well known, the kidney has to perform three major functions to maintain normal health. It helps in removing wastes, prevents leakage of essential elements and chemical compounds from the body, and provides homeostasis. However, prolonged exposure to chemical substances causes adverse health effects and damage of the renal system in animals and humans—a health disorder termed nephrotoxicity. This disorder has been found among workers and members of the public exposed to toxic chemicals, and because of improper medication. The chemical substances that cause damage to the renal system are called nephrotoxins. Reports have indicated that the nephrotoxic effect of chemical substances, including drugs, has become more profound in workers and patients who have a history of renal impairment. Also, some drugs are known to affect renal function in more than one way. Chemical substances such as toxic metals, organic compounds, and pesticides have caused global concern as nephrotoxicants. Prolonged occupational exposure to metals like cadmium, lead, and mercury has also caused renal disorders.[1–5]

10.2 CHEMICAL SUBSTANCES AND RENAL INJURY

It is well established that toxic nephropathies are not restricted to a single type of renal injury. Some chemicals target one discrete anatomical region of the kidney and may affect only one cell type. Chemical insult to the kidney may result in a spectrum of nephropathies that are indistinguishable from those that do not have a chemical etiology. Nephrotoxicity and neural disorders in animals and humans have occurred due to prolonged exposure to chemical substances. These may be broadly categorized as:

therapeutic agents: analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, aminoglycosides, cephalosporins, amphotericin B, tetracyclines, penicillamine, lithium, and anticancer drugs;
chemical substances: ethylene glycol, organic chemicals and solvents, volatile hydrocarbons, chloroform, halogenated alkenes, bipyridyl herbicides, mycotoxins, and silicon; and
metals: arsenic, bismuth, cadmium, chromium, germanium, gold, lead, mercury, and uranium.

For purposes of users' understanding, the chemical substances may be listed as follows: adhesives, agent orange, aspartame, ammonia, arsenic, benzene, carbonless copy paper, carbon monoxide, carpet cleaning agents, copper-chromium-arsenate, (CCA), chemical warfare agents, chlorine, combustion products, dioxin, drugs, formaldehyde, gamma butyrolactone, gasoline, glues, heavy metals, herbicides, lead, lithium, methyl diisocyanate (MDI), methyl-ethyl-ketone (MEK), manganese, mercury, metals, methylene chloride, mixed toxic waste, mold, municipal sludge, mycotoxins, naphthalene, *n*-hexane, oil and gas field emissions, opiates, organic metals, paint, paint remover, Paxil, pentachlorophenol, pesticides (organochlorines, organophosphates, etc.), phenolic resins, polluted air, polychlorinated biphenyl (PCB), Prozac, psychiatric drugs (such as antidepressants, antipsychotics, tranquilizers, and sleep drugs), radiation injuries, solvents, styrene, toluene diisocyanate (TDI), toluene, toxic waste, trichloroethane, trichloroethylene, welding fumes, wood preservatives, and xylene.[1] Thus, the commonest nephrotoxic chemicals are hydrocarbons—present, for instance, in organic solvents, glues, fuels, paints, and motor exhausts. Exposure is common among groups of workers such as painters, printers, cabinet makers, fitters and mechanics, and electricians; in manufacturing; and in many other occupations. Hydrocarbon exposure through paint spraying may result in active proximal tubular damage, which may be reduced by improvement of protection at the worksite. However, renal impairment independent of tubular injury may result from chronic paint exposure, even with improved protection.[1a]

10.3 SYMPTOMS OF NEPHROPATHY

Nephrotoxic chemical substances cause adverse health effects. The vulnerability of kidney tubules and the nephrotoxic chemicals are known to be related to the nature of normal tubular function. The common symptoms of nephrotoxicity include memory disorders, concentration problems, slowed reaction time, sleep disorders, depression, confusion, personality changes, fatigue, numbness of the hands and feet, numerous neurological and psychiatric disorders, irrational behavior, and violent behavior. It has become increasingly evident during the last two decades that the kidney is adversely affected by prolonged periods of exposure to an array of environmental chemicals. Man is exposed to medicines, industrial and environmental chemicals, and a variety of naturally occurring substances. The level of exposure varies from minute quantities to very high concentrations. Exposure may be over a long period

of time or limited to a single event, and it may be due to a single substance or several chemical substances.

Lead and cadmium have been known to cause the kidney disorder chronic interstitial nephritis (CIN). Morphological studies indicate the infiltration of mononuclear cells, prominent interstitial fibrosis, and tubular atrophy. A progressive fibrosis of the interstitial tissue decreases the number of functional nephrons and also the rate of glomerular filtration and eventually leads to renal failure. Some of the chlorinated compounds—for instance, carbon tetrachloride and trichloroethylene—are also known to cause glomerular lesions leading to nephrotic syndrome and renal failure. Some chemical substances cause acute injury, while others produce chronic renal damage leading to end-stage renal failure and renal malignancies.

The extent and cost of clinically relevant nephrotoxicity has only started to become apparent during the last decade. However, the full extent of the economic impact of chemically induced or associated nephropathy is difficult to define because the diagnosis of early injury and the documentation of the cascade of secondary degenerative changes have not been adequately identified. Instead, most chemically associated renal disease is only identified as acute renal failure or chronic renal failure at a very late stage, when therapeutic intervention is impossible.

More importantly, at this stage the etiology may be obscured by lack of reliable information on the likely causative agents, the levels and duration of exposure, and other possible contributing and exacerbating factors. At present, epidemiological evidence indicates that nephrotoxicity leading to acute and/or chronic renal failure represents a substantial financial burden to society.[6] Indeed, there is some indication that chemical exposure could play a much greater influence in the very high incidence of end-stage renal disease. Also, the nephropathies caused by chemical substances are not restricted to a single type of renal injury. Some chemical substances target one discrete anatomical region of the kidney and may affect only one cell type, while it may be different with another chemical substance.

Chemical insult to the kidney presents a wide spectrum of nephropathies that are indistinguishable from those that do not have a chemical etiology, and the diseases associated with exposure to chemical substances have remained unrecognized. Examples include the nephropathies caused by cadmium, other environmental heavy metals, the organometallic compounds used as therapeutic agents, anticancer drugs, cyclosporin, analgesic abuse, and antibiotics.

The nephron and its related cells perform diverse physiological functions. It is the major organ of excretion and homeostasis for water-soluble molecules; because it is a metabolically active organ, it can concentrate certain substances actively. In addition, its cells have the potential to bioconvert chemicals and metabolically activate a variety of compounds. There are a number of other processes described in the following that establish the potential for cellular injury. Specific physiological characteristics are localized to specific cell types. This makes them susceptible to, and the target for, chemicals.

The effect of chemical substances on cells may be pharmacological, in which case the effect is dose related and occurs only as long as the concentration of the chemical substance is high enough to be active. Alternatively, the chemical substance

may cause damage to the cell. The cell responds to injury by repair and the kidney responds to cellular lesion by renal and extrarenal adaptation to compensate for loss of that cell function. Although there is a substantial capacity within the kidney for repair, there are also several conditions where damage becomes completely irreversible. In general, the proximal and distal tubules and urothelia can be repaired, but the glomeruli and medulla may have a significantly lower repair facility. It is therefore possible to initiate a series of degenerative changes as a result of interfering with one or more of the normal physiological processes.

The array of industrial chemicals, negligence during use, and the long-term health consequences need to be understood by workers. The rational understanding of the mechanism of nephrotoxicity in animals and man provides the basis for safe use. Reports of Kluwe et al.[7] and Porter and Bennett[8] indicate the type of adverse health effects vis-à-vis nephrotoxicity caused by aminoglycosides, halogenated hydrocarbons and aromatic amines produce chronic kidney injury in humans and species of mammals.

However, there is still a wide gap in the understanding of the nephrotoxic effects caused by certain therapeutic agents such as cyclosporin, analgesics, and nonsteroidal anti-inflammatory agents. Several chemical substances disturb the glomerular filtration rate (GFR) and related renal functions in animals and humans.

10.4 METALS AND NEPHROTOXICITY

It is well known that a large number of chemical substances, including toxic metals and metalloids such as arsenic, cadmium, lead, and mercury, cause cell injury in the kidney. With metal-induced neurotoxicity, factors such as metal-binding proteins, inclusion bodies, and cell-specific receptor-like proteins seem to influence renal injury in animals and humans. It is of interest to note that certain renal cell populations become the targets for metal toxicity, while others do not. In fact, the target cell populations handle the organic and common inorganic nephrotoxicants differently.[9]

Lead is known for its toxicity in several organ systems in animals and humans (especially children). Acute exposure to lead causes nephropathy, which is characterized by proximal tubular dysfunction. The affected tubules show alterations in mitochondrial structure and the development of cytosolic and nuclear inclusion bodies. Intracellular lead is associated with specific high-affinity proteins and can also bind to metallothionein. In contrast to acute exposures, lead nephropathy caused by chronic exposure is irreversible. The kidney damage includes interstitial fibrosis, hyperplasia, glomerulonephritis, and atrophy of the tubules, leading to renal failure. Exposure to lead for long periods causes renal neoplasm in animals. Studies have shown that lead interacts with renal membranes and enzymes and disrupts energy production, calcium metabolism, glucose homeostasis, ion transport processes, and the renin-angiotensin system, as well as other health disorders.[10] Metals have been associated with the regulation of the heme biosynthetic pathway in the kidney. Acute and chronic exposures to high concentrations of lead cause disturbances to renal heme biosynthesis.

Chronic exposure to methyl mercury results in increased urinary excretion of uro- and coproporphyrins in rats, mediated via inhibition of ferrochelatase. Acute

treatment of laboratory rats with other metals such as nickel, platinum, tin, antimony, bismuth, and cobalt has caused induction of heme oxygenase, followed by decreased microsomal heme content. The stimulation in the kidney[11] with Pb remains a large environmental issue in North America because of its significant hematological actions in children, although its renal actions may be of greater importance than previously thought, underlining the need for vigilance. Similarly, prolonged periods of exposure to diquat and paraquat have caused acute renal failure.[11a]

Long-term exposure to heavy metals and some halogenated hydrocarbons causes progressive degenerative changes in the kidney, possibly leading to renal insufficiency. The screening tests most widely used to assess the integrity of the kidney are the estimation of serum creatinine, blood urea nitrogen (BUN), and the quantitative or semiquantitative measurement of total proteinuria lack sensitivity. They do not permit the detection of renal disturbances at a stage when removal from exposure may prevent progression of the disease and are not suitable to determine the no-effect levels of potentially nephrotoxic chemicals. During the last decades, new markers have been proposed for the early detection of structural and/or functional changes at various sites of the renal parenchyma. Some tests mainly attempt to assess the integrity of the glomerulus, the proximal tubule, the loop of Henle, and distal tubule. Workers exposed to cadmium develop a persistent low proteinuria. This has been linked with the age-related decline of the glomerular filtration rate (GFR). The study of dose effects and response relationships based on a large battery of renal markers has allowed better determination of the internal dose of cadmium that is not associated with significant renal risk.[5]

Exposures to chemical substances such as carbon tetrachloride, 1,1-dichloroethylene, paradichlorobenzene, ethylbenzene, monochlorobenzene, tetrachloroethylene, toluene, 1,1,2-trichloroethane, xylenes, cadmium, and lead are known to cause adverse effects on the kidney. The kidney is unusually susceptible because of its role in filtering harmful substances from the blood. Some of these toxicants cause acute injury to the kidney, while others produce chronic changes that can lead to end-stage renal failure or cancer. Furthermore, evaluation of the nephrotoxicity of complex industrial waste mixtures with organic chemicals and metals requires more studies.

It has become increasingly apparent that a number of chemical substances cause adverse effects on one or more of the anatomical elements of the kidney. These include the glomerulus; proximal, intermediate, and distal tubules; and medullary, endothelial, and urothelial cells. While the proximal tubular cells have self-repairing ability, the same is not true with glomerular epithelium and the medullary interstitial cells. Reports have indicated that cadmium and lead cause renal tubular dysfunction in animals and humans.[12,13] Cell culture studies show that cadmium increases cell death.

The preceding reports unequivocally suggest the need for greater vigilance to avoid exposure to these toxic metals by all and, especially, children. Awareness about metal toxicity and children's health is very important because certain metals, like cadmium, are known to cause significantly higher toxic actions in children and on the developing central nervous system. Similar is the global concern about metals like cobalt, lead, and mercury.

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Conclusions

Tens of thousands of tonnes of different chemical substances are manufactured, used, transported, stored, and disposed of in different countries around the world. The number of accidents, health hazards, and chemical disasters has been increasing. Although most of these accidents occur at fixed facilities where the chemical hazards are known, emergency medical personnel are increasingly more likely to be involved in incidents in which occupational workers and victims have been exposed to an unknown or incorrectly identified chemical hazard. Emergency medical technicians, therefore, must learn to deal with presenting symptoms and provide basic supportive medical care for complications (respiratory, cardiovascular, and neurological) that are most likely to cause a serious threat to life and end in human fatalities.

Students, workers, supervisors, managers, and administration should comply with the chemical safety management group/team. This is applicable to laboratories, university departments, factories, and industrial units where exposure to chemical substances is likely and precautions are necessary. People should be fully informed of the hazards involved and trained in appropriate safe working practices, globally harmonized system (GHS) for classification and labeling of chemicals, and first-aid measures.

The 1992 United Nations Conference on Environment and Development (UNCED) (Earth Summit), the 2002 World Summit on Sustainable Development (WSSD), and the Intergovernmental Forum on Chemical Safety (IFCS) have all endorsed the need for the proper management of chemical substances and have set a goal of 2008 for implementation. The GHS hazard classification criteria have been adopted by consensus for physical hazards (flammability, explosivity, etc.) and key health and environmental effects, including acute toxicity, carcinogenicity, germ cell mutagenicity, reproductive, developmental toxicity, respiratory and skin sensitization, skin and eye irritation, target organ/systemic toxicity, and aquatic toxicity. Standardized label elements (symbols, signal words, and hazard statements) for each of these hazard classes have been developed and agreed upon, along with a standard format and approach to presentation of GHS information in safety data sheets. The GHS document also includes guidance on other issues relevant to implementation of the system, including product identifiers, confidential business information, and precedence of hazards.

In fact, each individual or industrial worker, the supervisor, and the manager should have appropriate access to information concerning the chemical substance that he or she uses in the workplace. This is particularly necessary during the handling of hazardous materials and activities in their communities. Working with any chemical substance involves a degree of risk. Even though a chemical substance may not be considered hazardous by today's standards, all employees are advised to minimize their exposure to chemical substances by using established safe practices. The kinds and types of chemical substances used in industries in recent years and the newer and newer chemical substances introduced to the world market each year are

causing concerns about health. Many of the chemical substances are known to cause health disorders to the users. The prolonged periods of their usage are known to cause a significant number of health impairments every year and in every country of the globe. Industrial workers and the general public exposed to chemical substances due to leakage, improper storage, improper handling, improper transportation from workplace to disposal areas, and many other mistakes have caused acute and chronic health impairments and human tragedies.

In fact, public concerns involving different chemical substances are increasing each year. In view of this, supervisors, laboratory safety officers, employers, manufacturers, industries, regulatory agencies, and related government departments are required to improve the safe management of chemical substances at workplaces and homes to prevent health impairments. Therefore, to follow and fulfill the objectives of chemical safety management, there is a need to provide essential information to each industrial worker. These include but are not limited to the following:

- information on physical and chemical properties and on health effects of chemicals that may be encountered in acute environmental or occupational exposures;
- accurate, concise management information and treatment for patients acutely exposed to environmental toxicants;
- guidelines for effective decontamination of acutely exposed patients, while protecting others from secondary contamination;
- guidelines for patient care and follow-up;
- guidelines for reporting that encourage emergency department physicians to consider the patient as a sentinel case of environmentally or occupationally caused disease;
- information for persons potentially exposed during a hazardous chemical release incident;
- elementary and general knowledge essential for every occupational worker during handling, storage, and disposal activities;
- health impairments likely to result from exposure;
- nature of the chemical substance and product identification;
- hazard identification: as a corrosive agent, as a flammable substance, as an explosive, as a carcinogen, as a mutagen, as a teratogen;
- waste disposal procedures for chemical substances away from the workplace to prevent pollution;
- regular evaluations and patrols by qualified and trained personnel to ascertain the implementation of the chemical substances management plan in accordance with appropriate federal, state, and local regulations;
- Personal protections: eye protection (safety glasses), hand protection (gloves); body protection (appropriate working protective dress);
- occupational workers provided with immediate approach and contact numbers; and
- emergency medical treatment and first aid, the decontamination area and clean treatment area, transport to medical facility, adherence to safe management procedures and regulations, and qualified and trained personnel to

prepare chemical substances, preparation of reports, safety data sheets, and documentation of chemical hazards.

CHEMICAL SAFETY GUIDELINES

Use, storage, transportation, and disposal of different chemical substances essentially require basic knowledge to achieve safety. These may be listed as:

- Knowledge + common sense + caution = chemical safety.
- Follow the guidelines and material safety data sheet (MSDS) during work with chemical substances.
- There is no option to safe work practice without knowledge and caution.
- Always assume that any unfamiliar chemical substance is hazardous.
- Know all the hazards of the chemicals with which you work:
  - Perchloric acid is a corrosive, an oxidizer, and a reactive chemical.
  - Benzene is an irritant, flammable, toxic, and carcinogenic.
- Consider any mixture to be at least as hazardous as its most hazardous component.
- Never use any chemical substance that is not properly labeled.
- Follow all instructions about chemical safety precisely and regularly.
- Minimize exposure to any chemical substance regardless of its hazard rating.
- Use personal protective equipment (PPE) as appropriate during work.
- Above all, use common sense at all times and at all workplaces.
- Minimize the duration of exposure to all unknown chemical substances.
- Avoid repeated exposure to chemical substances of unknown nature.
- The potential hazard of any chemical substance or combination of chemical substances cannot be underestimated.
- Assume that a mixture or reaction product of chemical substances is more hazardous than any single component or reactant.

SAFE-HANDLING GUIDELINES

Users should treat all chemical substances and equipment with caution and respect. When working with chemical substances, remember to do the following:

- Remove and use only the amount of chemical substance required for the immediate job at hand.
- Properly seal, label, and store chemical substances in appropriate containers.
- Keep the containers clearly marked and in a well-ventilated area.
- Check stored chemical substances for deterioration and broken containers.
- Learn how to dispose of waste chemical substances safely, legally, and at predetermined places to meet waste disposal requirements.
- Clean up spills and leaks of chemical substances immediately.
- Know what to do in an emergency caused by chemical substances.

- Do not store chemical substances near heat or sunlight or near substances that might initiate a dangerous reaction.
- Do not transport unprotected chemical substances between the work area and other areas.
- Use a tray, rack, cart, or rubber carrier for in house transfer.
- Always use a secondary container during the transport of hazardous or highly odorous chemical substances and on an elevator.
- Do not pour hazardous chemical substances down the sink in the working laboratory or elsewhere.
- Do not put fellow workers or yourself in danger by negligence in the management of chemical substances.
- Participate in appropriate safety training on a regular basis.
- Students and occupational workers require continued attention and education.
- Students and workers should stop all kinds of illegal or irresponsible handling of chemical substances in the laboratory and work places.

MINIMIZE EXPOSURE AND REDUCE RISKS

- Students and workers should know how to read and understand material safety data sheets (MSDSs).
- Use safe procedures along with recommended fume hoods, shielding, spill protection, gloves, and other types of personal protective equipment.
- Students and workers should be taught about the concept of the chemical hygiene plan.
- No individuals should carry out experiments involving hazardous materials or procedures while alone.
- Students and workers should know what to do when emergencies occur, including escape routes, emergency phone numbers and phone calls, and the location and use of emergency equipment (e.g, alarms, eyewashes, showers, fire extinguishers, and spill kits).

HYGIENE AND CHEMICAL SAFETY

Good personal hygiene helps to minimize exposure to hazardous chemical substances. Observe the following guidelines while using and after use of chemical substances:

- Wash hands frequently and before leaving the laboratory.
- Wash hands before eating, drinking, smoking, or applying makeup.
- Do not keep food or food containers anywhere near chemical substances.
- Do not use laboratory equipment to serve or store food or drinks.
- Remove contaminated clothing immediately.
- Do not use the clothing again until it has been properly decontaminated.
- Follow all special precautions suggested during the use of chemical substances.

- Do not wear contact lenses while working with chemical substances, especially corrosives or volatile solvents.

Safety committees or teams can be a valuable asset and serve as an educational resource. All students should have access to information (MSDSs, books, etc.), know about the hazards of the substances they handle, and be prepared to respond in emergencies. For students conducting research, thorough risk assessments must be carried out to evaluate potential hazards associated with planned experiments. In the event of an accident, formal review of the incident and appropriate follow-up actions must occur. A safe environment must be provided in all classrooms and laboratories.

Once it is recognized that the ultimate responsibility for safety lies within an institution, the management and administration should clearly establish the procedures and policies to achieve chemical safety. An institution's chemical hygiene/laboratory safety plan should include standard safety rules and procedures, descriptions of safety committees, and emergency procedures. An emergency reporting system that is easily accessible at all times to persons working in laboratories must be maintained. Regular inspections should be performed, and problems must be addressed by management. Laboratory-specific safety rules, such as eye protection, should be posted and rigorously enforced. Appropriate facilities for safely handling and storing chemicals must be available. Laboratory operations, safety-related equipment, and the disposal of unwanted, hazardous, and waste materials must be in compliance with governmental regulations.

To achieve the goal of safe use of chemical substances by different sections of society (e.g., students, researchers, skilled and semiskilled workers, and householders), it is important to provide written instructions on the properties of the chemicals. The factors to be considered to evaluate the possible risks of hazardous chemical substances could be either general or specific:

- General factors
  - What is the nature of the hazard?
  - What is the nature of the exposure?
  - What control measures are in place to minimize risk?

- Specific factors
  - What are the body systems involved: eyes, skin, lungs?
  - What are the possible effects of exposure: irritation, burns, breathing difficulties, death?
  - Are the effects of the chemical substance short term or long term?
  - Instructions and information should be collected and stored in a place easily accessible at the workplace.
  - Every container and package of chemical substances in the workplace must have an appropriate and properly understandable label.
  - Label containers and packages with the name of the chemical substance or preparation.
  - Label containers and packages with name, address, and telephone number of the source of the product and supplier.

- Label containers and packages with composition and information on ingredients.
- Provide information about physical and chemical properties and their stability and reactivity.
- Provide information about the toxicological studies and data.
- Hazards identification includes (1) spillage and accidental release measures; (2) proper methods of handling, storage, transportation, and waste disposal; (3) personal protection; and (4) first-aid measures and fire fighting.

Glossary

Abatement: Reducing the degree or intensity of, or eliminating, pollution

Abiotic: Nonbiological

Absorbance: The logarithm to the base 10 of the reciprocal of transmittance

Absorbate: Substance or chemical that has been retained by the process of absorption

Absorbent: Material in which absorption occurs

Absorption: Movement of substances into the blood vascular system or into the tissues of the organism

Acclimatization: The physiological and behavioral adjustments of an organism to changes in its environment

Accretion: A phenomenon consisting of the increase in size of particles by the process of external additions

ACGIH: American Conference of Governmental Industrial Hygienists

Acid rain: The result of sulfur dioxide (SO_2) and nitrogen oxides (NOx) reacting in the atmosphere with water and returning to Earth as rain, fog, or snow

Action level: A level of the chemical similar to a tolerance level except that it is not established through formal regulatory proceedings. It is an informal judgment by a regulatory agency on what amount of a chemical should be allowed in food products

Active ingredient: In any pesticide product, the component that kills or otherwise controls target pests. Pesticides are regulated primarily on the basis of active ingredients

Acute bronchitis: Inflammation of the tubes that carry air into the lungs

Acute dermal toxicity: Adverse effects occurring within a short time of dermal application of a singular dose of a test chemical

Acute exposure: Exposure to chemical substances for 14 days' duration or less, as specified in the protocol

Acute exposure: A single exposure to a toxic chemical substance that may result in severe biological harm or death. Acute exposures are usually characterized as lasting no longer than a day, as compared to continued exposure over a period of time

Acute inhalation toxicity: Adverse effects produced by a test chemical following an inhalation exposure for a period of 4 hours

Acute oral toxicity: Adverse effects produced within a short time of oral administration of a single dose of a test chemical or multiple doses given within 24 hours

Acute test: A test lasting for a short period of time—14 days

Acute toxicity: The capacity of a substance to cause adverse health effects or death as a result of a single or short-term exposure

Additive effect: A biological response to exposure to multiple substances that equals the sum of responses of all the individual substances

Adenoma: A benign tumor of glandular tissue; can be precancerous in cases such as polyps in the colon

ADH: Antidiuretic hormone

ADI: Acceptable daily intake; the amount of a specific food additive or contaminant (e.g., pesticide) thought to be the maximum level that should be consumed on a daily basis. ADI values are normally determined by experts of the WHO/FAO Codex Alimentarius Committee

ADME: Absorption, distribution, metabolism, and distribution

ADR: Adverse drug reaction

Adsorbate: Chemical that has been retained by the process of adsorption

Adsorbent: A solid material on the surface of which adsorption takes place

Adsorption: A physical process in which molecules of gas of dissolved chemicals or liquids adhere in an extremely thin layer to the surfaces of solid bodies with which they are in contact

Adverse health effect: A change in body functions or cell structure that might lead to disease or health problems

AE: Adverse event

AEGLs: Acute exposure guideline levels

Aerobic: Requiring oxygen

Aerosol: Suspension of tiny particles of solid, liquid, or gaseous matter

Aetiology The science of cause or origin of a disease

Aflotoxin: Toxins produced by common molds (e.g., *Aspergillus flavus*) and species in different types of foods

Agent Orange: 2,4-dichlorophenoxyacetic acid (2, 4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T); dioxin

Agglomeration: A process of contact and adhesion whereby the particles of a dispersion form clusters of increasing size

AIN: Acute interstitial nephritis

Air pollution: Contamination of atmospheric air with substances or chemicals not considered suitable for health

Algicide: A pesticide that controls algae

Alveoli: Tiny sac-like air spaces in the lung where carbon dioxide and oxygen are exchanged

Allergy: An altered immune response to a specific substance on re-exposure

Ambient air: Air surrounding on all sides

Amino acids: Building blocks of protein by cells; there are about 20 amino acids

Ames test: A method of an experiment performed using bacteria as a test system to determine the mutagenic potential of a substance or chemical

Anaerobic: Requiring the absence of oxygen

Analyte: Any chemical substance measured in the laboratory

Analytic epidemiologic study: A study that evaluates the association between exposure to hazardous chemical substances and disease by testing scientific hypotheses

Anemia: A condition suggesting lack of red blood cells (RBCs); decreased red cell production resulting in a deficiency in the oxygen-carrying capacity of the blood

Angioedema: A reaction in the skin and underlying tissue showing swelling and red blotches

Antagonistic: Reduction of the effect of one chemical by another when they interact

Antagonistic effect: A biological response to exposure to multiple substances that is less than would be expected if the known effects of the individual substances were added together

Antibodies: Specific proteins produced by the body's immune system that bind with foreign proteins (antigens)

Antigen: A foreign substance that provokes immune response when introduced into the body; the body reacts by making antibodies

Anthropogenic: Effects produced as a result of human activities

Aphotic zone: The deeper parts of lakes, seas, or oceans where light does not penetrate

Aphytic zone: Parts of the lake floor where vegetation is not available

Aplastic anemia: Bone marrow failure with markedly decreased production of white blood cells, red blood cells, and platelets, leading to increased risk of infection and bleeding

Application factor: Number used to estimate concentration of a substance or chemical that will not produce significant adverse effects to a population during chronic exposure. The factor is based on the formula: application factor = maximum allowable toxicant concentration (MATC) ÷ (96 – h LC_{50})

Aquaculture: Breeding and rearing of fish in captivity; also termed pisciculture

Aquatic organism: Organisms related to living water bodies

Aqueous: Related to watery solution

Arboreal: Related to plants

ARF: Acute renal failure

Aromatic: Technical term for a compound or chemical that contains one or more benzene rings

Aromatic amines: Petrochemical compounds with a pungent odor (known to produce cancer)

Ash: Mineral content of a product that remains after complete combustion

Asphyxiant: A vapor or gas that can cause unconsciousness or death by suffocation; most are associated with a lack of sufficient oxygen to promote life

Asthma: Respiratory condition caused by narrowing of the airways; symptoms include recurrent attacks of wheezing, coughing, shortness of breath, and labored breathing

Atmosphere, an: A unit of pressure equal to the pressure exerted by a vertical column of mercury 760 mm high at a temperature of 0° under standard gravity

Atmosphere, the: The gaseous envelope surrounding a planet; the Earth's atmosphere is surrounded by a whole mass of air largely composed of oxygen (20.9%) and nitrogen (79.1%) by volume and carbon dioxide (0.03%) and traces of noble gases, water vapor, organic matter, suspended solid particles, etc.

Atmospheric dispersion: The mechanism of dilution of gaseous or smoke pollution leading to progressive decrease of pollutants

ATSDR: Agency for Toxic Substances and Diseases Registry

Autoimmunity: A condition in which the immune responses of an animal are directed against its own tissues

Autotrophic: Related to those organisms that produce their own organic constituents from inorganic compounds utilizing sunlight for energy or by oxidation processes

Bactericide: A pesticide used to control or destroy bacteria

Basal diet: Ration for adults and starter ration for the young, appropriate to the species; it should meet the standard nutritional requirement

Base pair mutagens: Chemicals or agents that produce a base change in the DNA

BEA: 2-Bromoethalamine

BEI: Biological exposure index

BLL: Blood lead level

BEN: Balkan endemic nephropathy

Benign: Not cancerous; cannot invade neighboring tissues or spread to other parts of the body; a condition of growth that is harmless

Benign tumor: A slow growing set of cells with the abnormal look of a tumor

Bioaccumulation: A process whereby a living organism acquires and stores chemical substances through bioconcentration after ingestion; a process where chemical substances are retained in fatty body tissue

Bioaccumulants: Substances that increase in concentration in living organisms as they take in contaminated air, water, or food because the substances are very slowly metabolized or excreted

Bioaccumulation factor: The ratio of concentration of a chemical in an organism to its concentration in the food

Bioassay: The quantitative measurement of the effects of a chemical substance on the organism under standard conditions

Bioavailability: Availability or presence of a chemical or metabolite in the body of the animal

Biochemical: A substance or chemical produced by a living organism or system

Biochemical oxygen demand (BOD): The amount of oxygen used for biochemical oxidation by a unit volume of water at a given temperature and for a given period of time; BOD finds application for the measurement of degree of water pollution

Biocide: A general term for any substance that kills or inhibits the growth of microorganisms (mold, slime, bacterium, fungus)

Bioconcentration: A process whereby living organisms acquire chemicals from water through gills or integument and store them in their bodies at concentrations higher than in the environment

Biodegradable: The capability of an organism or biological system to break a chemical substance into simpler chemicals

Biodegradation: The decomposition or breakdown of a chemical substance through the action of microorganisms—for instance, bacteria, fungi, or other natural physical processes like sunlight

Biologic monitoring: The estimation of hazardous chemical substances in biological materials (such as blood, hair, urine, or breath) to determine whether

exposure has occurred. A blood test for lead is an example of biologic monitoring

Biologic uptake: The transfer of substances from the environment to plants, animals, and humans

Biological oxygen demand (BOD): An indirect measure of the concentration of biologically degradable material present in organic wastes. It usually reflects the amount of oxygen consumed in 5 days by biological processes breaking down organic waste

Biological pesticide: A chemical substance derived from plants, fungi, bacteria, or other non-man-made synthesis that can be used for pest control

Biomagnification: A phenomenon where the bioaccumulated chemical substances increase in concentration as they pass upward through two or more trophic levels

Biomedical testing: The testing of persons or workers to find out whether or not a change in the body function might have occurred because of exposure to hazardous chemical substances

Biota: The plants and animals in an environment, some of which might be sources of food, clothing, or medicine for people

Biotechnology: The application of living organisms to produce new products and substances

Body burden: The total amount of a substance in the body. Some substances build up in the body because they are stored in fat or bone or because they leave the body very slowly

Bone marrow: A substance with the consistency of thick blood found in the body's hollow bones, such as legs, arms, and hips. Marrow produces platelets, red blood cells, and white blood cells—the primary agents of the body's immune system

Bowman capsules: The outer cortex of the kidney; the main units for blood filtering

Breathing zone: The location in the atmosphere at which individual animals and humans breathe

Bronchiole: The smaller airways of the lungs

Bronchiolitis: Inflammation of the bronchioles, usually caused by a viral infection

Bronchodilator: A drug that relaxes the smooth muscles of the airways and relieves constriction of the bronchi

Bronchopulmonary: Pertaining to the lungs and air passages

BUN: Blood urea nitrogen

Cancer: The injurious malignant growth of potentially unlimited size of cells and tissue invading local tissues and spreading to distant areas of the body

Cancer effect level (CEL): The lowest dose of chemical in a study or group of studies that produces significant increases in the incidence of cancer or tumors between the exposed population and its appropriate control

Cancer risk: A theoretical risk for getting cancer if exposed to a chemical substance every day for 70 years (a lifetime exposure); the true risk might be lower

Capillaries: The tiniest blood vessels; capillary networks connect the arterioles (the smallest arteries) and the venules (the smallest veins)

Carcinogen: A chemical capable of inducing cancer

Carcinogenesis: A biological process involving the transformation of a normal cell into a cancer cell

Carcinoma: A malignant tumor of the cells that involves lung, gut, skin, and epithelial tissues; ranges to about 90% of all types of cancer

CAS registry number: A unique number assigned to a substance or mixture by the American Chemical Society Abstract Service

Case study: A medical or epidemiologic evaluation of one person or a small group of people to gather information about specific health conditions and past exposures

CCPR: Codex Committee on Pesticide Residues

CCRIS: Chemical Carcinogenesis Research Information System

CDDs: Chlorinated dibenzo-*p*-dioxins (also see CFCs)

CDFs: Chlorinated dibenzofurans (also see CFCs)

Cell: The smallest structural unit of all living organisms

Ceiling value: A concentration of a substance that should not be exceeded, even instantaneously

CERCLA: Comprehensive Environmental Response, Compensation, and Liability Act of 1980. CERCLA, also known as Superfund, is the federal law that concerns the removal or cleanup of hazardous substances in the environment and at hazardous waste sites. ATSDR, which was created by CERCLA, is responsible for assessing health issues and supporting public health activities related to hazardous waste sites or other environmental releases of hazardous substances. This law was later amended by the Superfund Amendments and Reauthorization Act (SARA)

CFCs: Chlorofluorocarbons. A family of inert, nontoxic, and easily liquefied chemicals used in refrigeration, air conditioning, packaging, and insulation, or as solvents and aerosol propellants. Because CFCs are not destroyed in the lower atmosphere, they drift into the upper atmosphere, where their chlorine components destroy ozone

CFR: *See* Code of Federal Regulations

Chemical oxygen demand (COD): A measure of the oxygen required to oxidize all compounds and organic and inorganic matter in a sample of water. COD is expressed as parts per million of oxygen taken from a solution of boiling potassium dichromate for 2 hours. The COD test is used to assess the strength of sewage and waste

Chlorinated hydrocarbons: (1) Chemical substances containing only chlorine, carbon, and hydrogen. These include a class of persistent, broad-spectrum insecticides that linger in the environment and accumulate in the food chain. Among them are DDT, aldrin, dieldrin, heptachlor, chlordane, lindane, endrin, Mirex, hexachloride, and toxaphene. Other examples include TCE, which is used as an industrial solvent. (2) Any chlorinated organic compounds, including chlorinated solvents such as dichloromethane, trichloromethylene, and chloroform

Cholinesterase: The enzyme found in animals that regulates nerve impulses by the inhibition of acetylcholine; cholinesterase inhibition in animals produce a

variety of acute symptoms, such as nausea, vomiting, blurred vision, stomach cramps, and rapid heart rate

CHRIS: Chemical Hazards Response Information System

Chromatid: One of the two copies of the chromosome after the S phase

Chromatid-type aberration: A type of aberration; the damage expressed as breakage of single chromatids at the same locus

Chromosome: Structure found in the nucleus of a cell; these structures bear the DNA (deoxyribinucleic acid) from which genes are made. Genes carry the genetic code of the organism

Chromosome-type aberration: The damage expressed in both sister chromatids at the same locus

Chronic: Occurring over a long period of time; frequently recurring

Chronic exposure: Exposure to a chemical substance for more than 1 year

Chronic toxicity: The capacity of a substance to cause adverse or harmful effects in the organism after long-term exposure

CIN: Chronic interstitial nephritis

CNS: Central nervous system—the part of the nervous system that consists of the brain and the spinal cord

Co-carcinogen: A chemical substance or agent that assists carcinogens to cause cancer

Code of Federal Regulations (CFR): A document that codifies all rules of the executive departments and agencies of the federal government. It is divided into 50 volumes, known as titles. Title 40 of the CFR (referenced as 40 CFR) lists all environmental regulations

Cohort study: A study in which a group of people with a past exposure to chemical substances or other risk factors are followed over time and their disease experience compared to that of a group of people without the exposure

Colic: Acute abdominal pain, especially in infants

Complete carcinogens: Substances or chemicals that will both initiate and promote cancer

Concentration: The amount of a substance present in a certain amount of soil, water, air, food, blood, hair, urine, breath, or any other medium

Condensation: The process of converting a chemical in the gaseous phase to a liquid or solid state by decreasing temperature, increasing pressure, or both

Congenital: Associated with a condition that exists before birth of the organism or animal

Contact dermatitis: A condition where skin outbreaks are caused by direct contact with a substance

Contaminant: A chemical substance present in an environment at levels sufficient to cause harmful or adverse health effects to organisms, animals, and humans

Contamination: Introduction into water, air, and soil of microorganisms, chemicals, toxic substances, wastes, or wastewater in a concentration that makes the medium unfit for its next intended use. Also applies to surfaces of objects, buildings, and various household and agricultural use products

Convulsion: Abnormal and involuntary jerks and quick movements of the body

COPD: Chronic obstructive pulmonary disease

Corrosive: Any liquid or solid that causes visible destruction or irreversible alteration of skin tissue at the place of contact

Cost-benefit analysis: A quantitative evaluation and decision-making technique where comparisons are made between the costs of a proposed regulatory action on the use of a substance or chemical with the overall benefits to society of the proposed action, often converting both the estimated costs and benefits into health and monetary units

CPSC: Consumer Product Safety Commission

Cumulative toxicity: The adverse effects caused by substances or chemicals after repeated doses, prolonged exposure, or increased concentration of the chemical or metabolites in susceptible tissues of animals

Cyanosis: Bluish color of the skin due to insufficient oxygen in the blood

Cystic fibrosis: A serious genetic disease of excretory glands, affecting lungs and other organs; it causes production of very thick mucus that interferes with normal digestion and breathing

Cytogenetics: A discipline of science linking the study of heredity with that of the physical appearance of the chromosomes

Cytolysis: The phenomenon where the cell undergoes destruction, particularly due to the disintegration of cell membrane

DART: Developmental and reproductive toxicology

DBCP: 1,2-dibromo-3-chloropropane

DCVC: *S*-(1,2-dichlorovinyl)-L-cysteine

Decibel: The unit used for the measurement of the intensity of sound on a logarithmic scale based on measurements of sound intensity in watts per square meter and related to a reference. For instance, 10 W/m^2 is the intensity of the quietest sound perceptible to the human ear

Decomposition: The breakdown of chemical substances into other substances or parts of compounds usually associated with heat or chemical reactions

Delayed health effect: A disease or an injury that happens as a result of exposure to chemical substances that might have occurred in the past

Delney clause: An amendment enacted in 1958 to the Pure Food Act that prohibits the addition to food of all detectable amounts of a carcinogen

Dementia (senile dementia): An acquired progressive impairment of intellectual function

Density: The mass per unit volume of a substance or chemical

Dermal contact: Any contact with skin; touching

Dermal corrosion: A reaction producing irreversible tissue damage on the skin following the application of a test chemical substance

Dermal irritation: A type of irreversible and inflammatory change on the skin following exposure to chemical substances

Dermatitis: An inflammatory reaction of the skin caused by chemical substances and the associated chemical reaction on the body

Desorption: The process of freeing from an absorbed state

Detection limit: The lowest concentration of a chemical substance that can reliably be distinguished from a zero concentration

Detergent: A surface active agent used to remove dirt or grease from a surface

Detergents: The group of synthetic, organic, and water-soluble cleansing agents. Detergents are not prepared from fats and oils and are not inactivated by hard water

Developmental toxicity: The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism

Dioxin: A family of chemicals with related properties and toxicity. There are 75 different dioxins, or polychlorinated dibenzodioxins (PCDDs); 135 different furans, or polychlorinated dibenzofurans (PCDFs); and 209 different polychlorinated biphenyls (PCBs). Each different form is called a congener, a member of a family of compounds known chemically as dibenzo-*p*-dioxins. Concern about them arises from their potential toxicity as contaminants in commercial products. Tests on laboratory animals indicate that it is one of the more toxic anthropogenic (man-made) compounds; a term used interchangeably with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin or TCDD

Disease prevention: Measures used to prevent a disease or reduce its severity

Dispersoids: The particles of a dispersion

Disposals: The final placement or destruction of toxic, radioactive, or other wastes; surplus or banned pesticides or other chemicals; polluted soils; and drums containing hazardous materials from removal actions or accidental releases. Disposal may be accomplished through use of approved secure landfills, surface impoundments, land farming, deep-well injection, ocean dumping, or incineration

Dissolved oxygen (DO): Oxygen molecules that are dissolved in water; the unit of expression is parts per million (ppm)

Diuresis: Increased excretion of urine

Diuretic: A drug that promotes the excretion of salt and water by the kidney

Diurnal: A reaction that is recurring daily

DNA: Deoxyribonucleic acid (*see* Chromosome)

Dominant lethal mutation: The mutation occurring in a germ cell that does not cause dysfunction of the gamete, but is lethal to the fertilized egg or developing embryo

Dosage: A composite term indicating the dose (size), its frequency, number of doses, and duration of dosing

Dosage/dose: (1) The actual quantity of a chemical administered to an organism or to which it is exposed. (2) The amount of a substance that reaches a specific tissue (e.g., the liver). (3) The amount of a substance available for interaction with metabolic processes after crossing the outer boundary of an organism

Dose: The amount, quantity, and volume of a chemical substance administered once to an organism or animal. Dose is a measurement of exposure and is often expressed as milligram (amount) per kilogram (a measure of body weight)

Dose response: How an organism's response to a chemical substance (toxins) changes as its overall exposure changes. For instance, a small amount of X chemical substance causes drowsiness, but a large dose X becomes fatal (X means any toxic chemical substance)

Dose–response relationship: The quantitative relationship between the amount of exposure to a chemical substance and the extent of toxic injury or disease in body function or health (response) produced

DTPA: Diethylenetriamine pentaacetic acid

Dust: Chemical substances consisting of small, very fine, solid particles in the air

Dysplasia: Abnormal development or growth

EC_{50}: The calculated concentration of a substance or chemical that would kill 50% of an exposed population of animals

Ecology: The branch of science dealing with interrelationships of different organisms and their environment

Ecosystem: A complex system where different biological communities and their nonliving environmental surroundings function independently and interact

ECP: Exposure control plan

Edaphic factor: A composite of physical and biological characteristics of the soil that disturbs the ecosystem

Edema: Abnormal accumulation of fluids within tissues, resulting in swelling

EDTA: Ethylenediaminetetraacetic acid

Effluent standard: The maximum amount of a specified pollutant permitted in effluents

Elute: To remove a sorbed chemical substance from a sorbent by means of a fluid

Embryotoxic: The adverse health effects on the growing embryo

Embryotoxicity and fetotoxicity: Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred

EMIC: Environmental Mutagenesis Information Center

Emission: The kind of pollution discharged into the atmosphere from smokestacks, other vents, and surface areas of commercial or industrial facilities; from residential chimneys; and from motor vehicles, locomotives, or aircraft exhausts

Emission mixture: The total amount of a substance or chemical discharged into the air from a stack, vent, or discrete source

Emphysema: Chronic lung disease in which there is permanent destruction of alveoli

Encephalopathy: Any disease of the brain; a condition characterized by altered brain function and structure

Environment: The physical, chemical, and biotic conditions surrounding an organism or animal

Environmental impact statement: A document required of federal agencies by the National Environmental Policy Act for major projects or legislative proposals significantly affecting the environment. A tool for decision making, it describes the positive and negative effects of the undertaking and cites alternative actions

Enzyme: A protein produced by living cells; enzymes regulate the rate of chemical reactions without being altered in the process

EPA: U.S. Environmental Protection Agency

Epidemiology: The discipline of science studying the distribution of disease or other health-related states and events in human populations, as related to age, sex, occupation, ethnicity, and economic status in order to identify and alleviate health problems and promote better health

ESRD: End-stage renal disease

Estuary: Region of interaction between rivers and near-shore ocean waters, where tidal action and river flow mix fresh and salt water. Such areas include bays, mouths of rivers, salt marshes, and lagoons. These brackish water ecosystems shelter and feed marine life, birds, and wildlife

ET_{50}: The calculated time to kill 50% of an exposed population with a specific concentration of a substance or chemical

EU: European Union

Excretion: The physiological process in which the chemical or metabolite is eliminated from the body through urine, feces, sweat, or exhaled gas

Eye corrosion: The production of irreversible tissue damage in the eye following the anterior surface contact of a substance or chemical

Eye irritation: Production of an irreversible change in the eye

Fetotoxic: Adverse health effects to the fetus

FFDCA: Federal Food, Drug, and Cosmetic Act

Fiber: A solid particle; normally, length is at least three times its width and the hazard of a particle depends upon the size of the fiber

FIFRA: Federal Insecticide, Fungicide, and Rodenticide Act (enacted June 25, 1947)

Flammable: Any chemical substance, liquid or solid, that has a flash point of 100°F or below; any solid that can sustain fire and ignite readily; any material that can be ignited easily and will burn rapidly

Flash point: The temperature at which a liquid will generate sufficient vapors to promote combustion. Generally, the lower the flash point is, the greater the danger of combustion is

Flue gas: The air coming out of a chimney after combustion in the burner it is venting. Flue gas includes, for example, nitrogen oxides, carbon oxides, water vapor, sulfur oxides, particles, and many chemical pollutants

Fluorocarbons (FCs): The organic compounds analogous to hydrocarbons in which one or more hydrogen atoms are replaced by fluorine. FCs were once used in the United States as a propellant for domestic aerosols and are now found mainly in coolants and some industrial processes. FCs containing chlorine are called chlorofluorocarbons (CFCs). These are believed to be modifying the ozone layer in the stratosphere, and are responsible for allowing more harmful solar radiation to reach the Earth's surface

Foam: A gas in liquid dispersion

Fog: A visible aerosol in which the dispersed phase is liquid

Food chain: The order of organisms in which each organism feeds on the member below it; the lowest order could be an alga or a plant

FQPA: The Food Quality Protection Act

Fume: Very fine and small solid particles generated by condensation of vapors from the gaseous state, generally after volatilization from melted chemicals at high temperature; particle diameter is generally less than 1 μm

Fumigants: Toxic chemical substances in vapor form. Fumigants are used for the control of rodents, insects, and vectors of diseases

GAG: Glycosaminoglycan

Gas: One of the three states of aggregation of matter having no independent shape or volume but with a property of indefinite expansion

Gastrointestinal (GI) tract: Pertaining to the stomach, small and large intestines, colon, rectum, liver, pancreas, and gallbladder

GBM: Glomerular basement membrane

GCP: Good clinical practice

Gene: The part of a DNA molecule that carries the information defining the sequence of amino acids in a specific polypeptide chain; in simple words, the chromosome that carries a particular inherited characteristic

GENE-TOX: Genetic toxicology/mutagenicity data bank

Genome: A term referring to all the genes in a cell

Genotoxic: A chemical substance causing damage to the genetic material of living organisms and animals

GFR: Glomerular filtration rate

Global warming: An increase in the near-surface temperature of the Earth. Global warming has occurred in the distant past as the result of natural influences, but the term is most often used to refer to the warming predicted to occur as a result of increased emissions of greenhouse gases. Scientists generally agree that the Earth's surface has warmed by about 1°F in the past 140 years. The Intergovernmental Panel on Climate Change (IPCC) recently concluded that increased concentrations of greenhouse gases are causing an increase in the Earth's surface temperature and that increased concentrations of sulfate aerosols have led to relative cooling in some regions, generally over and downwind of heavily industrialized areas

Glomeruli: Network of tiny blood vessels in the kidneys where the blood is filtered and waste products are removed

GLP: Good laboratory practice

GMP: Good manufacturing practice

GRAS: Generally recognized as safe. The level of a chemical substance generally recognized as safe (the term refers to food additives and related substances). This designation by the U.S. FDA refers to a chemical or substance (including certain pesticides) added to food that is considered safe by experts and thus is exempted from the usual FFDCA food additive tolerance requirements

Greenhouse effect: The warming of the Earth's atmosphere attributed to a buildup of carbon dioxide or other gases; some scientists think that this buildup allows the sun's rays to heat the Earth while making the infrared radiation atmosphere opaque to infrared radiation, thereby preventing a counterbalancing loss of heat

Growth hormone (GH): The protein produced by the pituitary gland that promotes the growth of the whole body

GSH: Glutathione-SH

GUP: General-use pesticide

Habitat: The place where a population (e.g., human, animal, plant, microorganism) lives and its surroundings, both living and nonliving

Half-life: The term that denotes the time required for the elimination of one half of the total dose of a chemical from the body. For instance, the biochemical half-life of DDT in the environment is 15 years. Similarly, the time required for half of the atoms of a radioactive element to undergo self-transmutation or decay (half-life of radium is 1620 years)

Hazard: The ability of a chemical substance to cause injury; probability that a chemical substance or a physical agent can cause injury or adverse effects to animals or humans under a set condition; hazard is the inverse function of safety: hazard C (toxicity × bioavailability)

Hazard evaluation: A component of risk evaluation that involves gathering and evaluating data on the types of health injuries or diseases produced by chemical substances and exposure conditions

Hazardous ranking system: The evaluation of risks to public health and the environment related with rejected or uncontrolled hazardous waste sites and the principles of screening thereof by the U.S. EPA. The scorings are based on the potential of hazardous substances spreading from the site through the air, surface water, or ground water, and on other factors such as density and proximity of human population. Scorings of this kind help to decide the sites on the National Priorities List and related ranking

Hazardous substance: A kind of chemical substance or material (e.g., corrosive, ignitable, explosive, or chemically reactive) that may pose a threat to human health and/or environmental safety. Normally, the U.S. EPA designates typical hazardous chemical substances

H & E: Hematoxolin and eosin

HCBD: Hexachloro-1,3-butadiene

Heterotrophic: Organisms that require ready-made organic food materials from which they can produce most of their own constituents

Homeostasis: The inherent tendency present in an organ towards maintaining physical and psychological stability; the maintenance of constancy within a biological system either in terms of interaction between the organisms of a community or between the internal environment of an organism or individual

HPLC: High-performance liquid chromatography

HSDB: Hazard Substances Database, U.S. Library of Medicine

Hyaline membrane disease: A respiratory disease of newborns, especially premature infants, in which a membrane composed of proteins and dead cells forms and lines the alveoli, making gas exchange difficult or impossible

Hydrocarbons: Chemicals that consist entirely of hydrogen and carbon. Hydrocarbons contribute to air pollution problems like smog

Hyperplasia: Excessive growth of cells

Hypertension: High blood pressure

IARC: International Agency for Research on Cancer—a part of the World Health Organization

ICSCs: International chemical safety cards

IDLH: Immediately dangerous to life or health—the maximum environmental concentration of a chemical substance or contaminant from which one could escape within 30 minutes of time without any escape-impairing symptoms or irreversible health effects; also, concentrations of chemical substances if breathed continuously for at least 30 minutes in the air could cause irreparable damage to health

Immunity: The ability of an organism or animal to combat infections by parasites

Immunologic toxicity: The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals

Immunotoxic: Chemical substances that cause adverse health effects to the immune system

Incompatible chemical substances: Chemical substances that may cause dangerous reactions from direct contact with one another

Induction period: The length of time (at least 1 week) following a sensitization during which a hypersensitive state is developed by the animal

Inflammation: Response of the body tissues to injury; typical signs are swelling, redness, and pain

Ingestion: A process of swallowing food materials, water, drinks, and chemical substances knowingly, or unknowingly by accident

Inhalation: Breathing; people can take in chemicals by breathing contaminated air

Initiator: The substance or chemical that starts the process of tumor formation by causing permanent damage to the DNA

Insecticide: A pesticide compound specifically used to kill or prevent the growth of insects

Insecticide Act: Regulations containing many schedules and related sections for the manufacture, safe handling, transportation, and use of pesticides in India that has been in force since 1968

Integrated pest management (IPM): The application of pest control technologies to prevent unacceptable levels of pest damage and least possible hazard to persons, property, and the environment

Intra-arterial: Any chemical substance injected into an artery of an animal or a human

Intra-aural: Any chemical substance placed into the ear of an animal or a human

Intracerebral: Any chemical substance injected into the brain of an animal or a human

Intracervical: Any chemical substance placed in the cervix

Intraduodenal: Any chemical substance injected into the small intestine of an animal and a human

Intramuscular: Any chemical substance injected into a muscle of an animal or a human

Intraperitoneal: Any chemical substance injected into the abdominal cavity of an animal or a human

Intratracheal: Any chemical substance injected into the trachea

Intravenous: Any chemical substance injected into a vein of an animal or a human

In vitro: Studies carried out in isolation from living organisms; a process occurring in a test tube; isolated from the living organism and artificially maintained, as in a test tube

In vivo: Studies carried out within the living organism; a process occurring in the intact body of an organism or animal; occurring within the living organism

IPCS: International Program on Chemical Safety—a part of the World Health Organization, Geneva

IRED: Interim re-registration eligibility decision (regarding pesticide registration)

IRIS: Integrated Risk Information System

Iron: An essential mineral that is necessary for the transport of oxygen (via hemoglobin in red blood cells

IRPTC: International Register of Potentially Toxic Chemicals

Irritant: A chemical substance that can cause an inflammatory reaction to the eye, skin, respiratory system. An irritant can cause an acute effect from a single high-level exposure or chronic effects from repeated exposures

Itching: An uncomfortable sensation in the skin

ITER: International toxicity estimates for risk—a database of international risk values for chemical substances

Latency period: The period of time between exposure to something that causes a disease and the onset of the health effect. Cancer caused by exposure to chemical substances may have a latency period of 5–40 years

LDH: Lactate dehydrogenase

Lethal concentration (Lo) (LC Lo): The lowest concentration of a chemical substance in air that has been reported to have caused death in humans or animals

Lethal concentration (50) (LC_{50}): A calculated concentration of a chemical substance in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population

Lethal dose (Lo) (LD Lo): The lowest dose of a chemical substance introduced by a route other than inhalation that is expected to cause death in humans or animals

Lethal dose (50) (LD_{50}): The dose of a chemical substance that has been calculated to cause death in 50% of a defined experimental animal population

Leukemia: Any of a group of potentially fatal diseases involving uncontrolled growth of white blood cells. Leukemias are classified based upon rapidity of course of disease and cell type affected

LOAEL: Lowest-observed adverse effect level. The lowest dose of chemical in a study or group of studies that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control

LOEL: Lowest observed effect level. The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of an effect between the exposed population and its appropriate control group

Malformations: Permanent structural changes that may adversely affect survival, development, or function

Malignancy: State of being cancerous; malignant tumors can invade surrounding tissues and spread to other parts of the body

MCLG: Maximum contaminant level goal

Melting point: The temperature at which a solid chemical substance changes to a liquid

Metabolism: All the reactions of chemical substances that enable the body to work. For example, food is metabolized (chemically changed) to supply the body with energy. Chemical substances can be metabolized by the body and made either more or less harmful

Metastasis: Process of invasion and spreading of cancerous cells to other tissues

Mg/g: Milligrams per gram

Mg/cm^2: Milligrams per square centimeter (of a surface)

Mg/kg: Milligrams per kilogram

Mg/m^3: Milligrams per cubic meter; a measure of the concentration of a chemical in a known volume (a cubic meter) of air, soil, or water

Miticide: Chemical substances used to destroy mites that feed on plants and animals

Molluscicides: Chemical substances used to kill snails and slugs

Morbidity: Illness or disease; rate of incidence of disease

Mordants: Chemicals that are insoluble compounds that serve to fix a dye, usually a weak dye

Mortality: The rate of death

MRL: Minimal residue level (a level much below ADI), also referred as a minimal risk level (MRL); an estimate of the daily human exposure to a hazardous substance

MSDS: Material safety data sheet. Printed material on hazardous chemical substances and/or extremely hazardous substances. An MSDS provides information on physical properties, hazards to personnel, fire and explosion potential, safe handling recommendations, health effects, fire-fighting techniques, reactivity, and proper disposal. It was originally established for employee safety by OSHA

Mucus: A thick fluid produced by the lining of some organs of the body

Mutagenesis: Production of mutation occurring in the genetic store of organisms and animals because of toxic chemical substances

Mutagenic: Capability of a chemical substance to cause genetic damage such as mutations

Mutagens: Chemical substances that cause mutation

Mutation: Any heritable change occurring in the genetic material; change in the number, arrangement, or molecular sequence of a gene

Mycotoxins: Toxic chemical substances produced by fungus

Myeloma: Cancer beginning in plasma cells of bone marrow

Nasopharyngeal carcinoma: Cancer of the throat

Nausea: The urge to vomit

Necrosis: Mass death of areas of tissue surrounded by otherwise healthy tissue

Nematicides: Chemicals that kill nematodes (microscopic, worm-like organisms that feed on plant roots)

Neoplasm: Formation of new tissues associated with disease; the term denotes tumors

Nephron: The basic structural and functional unit of the kidney. The basic function of the nephron is to regulate water and soluble substances

Nephropathy: Kidney disease

Nephrotoxic: Chemical substances causing injury to kidneys

Neuropathy: A group of symptoms caused by abnormalities in motor or sensory nerves with symptoms of tingling or numbness in hands or feet, followed by gradual, progressive muscular weakness

NFPA: National Fire Protection Association

NIOSH: National Institute of Occupational Safety and Health. The U.S. Congress set up this institute in 1970 to play a key role to help in the protection of health of industrial workers. The agency conducts occupational-health research, inspects industries and manufacturing plants at the request of the employers and workers, collects data for its own decisions, and recommends standards for safe exposure to hazardous substances

Nitric oxide (NO): A gas formed by combustion under high temperature and high pressure in an internal combustion engine; it is converted by sunlight and photochemical processes in ambient air to nitrogen oxide. NO is a precursor of ground-level ozone pollution, or smog

Nitrogen oxide (NOx): NOx is formed as a result of photochemical reactions of nitric oxide in ambient air; it is a major component of photochemical smog. It is a product of combustion from transportation and stationary sources and a major contributor to the formation of ozone in the troposphere and to acid deposition

NOEC: No observed effect concentration. The highest tested concentration of a test substance or chemical at which no statistically significant lethal or other adverse effects are observed in animals

NOEL: No observed effect level is the highest test dose of a chemical substance that has been reported to have no harmful or adverse health effects on people or animals

NPL: National Priorities List—the U.S. EPA's list of the most serious uncontrolled or abandoned hazardous waste sites in the United States, updated on a regular basis

NSAID: Nonsteroidal anti-inflammatory drug

NTP: The National Toxicology Program is a part of the Department of Health and Human Services. NTP develops and carries out tests to predict whether a chemical will cause harm to humans

Ocular: Chemical substance placed in the eye

OEHHA: Office of Environmental Health Hazard Assessment
OSHA: Occupational Safety and Health Administration
Osteogenic sarcoma: Cancer associated with bone structures
Oxidation: Chemical addition of oxygen to break down pollutants or organic waste, for example, destruction of chemical substances such as cyanides, phenols, and organic sulfur compounds in sewage by bacterial and chemical means
Oxidative stress: Process whereby the metabolic balance of a cell is disrupted by exposure to environmental substances, resulting in accumulation of free radicals, which can damage the cell
Oxidizer: Chemical substance that causes oxygen to combine with another chemical substance; examples include oxygen and hydrogen peroxide
Ozone depletion: Destruction of the stratospheric ozone layer that protects the Earth from harmful effects of ultraviolet radiation. Depletion of ozone layer is due to the breakdown of certain chlorine- and/or bromine-containing compounds (chlorofluorocarbons or halons), which break down when they reach the stratosphere and then catalytically destroy ozone molecules
Ozone layer: Protective layer in the atmosphere, about 15 miles above the ground. The ozone layer absorbs some of the sun's ultraviolet rays, thereby reducing the amount of potentially harmful radiation that reaches the Earth's surface
PAHs: Polycyclic aromatic hydrocarbons
Parenteral: A general term meaning that a chemical substance was not administered orally. Usually, this means an intramuscular or intravenous route was used
Paresthesia: Abnormal physical sensations such as numbness, prickling, or tingling
Particle: A very small but discrete mass of solid or liquid matter
Particle concentration: Concentration expressed in terms of number of particles per unit volume of air or another gas
Particle size distribution: Relative percentage by weight or in number of each of the different size fractions of particulate matter
PAS: Periodic acid Schiff stain
PBBs: Polybrominated biphenyls
PCBs: Polychlorinated biphenyls
PEL: Permissible exposure limit; a legal limit set by OSHA on the length of time industrial workers may be exposed to a substance during an 8-hour time-weighted average day without adverse effects
Persistence: The quality of remaining for a long period of time (such as in the environment or the body). Persistent chemical substances—for example, DDT and PCBs, are not easily broken down
Pest: An insect, rodent, nematode, bacterium, virus, fungus, weed, and other organism that competes with humans for food or other resources. These are not beneficial but injurious to human health and environmental safety
PG: Prostaglandin
pH: The scale to measure acidity and alkalinity of a medium—for instance, in water, soil, or body fluid. pH is the hydrogen ion concentration. A truly neutral solution is neither acidic nor alkaline; pH of water is 7.0. pH of 0–2 is

strongly acidic, pH of 3–5 is weakly acidic, pH of 6-8 is neutral, pH of 9–11 is weakly basic, and pH of 12–14 is strongly basic

Pharmacokinetics: A term suggesting the quantitative uptake of drugs by the body; biotransformation, distribution, metabolism, and excretion from the body of animals or humans

Pheromones: Biochemicals used to disrupt the mating behavior of insects

PHG: Public health goal

Photocarcinogenesis: Carcinogenic effects associated with exposure to ultraviolet light

Photochemical reaction: Any chemical reaction initiated as a result of absorption of light

Photochemical smog: Type of air pollution due to photochemical reaction in the atmosphere

PIP: Pesticide information profiles

Pleurisy: An inflammation of the pleura, the lining of the lungs and chest cavity

Pneumoconiosis: Health conditions characterized by permanent deposition of substantial amounts of particulate matter in the lungs and by the tissue reaction to its presence; can range from relatively harmless forms of sclerosis to the destructive or fatal fibrotic effect of silicosis

Pneumonia: Inflammation of the lungs

Pollution: Generally, the presence of a chemical substance in the environment that, because of its chemical composition or quantity, prevents the functioning of natural processes and produces undesirable environmental and health effects. Under the Clean Water Act, for example, the term has been defined as the man-made or man-induced alteration of the physical, biological, chemical, and radiological integrity of water and other media

Pollution prevention: Identifying areas, processes, and activities that create excessive waste products or pollutants in order to reduce or prevent them through alteration or eliminating of a process. Such activities, consistent with the Pollution Prevention Act of 1990, are conducted across all U.S. EPA programs and can involve cooperative efforts with such agencies as the Departments of Agriculture and Energy

Polymer: A natural or synthetic chemical structure where two or more like molecules are joined to form a more complex molecular structure, such as polyethylene in plastic.

Polyploidy: A condition where the number of chromosomes in a cell is more than normal numbers

Polyuria: Excessive urination; may be a sign of diabetes

Polyvinyl chloride (PVC): A tough, environmentally indestructible plastic that releases hydrochloric acid when burned

POP: Persistent organic pollutants

Potentiation: The ability of one substance or chemical to increase the effect of another

ppb: Parts of a chemical substance contaminant per billion parts

ppm: Parts of a chemical substance contaminant per million parts

Precision: A degree of agreement of repeated measurements of the same property expressed in terms of dispersion of test results about the mean results obtained by repetitive testing of homogenous samples under specified conditions. The precision of a test method is expressed quantitatively as the standard deviation computed from the results of a series of controlled determinations

Procarcinogens: Chemical substances that are not carcinogenic by nature by themselves but upon undergoing body metabolism can become carcinogens

Promoters: Chemical substances or agents that do not cause cancer, but enhance the incidence of cancer on initiated cells

Protocol: The detailed plan with series of steps for conducting a scientific procedure

Pulmonary: Pertaining to the lungs

Purkinje cells: A specific type of nerve cell that carries each and every piece of information output by the cerebellum. These cells possess a great deal of control over the refinement of motor activities

PVC: Polyvinyl chloride

Pyrophoric: A chemical substance that ignites spontaneously in air at a temperature of 130°F (54.4°C) or below

Quality assurance and quality control (QA/QC): A system of procedures, checks, and audits to judge and control the quality of measurements and reduce the uncertainty of data. Some quality control procedures include having more than one person review the findings and analyzing a sample at different times or using different laboratories to see if the findings are similar

Quantitative risk assessment (QRA): A process that relies on mathematical modeling and estimations usually derived from animal test results and the probability of risk for a chemical substance at the low dose to which the human population is normally exposed

Radionuclide: A nuclide with radioactive properties

Radon: A naturally occurring radioactive inert gas that cannot be seen, smelled, or tasted, formed by radioactive decay of radium atoms in soil and rocks

RDA: Recommended daily allowance; the National Academy of Sciences sets the required nutrient values for healthy people in the United States. The values take into consideration the needs of all individuals

RDI: Recommended daily intake

Reactivity: The ability of a chemical substance to undergo a chemical reaction—for instance, combining with another substance; highly reactive substances are often hazardous; the tendency of a chemical substance to undergo a chemical change with the release of energy, often as heat

Recombinant DNA: The new DNA that is formed by combining pieces of DNA from different organisms or cells

Rectal: Pertaining to the rectum

Reduction: The process of removing oxygen from a chemical substance or addition of hydrogen

Registration: Process involving the scientific, legal, and administrative rules and regulations through which a governmental body (U.S. EPA, U.S. Food and

Drug Administration, Central Insecticide Board [CIB, India] and similar bodies in other countries evaluate the ingredients of pesticide formulations

REL: Recommended exposure limit (NIOSH exposure criteria)

Repellent: Any chemical substance that is used to drive away insects, bears, dogs, or other pests

Reproductive toxicity: Effects that may alter the normal reproductive processes of an animal—for instance, loss of fertility

Residue: The pesticide remaining in a product after natural or other processes

Respiratory distress syndrome: A lung disease that occurs primarily in premature infants; the newborn must struggle for each breath and blueing of its skin reflects the baby's inability to get enough oxygen; can also affect adults

Restricted-use pesticide (RUP): A pesticide that can be sold to or used by only certified applicators

RfD: Reference dose; a U.S. EPA estimate, with uncertainty or safety factors built in, of the daily lifetime dose of a substance that is unlikely to cause harm in humans

Risk: The predicted or actual frequency of occurrence of adverse effects caused by chemical substances that may cause harm under a set of conditions

Risk assessment: A process that evaluates the probability that harm will occur in a given set of conditions

Risk/benefit: The relation between the risks and benefits of a procedure or treatment

Rodenticide: A pesticide or other agent used to kill rats and other rodents or to prevent them from damaging food, crops, or forage

RPN: Renal papillary necrosis

RRRs (3R): Reduce, reuse, and recycle

RUP: *See* Restricted-use pesticide

Safe water: Water that does not contain harmful bacteria, toxic materials, chemicals, or substances, and is considered safe for drinking even if it may have taste, odor, color, and certain mineral problems

Safety: Practical certainty and very high probability that injury will not occur from the exposure to a hazard; the reverse function of the sum total of toxicity and bioavailability. Safety may be expressed as safety = $1 \div$ (toxicity $\times$ bioavailability)

Safety factor: A number, normally 100 or 1000, that is divided into the highest no-observed-effect dose arrived at using animal studies to set an acceptable daily intake level for humans

Sampling: A process consisting of the withdrawal or isolation of a fractional part of a whole. In the analysis of gas and polluted air, the separation of a portion of ambient atmosphere with or without the simultaneous isolation of the selected component

SARA: Superfund Amendments and Reauthorization Act. In 1986, SARA amended the CERCLA and expanded the health-related responsibilities of ATSDR. CERCLA and SARA direct ATSDR to look into the health effects from substance exposures at hazardous waste sites and to perform activities including health education, health studies, surveillance, health consultations, and toxicological profiles

Sarcoma: Tumors of connective tissues, muscles, fat cells, bones, and related organs

Sclerosis: A thickening or hardening of a body part, as of an artery, especially from excessive formation of fibrous interstitial tissue

Sensitizer: A chemical substance that on first exposure causes little or no reaction. However, repeated exposure induces a marked response not necessarily limited to the exposure site. This is usually associated with skin sensitization and exposure to chemical substances

SER: Smooth endoplasmic reticulum

Sex-linked genes: A set of genes located on the sex chromosomes (X and Y) of animals and humans

Short-term exposure limit (STEL): The maximum concentration to which workers can be continually exposed for up to 15 minutes. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily TLV-TWA may not be exceeded

Sister chromatid exchange: The genetic process leading to the formation of reciprocal exchange of DNA between the two DNA molecules of a replicating chromosome

Skin sensitization: An immunologically modulated cutaneous reaction to a substance or chemical by an animal. Response by humans to skin sensitization is observed in the form of erythema, edema, papules, pruritis, bullae, and vesicles, as with allergic contact dermatitis

Smog: Extensive atmospheric contamination by aerosols; the term is derived from combining the terms "smoke" and "fog"

Smoke: The small set of gas-borne particles from an incomplete combustion of a variety of materials; essentially consists of carbon and other combustible materials

Solubility: The amount of mass of a substance or chemical that will dissolve in a unit volume of solution; aqueous solubility is the maximum concentration of a chemical that will dissolve in pure water at a reference temperature

Solution: A mixture in which the components are uniformly dispersed

Solvent: A liquid capable of dissolving or dispersing one or more chemical substances; in certain instances the solvents can dissolve many different chemical substances—for instance, water, ethanol, acetone, hexane, and toluene

Soot: An agglomeration of particles of carbon impregnated with tar formed in the incomplete combustion of carbonaceous material

Sorbent: A solid or liquid medium in or upon which materials are retained by absorption or adsorption

Stack: A chimney, smokestack, or vertical pipe that discharges used air

Stack effect: Flow of air resulting from warm air rising, creating a positive pressure area at the top of a building and negative pressure area at the bottom. This

effect can overpower the mechanical system and disrupt building ventilation and air circulation

Static test: A test using aquatic organisms in which there is no flow of the test solution. The test solution remains unchanged throughout the period of testing

STEL: Short-term exposure limit—the maximum amount of the test chemical substance to which a worker may be exposed for 15 minutes

Subchronic delayed neurotoxicity: The repeated daily administration of a test chemical substance causing adverse health effects such as delayed onset of locomotor ataxia

Subchronic toxicity: Appearance of adverse health effects as a result of repeated daily dosing of test chemical substances to experimental animals through oral, dermal, or respiratory route for a period not exceeding 10% of the test animal's life span

Subcutaneous: Injection into the upper layers of the skin

Synergism: A phenomenon where exposure to more than one chemical can result in health effects greater than expected when the effects of exposure to each chemical are added together. In simple terms, 1 + 1 = 3. If chemicals have synergistic properties, the potential hazards of the chemicals should be re-evaluated, taking their synergistic properties into consideration

Systemic effects: Effects that require absorption and distribution of the toxicant to a site distant from its entry point

Target organ toxicity: This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular), extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical

TDI: Tolerable daily intake is the dose expressed on a body weight basis—milligrams per kilogram of body weight per day

TEA: Tetraethyl ammonium

TERA: Toxicology excellence for risk assessment

Teratogen: A chemical substance that causes structural defects and affects normal development, birth defects, and abnormalities in an animal

Teratogenicity: The biological process where chemical substances produce permanent structural and functional abnormalities to the fetus during the period of embryonic development

3MC: 3-methylcholanthrene

Threshold: The lowest dose of a chemical substance below which an adverse effect is not expected

Threshold level: Time-weighted average pollutant concentration values, exposure beyond which is likely to adversely affect human health

Threshold limit value (TLV): The concentration of a substance to which an average person can be repeatedly exposed without adverse effects. TLVs may be expressed in three ways: (1) TLV-TWA (time-weighted average), based on an allowable exposure averaged over a normal 8-hour workday or 40-hour workweek; (2) TLV-STEL (short-term exposure limit) or maximum concentration for a brief specified period of time, depending on a specific chemical substance (TWA must still be met); and (3) TLV-C (ceiling), exposure limit

or maximum exposure concentration not to be exceeded under any circumstances (TWA must still be met)

Tolerance: The amount of a chemical substance legally permitted in food products; tolerance limits are established through formal regulatory procedures—for instance, permissible residue levels for pesticides in raw agricultural produce and processed foods. The use of products with no indication of tolerance values is considered illegal

Toxic: Harmful to living organisms such as microorganisms, plants, animals, and humans

Toxic chemical: A chemical substance that can cause severe illness, poisoning, birth defects, disease, or death when ingested, inhaled, or absorbed by living organisms

Toxic cloud: Airborne plume of gases, vapors, fumes, or aerosols containing toxic materials

Toxicity: The intrinsic capability of a chemical or substance to cause injury or adverse effects to animals, humans, or plants. *Acute toxicity* involves harmful effects caused by chemical substances in an organism through a single or short-term exposure. *Chronic toxicity* is the ability of a chemical substance or mixture of substances to cause harmful effects over an extended period. *Subchronic toxicity* is the ability of the chemical substance to cause effects for more than 1 year but less than the lifetime of the exposed organism

Toxicokinetics: The quantitative uptake of xenobiotics by the body, its biotransformation, distribution, metabolism, and elimination from the body

Toxicological profile: The examination, summary, and interpretation of hazardous chemical substances to determine levels of exposure and associated health effects

TSCA: Toxic Substances Control Act

Tumor: Any abnormal mass resulting from the excessive multiplication of cells; tumors can be cancerous

Tumor, benign: Remains localized and normally does not spread to other parts of the body

Tumor, malignant: Cells break off, invade, and destroy surrounding tissues; cancerous tumors

TWA: Time weight average. The average concentration of a chemical substance in air over the total exposure period of time, which is usually an 8-hour workday

UCM: Urographic contrast medium

UDP: Uridine diphosphate

Ultraviolet rays: Radiation from the sun that can be useful or potentially harmful. UV rays from one part of the spectrum (UV-A) enhance plant life. UV rays from other parts of the spectrum (UV-B) can cause skin cancer or other tissue damage. The ozone layer in the atmosphere partly shields us from ultraviolet rays reaching the Earth's surface

U.S. EPA: U.S. Environmental Protection Agency

Vapor: The gaseous phase of matter normally from liquid or solid material and observed at normal temperature; most organic solvents evaporate and produce vapors

Vinyl chloride: A chemical substance used in producing some plastics that is believed to be oncogenic

Virtually safe dose (VSD): The dose of a chemical substance corresponding to the level of risk determined and accepted by regulatory agencies; the dose-to-risk relationship is based on a chemical dose–response curve

VOCs: Volatile organic compounds; any organic compound that evaporates readily to the atmosphere. VOCs contribute significantly to photochemical smog production and certain health problems

Volatility: The tendency of a liquid to evaporate into a gas or vapor. On inhalation, organic solvents are in the form of vapors

Vulnerable zone: An area over which the airborne concentration of a chemical substance is accidentally released and could reach a level of concern

Wastewater: The spent or used water from a home, community, farm area, or industry that contains dissolved or suspended matter

Water pollution: The presence of water sources that are polluted or contaminated with harmful or objectionable material that can damage the quality of water

Wheezing: Breathing with a rasp or whistling sound; a sign of airway constriction or obstruction

WHO: World Health Organization

Xenobiotics: The chemical substances that are pharmacologically and toxicologically active but foreign to organisms such as microorganisms, plants, birds, animals, and humans

Zero air: Atmospheric air purified to contain less than 0.1 ppm total hydrocarbons

Appendix A.1

TOXICITY RATING OF CHEMICAL SUBSTANCES[a]

Toxicity Rate	Dose	Adult Average Measure
Practically nontoxic	>15 g/kg	More than a quart
Slightly toxic	5–15 g/kg	Between a pint and quart
Moderately toxic	0.5–5 g/kg	Between an ounce and a pint
Very toxic	50–5000 mg/kg	Between a teaspoonful and an ounce
Extremely toxic	5–50 mg/kg	Between seven drops and a teaspoonful
Super toxic	<5 mg/kg	A taste (less than seven drops)

[a] Probable oral lethal dose for a human adult.

Source: Gleason, M. N. et al. 1969. *Clinical Toxicology of Commercial Products: Acute Poisoning,* 3rd ed. Baltimore, MD: Williams & Wilkins.

Appendix A.2

MATERIAL DAMAGE CAUSED BY AIR POLLUTION

Material	Pollutants
Metals	Air pollutants, SO_2, and acid gases cause damage—corrosion, surface damage, loss of metals, tarnishing
Building materials	Air pollutants, SO_2, acid gases, and particulates cause damage, discoloration, leaching
Paint and colors	Air pollutants, SO_2, acid gases, and H_2S cause damage to paint and paint discoloration
Textiles	Air pollutants, SO_2, and acid gases cause deterioration, reduced tensile strength and fading
Textile dyes	Air pollutants, ozone, and NO_2 cause deterioration, reduced strength, and fading
Rubber	Air pollutants, oxidants and ozone cause damage and cracking
Leather	Air pollutants, SO_2, and acid gases cause disintegration, and surface damage
Paper	Air pollutants, SO_2, and acid gases cause embitterment
Ceramics	Air pollutants cause changes in surface appearance

Appendix A.3

MAJOR GLOBAL CHEMICAL DISASTERS

With the ambitious growth of chemical industries to meet national and domestic needs, innumerable compounds are being manufactured. In fact, large volumes are produced, stored, and transported—often with less care and fewer precautions. A large number of chemicals thus produced are known to be toxic and potentially hazardous to man and the environment. In fact, several new instances indicate that chemical accidents have occurred all over the world due to one reason or another. It is clear in almost all cases that negligent, improper management leads to disasters where human health and environmental safety are in jeopardy. The ecological and environmental catastrophe that occurred in November 1986 at a pharmaceutical plant in Schweizerhalle, Basel, Switzerland, was a major ecological disaster that polluted the whole Rhine River with about 66,000 pounds of toxic chemicals. The following are some of the well documented chemical disasters:

October 4, 1918	Large-scale explosion due to ammonium nitrate at Morgan, New Jersey (now Sayreville)
July 26, 1921	Explosion due to ammonium nitrate in Krieweld, Germany (now in Poland)
March 1, 1924	A fire and several large explosions destroyed a warehouse containing ammonium nitrate in New Jersey
April 16, 1947	About 2600 tonnes of ammonium nitrate in sacks in the cargo ship *Grandcamp* exploded, killing several hundred people and setting fire to another vessel
July 28, 1947	The cargo ship *Ocean Liberty* with 3300 tonnes of ammonium nitrate and various inflammable products caught fire and exploded, killing 29 workers and causing serious damage
December 12, 1952, Chalk River, Ottawa, Canada	A partial meltdown of the reactor's uranium fuel core resulted after the accidental removal of four control rods. Although millions of gallons of radioactive water accumulated inside the reactor, there were no injuries
1953, Love Canal, Niagara Falls, New York	Disaster by chemical waste from chemical plants; by the 1990s, the town had been cleaned up enough for families to begin moving back to the area
October 7, 1957, Windscale Pile No. 1, north of Liverpool, England	Fire in a graphite-cooled reactor spewed radiation over the countryside, contaminating a 200-square-mile area
1957, South Ural Mountains	Explosion of radioactive wastes at Soviet nuclear weapons factory 12 miles from the city of Kyshtym forced the evacuation of over 10,000 people from a contaminated area; no casualties were reported by Soviet officials
1974, Decatur, Illinois	Propane explosion caused seven deaths and 152 injuries

1974, Flixborough, U.K.	Explosion in caprolactum plant resulted in 28 deaths and 89 injuries
1975, Beek, the Netherlands	Propylene explosion resulted in 14 deaths and 107 injuries
1976, Seveso, Italy	Dioxin/TCDD caused 193 injuries
1977, Chicago, Illinois	Hydrogen sulfide release resulted in eight deaths and 29 injuries
1978, Santacruz, Mexico	Methane fire resulted in 52 deaths
1978, Xilatopec, Mexico	Gas explosion in transit caused 100 deaths and 150 injuries
March 28, 1979, Three Mile Island, Harrisburg, PA	One of two reactors lost its coolant, which caused overheating and partial meltdown of its uranium core. Some radioactive water and gases were released. This was the worst nuclear-reactor accident in U.S. history
1979, Novosibirsk, USSR	Chemical plant accident resulted in 300 deaths
1980, Sommerville, U.S.	PCl_3 accident caused 300 injuries
1981, Tacoa, Venezuela	Oil explosion resulted in 145 deaths
1982, Taff, U.S.	Acrolein explosion occurs
1984, Sao Paulo, Brazil	Petro pipeline explosion causes 508 deaths
1984, Ixhuatepec	LPG tank explosion results in 452 deaths and 4258 injuries
December 2–3, 1984, Bhopal, India	Leakage of methyl isocyanate (MIC) gas in a pesticide plant causes exposure of half a million people to the deadly gas. More than 20,000 people died and more than 120,000 people still suffer from severe ailments
April 26, 1986, Chernobyl, Kiev, Ukraine	Explosion and fire in the graphite core of one of four reactors released radioactive material that spread over part of the Soviet Union, Eastern Europe, Scandinavia, and, later, Western Europe. Claimed dead total was 31. Total casualties are unknown. This is the worst such accident to date
1886, Devnya, Bulgaria	Fire in a chemical complex resulted in 17 deaths and 19 injuries
September 18, 1987, Goiânia, Brazil	244 people contaminated with cesium-137 from a cancer-therapy machine that had been sold as scrap. Four people died in the worst radiation disaster in the Western Hemisphere
1988, North Sea, U.K.	Pipe alpha oiling explosion caused 166 deaths
September 30, 1999, Tokaimura, Japan	Uncontrolled chain reaction in a uranium-processing nuclear fuel plant spewed high levels of radioactive gas into the air, killing two workers and seriously injuring one
September 21, 2001	About 200–300 tons of ammonium nitrate granules caused an explosion resulting in 31 people dead and 2,442 injured, 34 of them seriously
April 22, 2004, Ryongchon, China	Ryongchon disaster: A freight train carrying ammonium nitrate exploded near the Chinese border and killed 162 people and injured over 3000 others
August 9, 2004, Mihama, Japan	Nonradioactive steam leaked from a nuclear power plant, killing four workers and severely burning seven others.
July 17, 2007, Kashiwazaki, Japan	Radiation leaks, burst pipes, and fires at a major nuclear power plant followed a 6.8 magnitude earthquake near Niigata. Japanese officials, frustrated at the plant operators' delay in reporting the damage, closed the plant a week later until its safety could be confirmed. Investigations revealed that the plant had been built, unknowingly, directly on top of an active seismic fault

Appendix A.4

TRANSPORTATION AND GLOBAL CHEMICAL DISASTERS

Toxic Chemical	Country	Year
Crude oil, phenol	Markus Hook, U.S.	1975
Ammonia	Deer Park and Houston, U.S.	1976
Hydrogen bromide	Rockwood, U.S.	1977
Chlorine leakage	Youngstown, U.S.	1977
Propylene	San Carlos, Spain	1977
Oil, gas	Bantry Bay, Ireland	1979
Chlorine explosion	Mississauga, Canada	1979
Nitric acid leakage	Blythe, U.S.	1981
Chlorine	Montanas, Mexico	1981
Silicon tetra chloride	San Francisco, U.S.	1981
Butadine	Melbourne, Australia	1982
LPG explosion	Egypt	1983
Ammonia	Matamoros, Mexico	1984
PCB	Kenora, Canada	1985
Gasoline	Tamil Nadu, India	1985
Phosphoric acid	Maimisburg, U.S.	1985
Lead oxide	Hemel Hampstead, U.K.	1985
Phosphorous oxychloride	Pittsburg, U.S.	1987
Chlorine	Annan, USSR	1987
Gasoline	Herborn, Germany	1987
Explosives, explosion	Arzamas, USSR	1988
Pesticides	Chakhnounia, USSR	1988
Explosives	Sverdiorsk, USSR	1988
Toxic chemicals storage	Shenzhen, China	1993

Sources: UNEP (United Nationals Environmental Programme) compilation, *Manual on Emergency Preparedness,* Ministry of Enviornment and Forestry, Government of India; Workshop on Transportation of Dangerous Goods, New Delhi, India, October 18, 2001.

Appendix A.5

CHEMICAL SUBSTANCES, INDUSTRIES, AND POLLUTION

- Primary metallurgical manufacturing industries (viz., zinc, lead, copper, aluminum, and steel)
- Paper, pulp, and newsprint
- Pesticides
- Refineries
- Fertilizers
- Paints
- Dyes and color pigments
- Leather tanning and leather processing
- Rayon and synthetic fiber manufacturing
- Sodium/potassium cyanide-associated industries
- Basic drugs manufacturing
- Foundry industries
- Storage batteries (lead acid type)
- Acids/alkalis
- Plastics fabrication
- Rubber-synthetic manufacturing
- Cement processing and manufacturing
- Asbestos and associated operations
- Fermentation industry
- Electroplating industry

Appendix A.6

GLOBAL REGULATORY AGENCIES AND CHEMICAL SUBSTANCES

Air

Clean Air Act
National ambient air quality standards
Air toxics (HAPS)
Motor vehicle emission standards

Water

Safe Drinking Water Act
Clean Water Act

Food

Food Quality Protection Act
Federal Food, Drug and Cosmetic Act

Agrochemicals/Pesticides

Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), United States
Insecticide Act (Central Insecticide Board), Ministry of Agriculture, government of India, Control of Pesticides Act, No. 33 of 1980
Parliament of the Democratic Socialist Republic of Sri Lanka

Hazardous Waste

Resources Conservation and Recovery Act
Comprehensive Environmental Response Compensation and Liability Act
Superfund Amendments and Reauthorization Act

Sources: U.S. Environmental Protection Agency and U.S. Food and Drug Administration, 1999.

Appendix A.7

CHEMICAL SUBSTANCES AND ADVERSE HEALTH EFFECTS

Acid, acetic
- Uses: used to make acetates, plastics, acetate rayon, and as a solvent
- Health effects: skin is yellow where it comes in contact with the acid, burns on the lips and mouth, pain in the throat and stomach, difficulty in swallowing, nausea and vomiting, feeble pulse, diarrhea, and collapse

Acid, boric
- Uses: used as eyewash and in external ointments
- Health effects: nausea, diarrhea, headache, cold sweat, subnormal temperature, rash, and collapse

Acid, 2,4-dichlorophenoxyacetic (2,4-D)
- Uses: weed killer
- Health effects: causes irritation of eyes, intestinal disturbance, muscle stiffness, paralysis, and coma

Acid, hydrochloric
- Uses: extensive use in industry and in the laboratory
- Health effects: the lips and mouth on contact with the acid are usually white at first, but later turn brown; pain in the throat and stomach; difficulty in swallowing; nausea and vomiting; feeble pulse; diarrhea; and collapse

Acid, hydrocyanic
- Uses: gas used as a fumigant for citrus trees, and in ships and buildings against rodents and vermin; salts used for case-hardening steel
- Health effects: nausea and vomiting, feeble pulse, shallow breathing, dyspnea, cyanosis, convulsions, and collapse (possesses a peculiar peach-blossom odor)

Acid, hydrofluoric
- Uses: gas or liquid used for etching glass and in manufacture of fluorides
- Health effects: skin becomes yellow where it comes in contact with the acid, burns on the lips and mouth, pain in the throat and stomach, difficulty in swallowing, nausea and vomiting, feeble pulse, diarrhea, and collapse

Acid, nitric
- Uses: extensive use as a nitrating agent in making explosives and fertilizers
- Health effects: stains on the lips and mouth are first white, later turning to a deep yellow

Acid, oxalic
- Uses: used as an industrial bleach and as an oxidation-reduction standard
- Health effects: stains on the lips and mouth are first white, later turning to a deep yellow

Acid, phosphoric
- Uses: used in manufacture of many phosphates, and in engraving and lithography
- Health effects: stains on the lips and mouth are first white, later turning to a deep yellow

Acid, picric
- Uses: used in matches, explosives, the leather industry, and the manufacture of mordant textiles
- Health effects: causes skin to turn yellow where it contacts the acid, feeble pulse, nausea and vomiting, convulsions, and collapse

Acid, sulfuric
- Uses: the most widely used acid in chemical laboratories
- Health effects: stains on the lips and mouth are first white, later turning to a deep yellow

Alcohol, ethyl (grain alcohol)
- Uses: used in beverages, medicines, and extracts
- Health effects: the effects vary with individual patients; some become quarrelsome, some sentimental, and others fall asleep; nausea; vomiting; and depression

Alcohol, isopropyl
- Uses: used in medicines and extracts
- Health effects: the effects vary with individual patients; some become quarrelsome, some sentimental, and others fall asleep; nausea; vomiting; and depression

Alcohol, methyl (wood alcohol)
- Uses: used as solvent for shellacs and resins, in the manufacture of dyes and varnishes, as an antifreeze and a fuel, and for other uses
- Health effects: initial symptoms like those of ethyl alcohol; subsequently the patient develops nausea, vomiting, dizziness, headache, dilated pupils, delirium, and blindness

Ammonium hydroxide (ammonia water)
- Uses: used in cleaning and bleaching, removing stains, and home use
- Health effects: burns on the lips and mouth, severe pains in the throat and stomach, diarrhea, weak pulse, pallor, and collapse

Antimony trichloride
- Uses: used in medicine and in manufacturing
- Health effects: metallic taste in the mouth, pains in the abdomen, nausea, vomiting blood, and spasms of the fingers, arms, and legs, followed by collapse

Antimony potassium tartrate
Uses: used as an emetic and expectorant
Health effects: similar to antimony trichloride

Antu
Uses: rodenticide
Health effects: sharp drop in temperature and pulmonary edema

Arsenic
Uses: used in hardening metals and alloys, and as rat poisons, flypaper, tree and garden sprays, dyes, and for many other uses
Health effects: pain in the throat and stomach, nausea and vomiting, pallor, weak pulse, abdominal cramps, thirst, coma, convulsions, and collapse

Barium compounds (barium acetate, barium carbonate, barium chloride, barium sulfide, barium sulfite)
Uses: barium sulfide is used as a depilatory and in luminous paints
Health effects: nausea and vomiting, abdominal cramps, diarrhea, salivation, paralysis of the arms and legs, pallor, and weak pulse

Benzene hexachloride (BHC)
Uses: insecticide
Health effects: vomiting, diarrhea, convulsions, and difficulty in breathing

Bismuth compounds
Uses: used medicinally many times as bismuth dressings
Health effects: nausea and vomiting, salivation, a blue line at the junction of the teeth and gums, and swelling of the gums, tongue, and throat

Borates
Uses: used in cleansers, soaps, and detergents
Health effects: nausea, diarrhea, headache, cold sweat, subnormal temperature, rash, and collapse

Bromides
Uses: as drugs like sodium bromide, potassium bromide, and ammonium bromide
Health effects: mental confusion, nausea, vomiting, stomach pains, delirium, and coma

Cadmium
Uses: used for plating other metals and alloys
Health effects: nausea, vomiting, diarrhea, headache, stomach pains, and salivation

Calcium hydroxide and calcium oxide
Uses: in plasters, cements, mortars, water paints, for dehairing hides, and in insecticides
Health effects: pain in the throat and stomach, nausea and vomiting, thirst, pallor, weak pulse, and collapse

Carbon dioxide
- Uses: used in beverages and fire extinguishers, as solid dry ice, and as a refrigerant
- Health effects: headache, unconsciousness, and respiratory and cardiac failure

Carbon monoxide
- Uses: present in automobile exhaust and in some industrial gases
- Health effects: headache, bluish-red patches on body, unconsciousness, and cardiac and respiratory failure

Carbon tetrachloride
- Uses: used in extinguishers and dry cleaning, as a solvent, and for many other uses
- Health effects: nausea, vomiting, headache, dizziness, pallor, weak pulse, and subnormal temperature

Chloral hydrate
- Uses: used to induce sleep; also known as "knockout drops"
- Health effects: drowsiness, lassitude, cold hands and feet, nausea, vomiting, headache, stupor, and heart failure

Chlordane, dieldrin, DDT, heptachlor
- Uses: insecticides and pest control
- Health effects: overexcitability, tremors, convulsions, nausea, vomiting, weakness, depression, and coma

Chlorine and chlorine water
- Uses: used to disinfect and deodorize and as a bleach for wood, paper, pulp, cotton, and many other products
- Health effects: pain in the throat and stomach, nausea and vomiting, weak pulse rate, pallor, and difficulty breathing

Chloroform
- Uses: used as an anesthetic and analgesic
- Health effects: slow, weak pulse, becoming ever slower; pallor; diluted pupils; and paralysis of the heart

Copper compounds (copper acetate or cupric acetate, copper sulfate or cupric sulfate)
- Uses: uses are similar to those of copper aceto-arsenite, cupric acetate; cupric copper acetate or cupric acetate is used in the manufacture of pigments, fungicides, algaecides, and insecticides; copper aceto-arsenite is used as a pigment, an insecticide, and a wood preservative
- Health effects: all copper compounds cause nausea and vomiting, pallor, diarrhea, collapse, and heart failure

Creolin, creosote, and cresols
- Uses: used as water emulsion of phenolics (cresols) and as disinfectants, germicides, and deodorants
- Health effects: like phenol, these chemicals cause severe burns

Cyanides of potassium, sodium and other salts
- Uses: cyanide salts are used in silver and gold mining—the cyanide process; sodium cyanide is extensively used in industries for electroplating; calcium cyanide is used as a fumigant; potassium silver cyanide is used in silver plating; potassium ferrocyanide is used to achieve a blue color on cast bronze sculptures
- Health effects: nausea, vomiting, feeble pulse, shallow breathing, dyspnea, cyanosis, convulsions, coma with apnea, cardiac arrest, and death

Dinitro-*o*-cresol
- Uses: selective weed killer and insecticide
- Health effects: thirst, fatigue, excessive sweating, nausea, vomiting, abdominal pains, high temperature, difficulty in breathing, restlessness, convulsions, and prostration

Dinitrophenol
- Uses: selective weed killer and insecticide
- Health effects: thirst, fatigue, excessive sweating, nausea, vomiting, abdominal pains, high temperature, difficulty in breathing, restlessness, convulsions, and prostration

Ether
- Uses: used as general anesthetic, stimulant, solvent, and cleaning agent
- Health effects: causes slow, weak pulse, becoming ever slower; pallor; diluted pupils; and paralysis of the heart

Fluorides
- Uses: fluoride compounds are used in making steel, chemicals, ceramics, lubricants, dyes, plastics, and pesticides; fluorine and hydrogen fluoride are used to make certain chemical compounds; hydrofluoric acid is used for etching glass; fluorides are also added to drinking water, dental products, toothpaste, and mouth rinses
- Health effects: fluoride has both beneficial and detrimental effects on tooth enamel; causes burning, cramp-like pains in the abdomen; grayish-blue skin; feeble pulse; pallor; and collapse

Fluoroacetates
- Uses: rat poison
- Health effects: causes nausea, vomiting, mental uneasiness, epileptiform convulsions, uneven heart beat and respiration, exhaustion, and coma

Formaldehyde
- Uses: used in embalming fluids; for hardening; films; and as a germicide, antiseptic, and deodorant
- Health effects: nausea and vomiting, clammy skin, feeble pulse, pallor, burning in the mouth and throat, and collapse

Gasoline
- Uses: several uses; the largest is as fuel
- Health effects: nausea, vomiting, headache, giddiness, and affected vision

Hydrogen peroxide
Uses: used in medicine and also as a bleaching agent, an oxidizing agent, an antiseptic, and a catalyst
Health effects: nausea and vomiting, pallor, and feeble pulse

Hydrogen sulfide
Uses: used as a reducing agent
Health effects: nausea, vomiting, greenish face, feeble pulse, coma, and respiratory failure

Iodoform
Uses: used as an antiseptic
Health effects: headache; rapid, feeble pulse; pallor; dizziness; and collapse

Lead compounds
Uses: several uses in industry
Health effects: headache, metallic taste in mouth and throat, nausea, vomiting, blue line on the gums, constricted throat, diarrhea, anemia, and paralysis

Lye or sodium hydroxide
Uses: used extensively in industry and in the home
Health effects: burning effects on the lips and mouth, severe pains in the throat and stomach, diarrhea, feeble pulse, pallor, and collapse

Mercury compounds (mercuric oxide, red; mercuric oxide, yellow; mercurous chloride; mercury bichloride)
Uses: many uses in medicine and in various industries
Health effects: causes metallic taste in the mouth; nausea; vomiting; thirst; diarrhea; feeble pulse; slow, shallow breathing; and collapse

Naphthalene
Uses: used as moth balls and in dye, resin, and plastic industries
Health effects: restlessness, depression, twitching, urine is brown to black, feeble pulse, coma, and snoring

Phenol
Uses: as an antiseptic, disinfectant, and deodorant
Health effects: whitish burns on the mouth, pains in the throat and stomach, nausea, vomiting, dizziness, feeble pulse, shallow breathing, depression, and unconsciousness

Phosphorus, red, and phosphorus, white
Uses: used in fireworks and poisons for mice and rats
Health effects: causes nausea and vomiting, a garlic taste, headache, feeble pulse, diarrhea, vomiting, and collapse (phosphorus is luminous in the dark)

Potassium carbonate
Uses: used in the manufacture of soap, glass, and pottery
Health effects: nausea, vomiting, pain in the throat and stomach, feeble pulse, and collapse

Potassium chlorate
- Uses: used in the manufacture of matches, fireworks, and many other items
- Health effects: nausea, vomiting, pain in the throat and stomach, diarrhea, jaundice, feeble pulse, cyanosis, coma, and collapse

Potassium permanganate
- Uses: bleaching resins, waxes, oils, and fats
- Health effects: nausea; vomiting; rapid, feeble pulse; cold, clammy skin; and collapse

Silver nitrate
- Uses: manufacture of indelible inks and silver salts, used for resilvering mirror surfaces
- Health effects: nausea, vomiting, black vomitus, throat and stomach pain, feeble pulse, coma, and collapse

Sodium carbonate
- Uses: manufacture of soap, glass, and sodium salts and as a detergent and water (treatment) softener
- Health effects: nausea, vomiting, pain in the throat and stomach, feeble pulse, and collapse

Sodium fluoride
- Uses: insecticide
- Health effects: burning, cramp-like pains in the abdomen; grayish-blue skin; feeble pulse; and collapse

Sodium fluoroacetate
- Uses: rat poison
- Health effects: nausea, vomiting, mental uneasiness, epileptiform convulsions, uneven heart beat and respiration, exhaustion, and coma

Sodium hydroxide
- Uses: manufacture of paper and soap, in oil refining, and numerous other industries
- Health effects: burns on the lips and mouth; severe pains in the throat and stomach; diarrhea; feeble, weak pulse; and collapse

Sodium nitrate
- Uses: manufacture of diazo dyes
- Health effects: nausea, vomiting, flushed face, violent and lessened heart action, dilated pupils, and collapse

Thallium salts
- Uses: rat poisons and ant powders
- Health effects: severe abdominal pains, purplish gums, foul breath, salivation, and respiratory failure

Thiocyanates
- Uses: insecticide
- Health effects: respiratory difficulty and convulsions

Toxaphene
- Uses: insecticide
- Health effects: convulsions sometimes preceded by nausea, vomiting, weakness, lassitude, and amnesia

White lead
- Uses: used in putty and pigments
- Health effects: metallic taste, dry throat, nausea, vomiting, diarrhea, leg cramps, blue line on gums, feeble pulse, anemia, and paralysis

Zinc acetate; zinc chloride; zinc sulfate
- Uses: used in medicine and many industries
- Health effects: metallic taste, pain in the stomach, salivation, nausea, vomiting, bloody vomitus, purging, pallor, and collapse

Zinc phosphide
- Uses: rat poison
- Health effects: difficulty in breathing, nausea, vomiting, stomach pains, diarrhea, slow action of heart, and circulatory collapse

Appendix A.8

PEROXIDIZABLE CHEMICAL SUBSTANCES

Acetal
Acetaldehyde
Acrylamide
Acrylic acid
Acrylonitrile
Allyl ethyl ether
Allyl phenyl ether
Allyl vinyl ether
1-Allyloxy-2,3-epoxypropane
Benzyl-1-naphthyl ether
Benzyl butyl ether
Benzyl ethyl ether
Bis(2-ethoxyethyl) ether
Bis(2-methoxyethyl) ether
1,3-Butadiene
1,3-Butadiyne
2-Butanol
Buten-3-yne
Butyl ethyl ether
Butyl formate
Butyl vinyl ether
2-Chloro-1,3-butadiene
1-Chloro-2,2-diethoxyethane
2-Chloroacrynitrile
2-Chloroethyl vinyl ether
Chloroethylene
Chloroprene
Chlorotrifluoroethylene
Cinnamaldehyde
Crotonaldehyde
Cyclohexene
Cyclooctene
Cyclopropyl methyl ether
Decahydronaphthalene
Decalin
Di(2-propynyl)ether
Diacetylene
Diallyl ether
p-Dibenzyloxybenzene
1,2-Dibenzyoxyethane
Dibutyl ether
1,1-Dichloroethylene
Dicyclopentadiene
1,1-Diethoxyethane
1,2-Diethoxyethane
Diethoxymethane
3,3-Diethoxypropene
Diethyl ether
Diethyl ether
Diethyl fumarate
Diethylene glycol dimethyl ether
Diethylketene
Diglyme
2,3-Dihydrofuran
2,3-Dihydropyran
Diisopropyl ethera
1,1-Dimethoxyethane
1,2-Dimethoxyethane
1,1-Dimethoxypropane
2,2-Dimethoxypropane
3,3-Dimethoxypropene
2,2-Dimethyl-1,3-dioxolane
2,6-Dimethyl-1,4-dioxane
1,3-Dioxane
1,4-Dioxane
1,3-Dioxep-5-ene
1,3-Dioxol-4-en-2-one
Dipropoxymethane
Dipropyl ether
Divinyl acetylenea
Divinyl ether
1-Ethoxy-2-propyne
1,2-Epoxy-3-isopropoxy propane
2-Ethoxyethanol
2-Ethyl butanal
Ethyl isopropyl ether

Dibenzyl ether
Ethyl vinyl ether
2-Ethylacrylaldehyde oxime
Ethylene glycol dimethyl ether
2-Ethylhexanal
2-Ethylhexyl vinyl ether
2-Furaldehyde
Furan
Glyme compounds
4,5-Hexadien-2-yn-1-ol
2,4-Hexadienal
2,5-Hexadiyn-1-ol
2-Hexenal
Indole-2-carboxyaldehyde
Isobutyl vinyl ether
Isobutyraldehyde
Isopropoxypropionitrile
Isopropyl alcohol
Isopropyl ether[a]
Isopropyl propyl ether
Isopropyl vinyl ether
2-Isopropylacrylaldehyde oxime
Isovaleraldehyde
Limonene
1,5-*p*-Menthadiene
2-Methoxyethanol
Methoxy-1,3,5,7-cyclo octatetraene
2-Methoxyethanol
2-Methoxyethyl vinyl ether
Methyl acetylene
Methyl methacrylate
4-Methyl-1,3-dioxane
2-(1-Methylheptyl)-4,6 dinitrophenyl crotonate
Ethyl propenyl ether
2,3-Methyl-2-methylene butanal
4-Methyl-2-pentanone
2-Methyltetrahydrofuran
Methyl vinyl ether
2-Penten-4-yn-3-ol
a-Pentylcinnamaldehyde
Potassium[a] (forms yellow potassium peroxide on the surface)
Potassium amide
2-Propanol
Propionaldehyde
2-Propyne-1-thiol
Sodium amide[a]
Sodium 5,8,11,14,-eicosatetraenoate
Sodium ethoxyacetylide
Styrene
1,1,2,3-Tetrachloro-1,3,-butadiene
Tetrafluoroethylene
Tetrahydrofuran
Tetrahydronaphthalene
Tetrahydropyran
Tetralin
Tridecanal
1,3,3-Trimethoxypropene
3,3,5-Trimethyl-2-cyclo-hexene-1-one (isophorone)
Vinyl acetate
Vinyl acetylene
Vinyl chloride
Vinyl ethers
Vinyl pyridine
4-Vinylcyclohexene
Vinylidene chloride

[a] Forms peroxides rapidly upon storage.

Sources: From Bretherick, L. 1990. *Handbook of Reactive Chemicals Hazards*, 4th ed. London: Butterworth.

Appendix A.9

SHELF LIVES OF UNSTABLE CHEMICAL SUBSTANCES

Peroxide hazard on storage; discard after 3 months:

Isopropyl ether
Sodium amide
Vinylidene chloride
Divinyl acetylene, potassium metal

May cause peroxide hazard; discard after 1 year:

Acetal
Cumene
Diacetylene
Dioxane
Ethylene glycol dimethyl ether
Methyl isobutyl ketone (glyme)
Tetrahydronaphthalene
t-Butyl alcohol
Cyclohexane
Dicyclopentadiene
Ethyl ether
Metal acetylene
Tetrahydrofuran
Vinyl ethers

Hazardous to peroxide initiation of polymerization; discard after 1 year:

Butadiene
Chlorotrifluoroethylene
Indene
Tetrafluoroethylene
Vinyl chloride
Chlorobutadiene (chloroprene)
9,10-Dihydroanthracene
Styrene
Vinyl acetylene
Vinyl pyridine

Appendix A.10

TOXICITY TO THE HUMAN FETUS OF CHEMICAL SUBSTANCES AND DRUGS

Chemicals	Adverse Effects
Alcohols	Muscular hippotonia
Antibacterials	Deposition in bones
Streptomycin	Discoloration of teeth
Tetracyclines	Inhibition of bone growth
Sulfonamides	Eighth nerve damage (anemia)
Novobiocin	Hyperbilirubinemia
Erythromycin	Liver damage
Nitrofurantoin	Hemolysis
Anticoagulants	
Coumarin	Hemorrhage, death
Antidiabetics	
Tolbutamide	Thrombocytopenia
Chlorpropamide	Prolonged hypoglycemia
Phenoformin	Lactic acidosis
Insulin (shock)	Fatal
Ammonium chloride	Acidosis
Antihistamines	Infertility
Antithyroid drugs	Hypothyroidism
Barbiturates	Coagulation defects
Diphenyl hydrantoin	Withdrawal syndrome
Phenobarbital in excess	Neonatal bleeding, death
Diazepam	Hypothermia
Sedatives	Behavioral changes
Meprobamate	Retarded development
Meperidine	Neonatal depression
Primidone	Withdrawal symptoms
Heroin, morphine	Withdrawal syndrome
Reserpine	Nasal congestion, lethargy, respiratory depression, brachycardia
Phenothiazines	Hyperbilirubinemia, depression, hypothermia
Magnesium sulfate	Central depression, neuromuscular block
Chloroquine	Death
Organic solvents	Newborn depression
Salicylates (in large amounts)	Bleeding

Appendix A.11

RESPIRATORY IRRITANT CHEMICAL SUBSTANCES

Chemical Substance	Nature of Respiratory System Injury
Acetaldehyde	Upper airway injury; rarely causes delayed pulmonary edema
Acetic acid and organic acids	Ocular injury and upper airway injury
Acid anhydrides	Ocular injury and upper airway injury, pulmonary hemorrhage, bronchospa
Acrolein	Diffuse airway and parenchymal injury
Ammonia	Ocular injury, upper airway burn, and bronchiectasis
Antimony trichloride and antimony pentachloride	Pneumonitis, noncardiogenic pulmonary edema
Asbestos dust	Asbestosis, alveolar damage, diffuse pleural fibrosis, lung cancer
Beryllium dusts, fume	Acute upper airway injury, tracheobronchitis, chemical pneumonitis, beryllosis
Boranes (diborane)	Upper airway injury, pneumonitis
Cotton dust	Byssinosis
Crystalline silica	COPD, emphysema, silicosis, lung cancer
Cadmium	Tracheobronchitis, pulmonary edema, inflammatory changes, emphysema
Calcium oxide, calcium hydroxide	Upper and lower airway inflammation, pneumonitis
Chlorine	Upper and lower airway inflammation, pneumonitis, noncardiogenic pulmonary edema
Chloroacetophenone (tear gas)	Ocular and upper airway inflammation, lower airway and parenchymal injury with masssive exposure
o-Chlorobenzomalonitrile	Ocular and upper airway inflammation, lower airway injury with massive exposure
Chloromethyl ethers	Upper and lower airway irritation; a respiratory tract carcinogen
Chloropicrin	Inflammation of upper and lower airway
Chromic acid (Cr IV)	Nasal inflammation and ulceration, rhinitis, pneumonitis with massive exposure
Coal dust	Chronic bronchitis, pneumoconiosis, obstructive lung disease, focal emphysema, progressive massive fibrosis (PMF), coal workers' pneumoconiosis (CWP), silicosis
Cobalt	Acute bronchospasm, pneumonitis, chronic exposure leads to lung fibrosis, progressive massive fibrosis (PMF), coal workers' pneumoconiosis (CWP), silicosis
Formaldehyde	Ocular and upper airway irritation, bronchospasm in severe exposure, contact dermatitis
Hydrochloric acid	Ocular and upper airway inflammation, on heavy exposure lower airway inflammation

(continued on next page)

Chemical Substance	Nature of Respiratory System Injury
Hydrofluoric acid	Ocular and upper airway inflammation, tracheobronchitis, pneumonitis
Hydrogen bromide	Upper airway injury, pneumonitis with massive exposure
Isocyanates	Ocular, upper and lower inflammation, asthma, hypersensitivity pneumonitis
Lithium hydride	Pneumonitis, noncardiogenic pulmonary edema
Mercury	Ocular and respiratory tract inflammation, pneumonitis; central nervous system (CNS), kidney, and systemic effects
Methyl bromide	Upper and lower airway injury, pneumonitis, CNS depression, seizures
Nickel carbonyl	Lower respiratory irritation, pneumonitis, delayed systemic toxic effects
Nitrogen dioxide	Ocular and upper airway inflammation, noncardiogenic pulmonary edema, delayed onset bronchiolitis
Nitrogen mustards and sulfur mustards	Ocular, upper, and lower airway inflammation; pneumonitis
Osmium tetroxide	Severe ocular and upper airway irritation, transient renal damage
Ozone	Upper and lower airway inflammation; asthmatics are highly susceptible
Paraquat	Pulmonary fibrosis
Phosgene	Upper airway inflammation and pneumonitis; low doses cause delayed pulmonary edema
Phosphoric chlorides	Ocular and upper airway inflammation
Phosphoric sulfides	Ocular and upper airway inflammation
Selenium dioxide	Ocular and upper airway inflammation, pulmonary edema in massive exposure
Styrene	Ocular, upper, and lower airway inflammation; neurological impairments
Sulfur dioxide	Upper airway inflammation, bronchoconstriction, pneumonitis on massive exposure
Titanium tetroxide	Upper airway injury
Toluene 2,4-diisocyanate (TDI)	Asthma
Uranium hexafluoride	Upper and lower airway injury, bronchospasm, pneumonitis
Vanadium pentoxide	Ocular, upper and lower airway symptoms
Zinc chloride	Upper and lower airway irritation, fever, delayed onset pneumonitis

Appendix A.12

EXPLOSIVE CHEMICAL SUBSTANCES (IN OVERPRESSURIZED CONTAINERS)

Aluminum chloride
Aluminum lithium hydride
Ammonia solution
Ammonium hydroxide
Ammonium persulfate
Anisyl chloride
Aqua regia
Benzenesulfonyl chloride
Bleach
Bleaching powder
Calcium carbide
Calcium hydride
Calcium hypochlorite
Chloroform
Chromic acid
Cumene hydroperoxide
Cyclohexene
Diethyl pyrocarbonate
Dimethylamine
Formic acid
Hydrogen peroxide
Lauroyl peroxide
Lithium aluminum hydride
Lithium hydride
Nitric acid
Nitrosoguanidine
Peracetic acid
Phenol
Phosphorus trichloride
Potassium persulfate
Silicon tetrachloride
Sodium borohydride
Sodium dithionite
Sodium hydride
Sodium hydrosulfite
Sodium hypochlorite
Sodium peroxide
Sodium persulfate
Thionyl chloride
Urea peroxide
Zinc

Appendix A.13

FLAMMABLE CHEMICAL SUBSTANCES

A flammable chemical substance is a solid, liquid, vapor, or gas that ignites easily and burns rapidly in air. Many of the flammable chemicals used in laboratories are flammable liquids and organic solvents. The vapors of these chemical substances form ignitable mixtures with air. Based on the flash points of these chemicals, classifications are made. The flash point of a chemical substance is defined as the lowest temperature at which a fuel–air mixture present above the surface of a liquid will ignite, if an ignition source is present. The common flammable chemical substances include, but are not restricted to, acetone, benzene, cyclohexane, ethanol, ethyl acetate, ethyl ether, gasoline, hexane, isopropyl alcohol, methanol, propanol, tetrahydrofuran and toluene, and xylene.

Students and workers in laboratories should always remember three important words—*danger, warning,* and *caution* (or A, B, C)—while handling flammable liquids to avoid health effects and chemical disasters:

- *Danger* (A) denotes the highest degree of the chemical hazard. This includes chemical substances of classes 1A and 1B under flammable liquids and with flash points less than 73°F.
- *Warning* (B) denotes the intermediate degree of the chemical hazard. This includes chemical substances of class 1C flammable liquids with flash points at or above 73°F, but below 100°F.
- *Caution* (C) denotes the lowest degree of the chemical hazard. This includes chemical substances of class II flammable liquids with flash points at or above 100°F, but below 140°F.

All flammable chemical substances are classified according to flash point, boiling point, and ignition temperature:

- Flash point (FP) is the lowest temperature at which a flammable liquid gives off sufficient vapor to ignite.
- Boiling point (BP) is the temperature at which the vapor pressure of a liquid is equal to the atmospheric pressure under which the liquid vaporizes.
- Ignition temperature is the lowest temperature at which a chemical substance will ignite and burn independently of its heat source.

PRECAUTIONS

Students in the laboratory and workers in different workplaces must:

- strictly observe the properties of the chemical substances during use, storage, transportation, and waste disposal;
- use appropriate personal protective equipment (PPE);
- always take care to minimize vapors, which act as fuel, while using flammables;
- avoid negligence and know proper use of flammable liquids;
- avoid all conditions for a fire to occur at the workplace;
- maintain storage of minimum quantities of flammable chemical substances in the workplace; and
- keep fire extinguishers in easily approachable work areas, and be familiar with their use.

Flammable Chemical Substances

Chemical	Flash Point (°F)	Class
Acetone	0	1B
Benzene	12	1B
Butyl acetate	>72	1C
Carbon disulfide	–22	1B
Cyclohexane	–4	1B
Diethylene glycol	225	3B
Diethyl ether	–49	1A
Ethanol	55	1B
Heptane	25	1B
Isopropyl alcohol	53	1B
Methanol	52	1B
Pentane	<–40	1A
Toluene	40	1B

Appendix A.14

FLAMMABLE LIQUIDS

Solvent	Class	Flash Point	Boiling Point
Diethyl ether[a]	1A	–45	35
Ethyl ether[a]	1A	–45	35
Pentane[a]	1A	–40	36
Acetaldehyde[a]	1A	–38	21
Gasoline[a]	1B	–38	41
Propylene oxide[a]	1A	–37	35
Carbon disulfide[a]	1B	–30	46
Acrolein[a]	1B	–26	52
Hexane[a]	1B	–22	69
Ethylamine (70% solution)[a]	1A	–18	38
Acetone[a]	1B	–18	57
Diethylamine[a]	1B	–18	57
Petroleum ether[a]	1B	–18	35–60
Benzene[a]	1B	–11	80
Propanol-n[a]	1B	–8	49
Methyl ethyl ketone[a]	1B	–6	80
Ethyl acetate[a]	1B	–4	77
Toluene[a]	1B	4	111
Methanol[a]	1B	11	64
Propanol-iso[a]	1B	12	83
p-Dioxane[a]	1B	12	101
Ethanol (95%)[a]	1B	17	78
Ethanol (80%)[a]	1B	20	78
Ethanol (70%)[a]	1B	21	78
Ethanol (50%)[a]	1C	24	78
Amyl acetate[a]	1C	25	149
Xylene[a]	1C	32	144
Turpentine[a]	1C	35	149
Ethanol (20%)[a]	1C	36	78
Kerosene[b]	2	38	152–302
Acetic acid[b]	2	43	118
Ethanol (10%)[b]	2	49	78
Acetic anhydride[b]	2	54	140
Formaldehyde (37%)[b]	2	60	96
Dimethyl formamide[b]	2	67	153

[a] Flammable.
[b] Combustible.

Appendix A.15

FLAMMABLE CHEMICALS WITH CHARACTERISTICS

Chemical	Class	Flash Point (°F)	Boiling Point (°F)	Example
Ethyl ether	1A	<73	<100	
Flammable aerosols				
Acetone	1B	<73	100	
Gasoline, toluene, butyl alcohol	1C	73	<100	
Methyl isobutyl ketone, turpentine, cyclohexane	2	100–140		Kerosene
Mineral spirits	3A	140–199		Butyl cellosolve
Cellosolve	3B	200		Ethylene glycol, hexylene glycol

Appendix A.16

CLASSIFICATION OF FLAMMABLE LIQUIDS: FLASH POINT AND BOILING POINT

The flash point is the minimum temperature at which a liquid in a container gives off sufficient vapors to form an ignitable mixture with air at the surface of the liquid. The lower the flash point is, the easier it is to form an ignitable mixture.

Chemical	Class	Flash Point (°C)	Boiling Point
Ethyl ether	A	<23	<38
Gasoline, toluene, and ethanol (95–70%)	1B	<23	<38
Ethanol (50–20%)	1C	23–38	—
Combustible			
Fuel oil no. 1	2	38–60	—
Fuel oil no. 4	2A	60–93	—
Glycerine	3B	>93	—

Appendix A.17

INCOMPATIBLE CHEMICAL SUBSTANCES

Certain hazardous chemicals when stored or mixed together react violently. These chemical substances are unsuitable for mixing and are *incompatible*. During storage, classes of incompatible chemicals should be segregated from each other according to hazard class. In chemical laboratories, more often than not chemicals are stored alphabetically. This has led to the occurrence of several chemical disasters and explosions. It is important that incompatible chemical substances be handled, stored, and disposed of with care and caution and that no contact is made from one chemical to the other. The following are a few selected incompatible chemical substances. **Chemicals in column A should not come in contact with chemicals in column B:**

A. Chemical	B. Incompatible with
Acetic acid	Chromic acid, nitric acid, hydroxyl compounds, ethylene glycol, perchloric acid, peroxides, permanganates
Acetylene	Chlorine, bromine, copper, fluorine, silver, mercury
Acetone	Concentrated nitric and sulfuric acid mixtures
Alkali and alkaline earth metals: powdered aluminum or magnesium, calcium, lithium, sodium, potassium	Water, carbon tetrachloride or other chlorinated hydrocarbons, carbon dioxide, halogens
Ammonia (anhydrous), bromine	Mercury, chlorine, calcium hypochlorite, iodine, hydrofluoric acid (anhydrous)
Ammonium nitrate	Acids, powdered metals, flammable liquids
Chlorates, nitrates	Sulfur, finely divided organic or combustible materials
Aniline	Nitric acid, hydrogen peroxide
Arsenical materials	Any reducing agent
Azides	Acids
Bromine, chlorine	Ammonia, acetylene, butadiene, butane, methane, propane (or other petroleum gases), hydrogen, sodium carbide, benzene, finely divided metals, turpentine
Calcium oxide	Water
Carbon (activated)	Calcium hypochlorite, all oxidizing agents
Carbon tetrachloride	Sodium
Chlorates	Ammonium salts, acids, powdered metals, sulfur, finely divided organic or combustible materials
Chromic acid and chromium trioxide	Acetic acid, naphthalene, camphor, glycerol, alcohol, and flammable liquids in general
Chlorine dioxide	Ammonia, methane, phosphine, hydrogen sulfide
Copper	Acetylene, hydrogen peroxide

(continued on next page)

A. Chemical	B. Incompatible with
Cumene hydroperoxide	Acids (organic or inorganic)
Cyanides	Acids
Flammable liquids	Ammonium nitrate, chromic acid, hydrogen peroxide, nitric acid, sodium peroxide, halogens
Fluorine	Everything
Hydrocarbons (butane, propane, benzene)	Fluorine, chlorine, bromine, chronic acid, sodium peroxide
Hydrocyanic acid	Nitric acid, alkalis
Hydrofluoric acid (anhydrous)	Ammonia (aqueous or anhydrous)
Hydrogen peroxide	Copper, chromium, iron, most metals, their salts, alcohols, acetone, organic materials, aniline, nitromethane, combustible materials
Hydrogen sulfide	Fuming nitric acid, oxidizing gases
Hypochlorites	Acids, activated carbon
Iodine	Acetylene, ammonia (aqueous or anhydrous), hydrogen
Mercury	Acetylene, fulminic acid, ammonia
Nitrates	Sulfuric acid
Nitric acid (commercial grade)	Acetic acid, aniline, chromic acid, hydrogen sulfide, flammable liquids, flammable gases, copper, brass, and heavy metals
Nitrites	Acids
Nitroparaffins	Inorganic bases, amines
Oxalic acid	Silver, mercury
Oxygen	Oils, grease, hydrogen, flammable liquids, solids, gases
Perchloric acid	Acetic anhydride, bismuth and its alloys, alcohol, paper, wood, grease, oils
Peroxide (organic)	Acids (organic or mineral); avoid friction; store cold
Phosphorus (white)	Air, oxygen, alkalis, reducing agents
Potassium	Carbon tetrachloride, carbon dioxide, water
Potassium chlorate	Sulfuric acid and other acids, perchlorates
Potassium permanganate	glycerol, ethylene glycol, benzaldehyde, sulfuric acid
Selenides	Reducing agents
Silver	Acetylene, oxalic acid, tartartic acid, ammonium compounds, fulminic acid
Sodium	Carbon tetrachloride, carbon dioxide, water
Sodium nitrate	Ammonium nitrate and other ammonium salts
Sodium peroxide	Ethyl or methyl alcohol, glacial acetic acid, acetic anhydrite, benzaldehyde, carbon disulfide, glycerin, ethylene glycol, ethyl acetate, methyl acetate, furfural
Sulfides	Acids
Sulfuric acid	Potassium chlorate, potassium perchlorate, potassium permanganate (similar compounds of light metals, such as sodium, lithium)
Telurides	Reducing agents

Appendix A.18

IDENTIFICATION OF FLAMMABLE AND COMBUSTIBLE LIQUIDS

A flammable liquid is one that has a flash point below 100°F and a vapor pressure of more than 2068.6 mm:

class 1A: flash point below 73°F and boiling point at or below 100°F;
class 1B: flash point below 73°F and boiling point above 100°F; and
class 1C: flash point at or above 73°F, but below 100°F.

Combustible liquids comprise any liquid having a flash point at or above 100°F:

class 2: flash point at or above 100°F, but below 140°F;
class 3A: flash point at or above 140°F, but below 200°F; and
class 3B: flash point at or above 200°F.

FLAMMABLE LIQUID STORAGE CABINETS

Cabinets designed for the storage of flammable chemicals should be properly used and maintained. Read and follow the manufacturer's information and follow these safety practices:

- Cabinets must be grounded, if they are not sitting directly on concrete floors.
- Store only compatible chemicals inside the cabinet.
- Rooms and cabinets used to store flammables should be marked with conspicuous lettering: "FLAMMABLE—KEEP AWAY."
- Do not store paper, cardboard, or other combustible material in or on a flammable liquid storage cabinet.
- Flammable liquid storage cabinets are not intended for the storage of small cylinders of compressed or liquefied gases.

The manufacturer establishes quantity limits for various sizes of flammable storage cabinets; do not overload the cabinet. As a general rule, not more than 120 gal (454 L) of class 1, class 2, and class 3A liquids may be stored in a storage cabinet. Of this total, not more than 60 gal (227 L) may be of class 1 and class 2 liquids, and not more than 3 storage cabinets should be kept in a single room.

CORROSIVE STORAGE CABINETS

Corrosive chemicals should be kept in cabinets specifically designed to hold them. A wooden storage cabinet or metal cabinet treated with a corrosion-resistant coating is

available commercially. Read and follow the manufacturer's instructions and follow these safety practices:

- Store acids and bases in separate storage cabinets.
- Store organic and inorganic acids separately, either in different storage cabinets or separated by distance or barrier.
- Store nitric acid away from all other acids unless the cabinet has a separate compartment for nitric acid.

Source: Hazard Evaluation System and Information Service, California Department of Health Services (updated January 2007).

Appendix A.19

CHEMICALS: STORAGE AND HEALTH RISKS

Chemical	Nature of Risk
Acetic anhydride	Explosive potential, corrosive
Acetyl chloride	Corrosive, dangerous fire risk, reacts violently with water and alcohol
Acrylamide	Toxic by absorption, suspected carcinogen
Acrylonitrile	Flammable poison
Adipoyl chloride	Corrosive, absorbs through skin, lachrymator
Aluminum chloride (anhydrous)	Water reactive, corrosive
Ammonia, gas (corrosive)	Lachrymator
Ammonium bifluoride	Reacts with water, forms hydrofluoric acid
Ammonium bichromate	May explode on contact with organics; suspected carcinogen
Ammonium chromate	Oxidizer, poison; may explode when heated
Ammonium dichromate	Reactive; may cause fire and explosion
Ammonium perchlorate	Explosive, highly reactive
Ammonium sulfide poison	Corrosive, reacts with water and acids
Aniline carcinogen	Toxic, absorbs through skin
Aniline hydrochloride	Poison
Antimony oxide	Health and contact hazard
Antimony powder	Flammable as dust, health hazard
Antimony trichloride	Corrosive; emits hydrogen chloride gas if moistened
Arsenic compounds	Poison, carcinogen
Asbestos	Friable inhalation health hazard, carcinogen
Azide ompounds	Explosive in contact with metals, extremely reactive, highly toxic
Barium chromate	Poison
Benzene	Flammable, carcinogen
Benzoyl peroxide	Organic peroxide, flammable, oxidizer
Beryllium and its compounds	Poison; dust is P-listed and highly toxic; carcinogen
Bromine	Corrosive, oxidizer, volatile liquid
Cadmium compounds	Toxic heavy metal, carcinogen
Calcium fluoride (fluorspar)	Teratogen; emits toxic fumes when heated
Carbon disulfide	Flammable, toxic, P-listed, extremely hazardous
Carbon tetrachloride	Toxic, carcinogen
Chloral hydrate	Hypnotic drug, controlled substance
Chlorine poison gas	Corrosive
Chlorobenzene	Explosive limits 1.8–9.6%, toxic
Chloroform	Carcinogen; if old, forms deadly phosgene gas; inhalation and contact hazard

(continued on next page)

Chemical	Nature of Risk
Chlorosulfonic acid	Toxic (a/k/a sulfuric chlorohydrin)
Chromic acid	Strong oxidizer, poison
Collodion	Flammable, explosive when dry, nitrocellulose compound
Cuprous cyanide	Toxic
Cyanogen bromide	Poison, strong irritant to skin and eyes
Cyclohexene	Flammable, peroxide former
Dichlorobenzene	Toxic
Dichloroethane	Flammable, toxic
Dinitrophenol	Explosive; "bomb squad"
Dinitrophenyl hydrazine	Severe explosion and fire risk
Dioxane	Flammable, peroxide former
Ether, anhydrous	Flammable, peroxide former
Ether, ethyl	Flammable, peroxide former
Ether, isopropyl	Flammable, peroxide former
Ethylene dichloride	Toxic, contact hazard, dangerous fire risk, explosive in air 6–16%
Ethyl nitrate	Explosive; "bomb squad"
Ethyleneimine	Flammable, toxic, P-listed
Ferrous sulfide	Spontaneously ignites with air if wet
Formaldehyde (formalin)	Toxic, carcinogen, sensitizer
Gunpowder	Explosive
Hydrazine	Flammable, absorbs through skin, carcinogen, corrosive
Hydriodic acid	Corrosive, toxic
Hydrobromic acid	Corrosive, poisonous
Hydrofluoric acid	Corrosive, poisonous
Hydrogen	Flammable
Hydrogen sulfide	Gas poison, stench
Isopropyl ether	Flammable, highest risk peroxide former
Lithium aluminum hydride	Flammable, reacts with air, water, and organics
Lithium metal	Reacts with water, nitrogen in air
Mercaptoethanol	Flammable, corrosive, intense stench
Mercury compounds	Poisonous heavy metal
Mercury, liquid	Toxic heavy metal, carcinogen
Methylene chloride	Toxic, carcinogen, narcotic
Methyl ethyl ketone	Flammable, dangerous fire risk, toxic
Methyl iodide (iodomethane)	May be a narcotic; carcinogen, lachrymator
Methyl isocyanate	Flammable, dangerous fire risk, toxic
Methyl isopropyl ketone	Toxic
Methyl methacrylate	Flammable, vapor causes explosive mix with air
Naphthylamine	Combustible, toxic, carcinogen
Nickel oxide	Flammable as dust, toxic, carcinogen
Nicotine	Poison, P-listed, extremely hazardous
Nitrilotriacetic acid	Corrosive
Nitrobenzene	Highly toxic
Nitrocellulose	Flammable, explosive; call ETSI
Nitrogen triiodide	Explosive; "bomb squad"
Nitroglycerin	Explosive; "bomb squad"

Chemical	Nature of Risk
Osmium tetraoxide (osmic acid)	Highly toxic, P-listed, extremely hazardous
Pentachlorophenol	Extremely toxic
Perchloric acid	Powerful oxidizer, reactive
Phosphorus pentasulfide	Water reactive, toxic, incompatible with air and moisture
Phosphorus pentoxide	Oxidizer, toxic
Phosphorus, red	Flammable solid
Phosphorus, yellow or white	Air reactive, poisonous
Picric acid, trinitrophenol	Explosive when dry
Potassium cyanide	Poison, P-listed, extremely hazardous
Potassium perchlorate	Powerful oxidizer, reactivity hazard
Potassium sulfide	Flammable; may ignite spontaneously
Potassium, metal	Water reactive, peroxide former (orange fog/crystals)
Pyridine flammable	Toxic; vapor forms explosive mix with air
Selenium	Toxic
Silver oxide	Poisonous
Silver cyanide	Extremely toxic
Sodium metal lump	Water reactive; ignites spontaneously in dry, hot air; corrosive
Sodium arsenate	Toxic, carcinogen
Sodium arsenite	Toxic, carcinogen
Sodium azide	Poison, explosive reaction with metals, P-listed, extremely hazardous
Sodium borohydride	Flammable solid, water reactive
Sodium cyanide	Poison, P-listed, extremely hazardous
Sodium fluoride (bifluoride)	Highly toxic by ingestion or inhalation, strong skin irritation
Sodium fluoroacetate	Tox-X deadly poison
Sodium peroxide	Water reactive; may cause fire and explosion
Sodium sulfide	Fire and explosion risk
Strontium	Flammable, store under naphtha, reacts with water.
Tetrahydrofuran	Flammable, peroxide former
Thioacetamide	Toxic, carcinogen, combustible
Thionyl chloride	Corrosive
Thiourea	Carcinogen
Titanium trichloride	Flammable, fire risk
Triethylamine	Flammable, toxic, irritant
Trinitrobenzene	Explosive; “bomb squad”
Trinitrophenol	Explosive; “bomb squad”
Trinitrotoluene	Explosive; “bomb squad”
Uranium/uranyl compounds	Radioactive

Appendix A.20

STOREROOMS AND STORAGE OF CHEMICAL SUBSTANCES

Users and workers should know and strictly adhere to the following:

- Storerooms should be properly supervised by qualified persons.
- Relevant safety information, materials safety data sheets (MSDS), and proper handling, storage, and disposal methods should be available.
- Storerooms must have adequate security.
- No unauthorized individual should have access to the storerooms.
- All containers of chemical substances must have date and proper label.
- Do not store chemical substances in alphabetical order.
- Store chemical substances according to their hazard class.
- Separate incompatible chemical substances.
- Store chemical substances according to compatibility.
- Maintain a separate record of time-limited chemical substances.
- Reduce unnecessary storage of chemical substances.
- Do not store chemical substances near heat sources (ovens or steam pipes).
- Do not store chemical substances in direct sunlight.
- Maintain reagent labeling and container integrity.
- Never store food products in refrigerators intended for laboratory use.
- Identify safe cylinder storage areas for high-pressure cylinders and gas cylinders.
- Do not store gas cylinders in stairwells or exit corridors.
- Provide all cylinders secured chains and keep in upright positions at all times.
- Do not use cylinders that have no regulator valve.
- Segregate empty cylinders and mark "EMPTY" or "MT."
- Never lay a cylinder down as the top valve may be damaged.
- A communication system to the main office or an emergency system should be provided.
- Fire extinguishers of the approved type should be positioned near an escape route.

FLAMMABLE LIQUIDS

- There should be separate storage cabinets for flammable liquids in approved safety cabinets.
- Do not use refrigerated storage and freezers for flammable liquids.
- Store flammable and combustible liquids in appropriate containers according to their characteristics.
- Always wear the prescribed personal protective equipment (PPE; lab coats, safety goggles, gloves, etc.).

Appendix A.21

STORAGE OF CHEMICAL SUBSTANCES

Many chemical hazards in laboratories, factories, and workplaces have been now well known because of improper methods of storage of chemicals and negligence in the proper management of toxic chemicals. While using, handling, storing, transporting, and eventually disposing of toxic chemicals, each student, industrial worker, and concerned management must be careful and responsible, and follow the procedures and instructions completely. The following points may help in the safe use of chemical substances as well as to contain possible chemical and health hazards both at the workplace and in the living environment:

- Design separate storage areas for flammable solvents, corrosive liquids, reactive chemicals, explosive chemicals, and chemical carcinogens.
- Properly inspect chemical containers and packages before use and also periodically.
- Ensure that the label on the chemical container is legible and intact.
- Labels on the containers must indicate the date of manufacture, date of expiration, and the last date of use.
- Practice storage of minimum chemicals and containers on shelves at workplaces.
- Conduct periodical checks of new chemicals and disposal of old, unused chemicals.
- Store all containers with chemical substances on shelves at shoulder height that are sturdy and painted.
- DO NOT store chemical substances on bench tops.
- DO NOT store acids and bases together on laboratory shelves. Segregate acids from bases.
- Store chemical substances according to their primary hazard classification.
- Store chemical substances in a cool, dry, properly ventilated storage area away from direct sunlight.
- Store incompatible chemical substances separately.
- Store chemical carcinogens in well designated areas or cabinets with proper labels.
- Store volatile chemical substances in a well ventilated storage area.
- DO NOT store flammable liquids near sources of heat, ignition, strong oxidizing agents, explosives, reactive chemicals, and open exits.
- Separate the storage areas away from flammable solvents and corrosive liquids.
- Always keep fire extinguishers ready and available in sufficient numbers

- Store compressed gas cylinders in a secure, upright position in a ventilated and dry place.
- Advise workers about the consequences and hazards of negligence during the use of chemical substances in the workplace and provide proper training.
- Store corrosive substances in a cool, dry, and well ventilated area away from direct sunlight.
- Use storage materials that are resistant to corrosion.
- Store caustic and corrosive materials near the floor to avoid danger.

Appendix A.22

LABELS ON CHEMICAL STORAGE CONTAINERS

- All containers and packages of chemical substances must have proper labels and compliance signs.
- The labels must be legible, with the name of the chemical, date of manufacture, date of expiration, and date of receipt in the laboratory or workplace.
- Label all chemical containers with hazard details and hazard warnings as flammable, corrosive, organic peroxide, oxidizer, pyrophoric, unstable (reactive), water reactive, combustible liquid, compressed gas, explosive, acids, and/or incompatible.
- Label all chemical containers appropriately and legibly as carcinogenic (causing cancer), irritant (to eyes, lungs, nose, throat), corrosive (acid/base), sensitizer, hepatotoxin (causing liver damage), nephrotoxin (causing kidney damage), neurotoxin (damaging the nervous system), or respiratory toxicant (causing lung damage).
- Label all containers of chemical wastes with proper labels.
- Discard chemical containers that have no proper labels, illegible labels, or missing labels.
- Discard waste chemical substances at proper waste-disposal units and inform supervisors or managers.
- Use appropriate signal words to indicate the degree of hazard as "DANGER" (most serious hazard), "WARNING" (moderate hazard), or "CAUTION" (lesser degree of hazard).
- Wash hands, face, and exposed parts of the body thoroughly after handling.
- Avoid contact of chemical substances with eyes, skin, and clothing.
- Use chemical substances according to the directions and only with adequate ventilation.
- Keep chemical substances away from heat, sparks, and flame.
- Keep away from contact with clothing and other combustible materials.

Appendix A.23

ACIDS AND ALKALIS: PRECAUTIONS DURING USE

Nitric acid. Nitric acid is a strong acid. Known as *aqua fortis* to the ancient alchemists, it is the most often used acid in etching. It bites all metals, including lead and silver, except for aluminum plates and most stainless steels. It will also bite all organic matter. This acid is very sensitive to temperature changes (never leave it in sunlight). Nitric acid should be kept in a jar or carboy made of glass or stoneware closed with a ground glass stopper (the inside of the stopper may be slightly oiled) or with a special plastic plug. It must be remembered that this acid is sensitive to light and can be ruined by too much exposure to light. Because of this, it should be kept in a dark place. The vapors of nitric acid are very toxic.

Sulfuric acid (vitriol oil). Sulfuric acid is a strong, colorless liquid when pure. This acid bites violently all organic matter and all the metals usually used in print making except for copper and lead. It is also used to clean the glass surfaces of plates used for photo-engraving. Sulfuric acid is more dangerous to use than nitric acid. If water is poured into this acid, it will splatter and heat up. Always pour the acid into water and never pour water into the acid.

Hydrochloric acid. Hydrochloric acid is a strong acid that is colorless and easily water soluble. It is corrosive, but on contact it does not burn one's skin like nitric and sulfuric acids. Accumulation of vapors of hydrochloric acid in workplaces is dangerous as they may cause an explosion.

Phosphoric acid (orthophosphoric acid). Phosphoric acid is colorless and odorless. It is a good acid for scouring ferrous metals and for lithography work.

Hydrofluric acid. Hydrofluric acid is colorless and highly corrosive. It bites all metals as well as glass and ceramics. It is kept in a gutta-percha or plastic container. Usually, it is used in diluted form to etch on glass and ceramics as well as to scour cast iron.

Chromic acid. Chromic acid or chromic anhydride is water soluble. It is available in the form of dark red needles. These crystals are highly soluble, very caustic, and act as oxidizing agents. The acid made from these crystals attacks any organic matter. When in its solid form (crystals), it can cause autocombustion phenomena when put in contact with paper. It is used as a component in litho and offset solutions.

Several acids are normally weak and mild. These include *citric acid, oxalic acid, tartaric acid, gallic acid,* and *hydrofluosilic acid.*

Alkalis/Bases

Soda or *caustic soda* is sold in stoppered flasks. Soda absorbs humidity and therefore must be kept in an air-tight plastic box and not in bottles with a ground-glass stopper. Caustic soda will attack aluminum, zinc, tin-plated and galvanized iron, enamel, and all organic matter.

Potash or *caustic potash* is similar to caustic soda, but is more sensitive to atmospheric humidity than soda.

Ammonia is a concentrated solution of ammonia gas and has a strong distinctive smell. It is a very volatile substance and must be kept in a flask with a ground-glass stopper and in a cool place. It is used as a cleaning agent in litho-offset.

Appendix A.24

EXPOSURE LEVELS, INDICATIONS, AND EMISSION CONTROLS

Low exposure: no visible haze in the workplace; no visible soot deposits; no complaints or reports of irritancy or other ill effects; CO_2 levels less than 800 ppm and/or CO less than 8 ppm and NO_2 levels less than 50% of the exposure limit of 1 ppm (ceiling); controls likely to be adequate; periodic reevaluation required

Medium exposure: occasional white, blue, or black smoke visible in the workplace; soot deposits visible; a few complaints of irritancy or other ill effects; CO_2 levels near 800 ppm and/or CO levels approaching 10 ppm or NO_2 levels approaching the exposure limit; controls may not be adequate; additional assessment for other contaminants or additional controls will likely be required

High exposure: permanent white, blue, or black smoke; heavy soot deposits, especially near emission points; widespread worker complaints; CO_2 levels in excess of 1000 ppm and/or CO levels in excess of 10 ppm or NO_2 levels above the exposure limit; controls likely not adequate; immediate cessation of operations and decision on new control strategy before resuming; reevaluation required

Appendix A.25

STANDARD WORK PRACTICES AND GOOD MANAGEMENT OF CHEMICALS

The general guidelines are not, by themselves, adequate for chemical substances with high acute toxicity or high chronic toxicity, such as heavy metals, chemical carcinogens, or reproductive toxins. Students and workers must follow standard work practices to contain health and environmental disasters:

- Wear eye protection at all times where chemicals are used or stored.
- Wear a lab coat or other protective clothing (e.g., aprons).
- Wear gloves selected on the basis of the hazard. Inspect them before use. Wash reusable gloves before removal. Turn disposable gloves inside out carefully when removing to avoid contaminating hands.
- Wash hands immediately after removing gloves, after handling chemical agents, and before leaving the lab, even though gloves were worn.
- Lab coats and gloves should be worn only in the lab. They should not be taken outside the lab to lunchrooms or offices or worn outdoors. Lab coats should be cleaned frequently.
- Confine long hair and loose clothing.
- Wear sturdy shoes that cover feet completely.
- Do not store or prepare food, eat, drink, chew gum, apply lip balm or cosmetics, or handle contact lenses in areas where hazardous chemicals are present.
- Check with the supervisor regarding contact lens policy in the lab. If wearing them is acceptable, take appropriate precautions such as informing other lab occupants and having a suction-type removal device in the first-aid kit.
- Food should be stored in cabinets or refrigerators designated for such use only.
- Never pipette or start a siphon by mouth.
- Label all chemical containers.
- Chemical storage should be by hazard class. Chemicals should not be stored merely by alphabetical order.
- Never smell or taste chemicals. Again, label containers properly to avoid confusion about contents.
- Keep work areas clean and uncluttered.
- Keep personal belongings away from chemicals.
- Obtain a material safety data sheet for each chemical and consult it before the chemical is used.
- Know the emergency procedures for the building, the department, and the chemicals being used.

- Vent into local exhaust devices any apparatus that may discharge toxic vapors, fumes, mists, dusts, or gases. Never release toxic chemicals into cold rooms or warm rooms that have recirculating atmospheres.
- Use chemical fume hoods or other engineering controls to minimize exposure to airborne contaminants.
- Properly handle, collect, and dispose of surplus and waste chemicals.

The worker should observe the following:

- Eye protection and gloves should be used for handling hazardous chemicals.
- Lab workers should wash their hands immediately after removing gloves, after handling chemical agents, and before leaving the laboratory.
- Lab coats should be worn fully fastened.
- Lab coats and gloves should be worn only in the lab. They should not be taken outside the lab to lunchrooms or offices and are not worn outdoors.
- Following a significant chemical exposure to skin or clothing, lab workers should be instructed to use the safety shower immediately.
- Eating, drinking, smoking, gum chewing, and applying cosmetics should be prohibited in the work area.
- Food storage should be prohibited in the work area.
- Food should be stored in cabinets or refrigerators designated for such use only.
- Mechanical pipetting devices should be used and mouth pipetting prohibited.
- All hazardous chemicals should be used in a chemical fume hood.
- All containers of hazardous chemicals should be labeled in accordance with OSHA hazard communication standards. Each container of and/or apparatus with hazardous chemical contents in the lab should be labeled with the following information:
  - identity of the hazardous chemical substances; and
  - hazard warnings in words, pictures, symbols, or a combination thereof that provide at least general information regarding the hazards of the chemical.
- Chemical storage should be by hazard class and NOT in alphabetical order.
- Chemicals should be dated on receipt and opening.
- Chemicals should be removed when the expiration date is exceeded, especially in the case of peroxide formers.
- Incompatible materials should be physically separated.
- Flammable materials in amounts exceeding 10 gal should be stored in a storage cabinet for flammables.
- Acids and bases should be stored on low shelves or in acid/base cabinets. Plastic-coated bottles and plastic trays should be used to minimize the effects of leaks.
- Shock-sensitive, detonable compounds (such as sodium azide, dry picric acid) or extremely poisonous materials (such as cyanides, osmium tetroxide, cacodylic acid, tetrodotoxin, picrotoxin, ricin) should be stored in locked cabinets. DEA-regulated substances (e.g., pentobarbital, phenobarbital)

should be locked in cabinets with keys accessible only to authorized lab workers.

- Designated work areas should be established for handling materials with a high degree of acute toxicity (such as chemicals with corrosive effects, e.g., nitric, sulfuric, and hydrochloric acids; hydrofluoric acid; sodium hydroxide; or chemical asphyxiants such as carbon monoxide and hydrogen sulfide).

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Environmental and Occupational Health & Safety

SAFE USE OF CHEMICALS

A Practical Guide

Learn How to Use Chemicals Safely in the Workplace, Home, and Laboratory

Occupational workers frequently use, store, and dispose of toxic chemicals without knowing the possible consequences, both for the workplace and the environment. Improper use or misuse of chemical substances can result in health disorders, fatalities, or chemical disasters. **Safe Use of Chemicals: A Practical Guide** presents quick and comprehensive instruction to those who work with potentially dangerous substances and provides them with the information they need to avoid the hazards associated with handling these chemicals.

Thoroughly referenced from a wide variety of sources, this book contains information on industrial solvents, pesticides, metals, air pollutants, and toxic gases and drugs, as well as other substances. The information presented for each chemical substance is concise yet thorough and does not require advanced training to comprehend. For each chemical, the author provides the CAS number, IUPAC name, molecular formula, synonyms, uses and exposures, toxicity and health effects, the exposure limits, and methods of proper storage and disposal. Tables and appendices are included where appropriate.

T.S.S. Dikshith is a member of the World Health Organization (WHO) Task Group on Environmental Health Criteria Documents and the International Program on Chemical Safety and has worked in several laboratories in the United States, France, Germany, and Canada. By following the guidelines established in this text, those who work with chemical substances are able to minimize the risk of disaster and protect themselves

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