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CHAPTER 3

Principles of Environmental and Occupational Hazard Assessment

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EXPOSURE AND DOSE

A fundamental precept of human toxicology is that the intensity of toxic action is a function of the concentration of the toxic agent that reaches a target organ or tissue. The relationship between concentration and intensity of effect is commonly referred to as the *dose-response relationship* for a given substance. *Dose* is defined as the amount or mass of contaminant that is absorbed or deposited in the body over an increment of time. The *total dose* experienced by an individual refers to the sum of doses resulting from all environmental contact with a contaminant received by a person over a given time interval (1).

Biological measures of a chemical or its metabolites in various matrices, such as blood or urine, are seeing increased application as more direct indicators of dose (i.e., biological exposure indices). But in many instances, it is not practical to assess exposure by using exhaled air, blood, urine, or other biological specimens. It is often necessary to rely on exposure measurement as a surrogate for estimating dose. In the workplace and related environments, exposure measurement serves as a bridge between conditions of work and potential toxic effect (2).

The concept of *exposure* is formally defined as an event that occurs when there is contact between a human and the environment with a contaminant of specific concentration for an interval of time. The unit of expression for exposure is: concentration × time (1,3). Exposure (or dose) profiles describe the exposure concentration (or dose) as a function of time. Expressed differently, concentration and time are used to depict exposure while amount and time characterize dose (3). It is necessary to measure or estimate the exposure (dose) to appreciate the potential health effects from a substance.

To use exposure as a surrogate for dose, certain assumptions are required to relate the duration of an exposure to expected effect (2). The implied assumption, called *Haber's rule*, states that the effect is proportional to cumulative dose. Dose is estimated by exposure concentration times the duration of the exposure (3). This straightforward relationship is used to express exposure as a function of contaminant concentration and time. What is lost in this expression is an appreciation for any variation in concentration that occurred during the averaging time. In an occupational setting, this relationship has resulted in the use of 8- or 40-hour averaging times to express acceptable levels of employee exposure. In certain instances, this concept has been expanded to express cumulative exposure over extended periods, such as parts-per-million (ppm)—years. For example, Haber's rule implies that exposure to 100 ppm for 5 years is dose-equivalent to an exposure of 500 ppm for 1 year. Time-weighted averages (TWAs) are widely used in exposure assessments, especially as part of risk assessments for carcinogens.

EXPOSURE AND HEALTH STANDARDS

Measurement of exposure as a surrogate measure of dose serves as the basis for establishing occupational exposure limits. Most of these limits are based on an 8-hour averaging time, although shorter averaging times also are used. Short-term (15-minute) exposure limits (STELs), are recommended for fast-acting substances or when dose rate may be critical to health impact. Established exposure limits include recommended limits set by professional societies or other nongovernmental bodies, as well as regulatory limits (standards) enforced by regulatory agencies.

Threshold Limit Values

Industrial hygienists employed by governmental agencies formed a group dedicated to the establishment of principles and policies for governing employee exposures to airborne chemicals. This group, named the American Conference of Governmental Industrial Hygienists (ACGIH), composed a list of chemical exposure limits that eventually became accepted as threshold limit values (TLVs) intended to serve as exposure guidelines for worker protection. The ACGIH has defined three categories of TLVs: (a) the TWA (TLV-TWA), (b) the short-term exposure limit (TLV-STEL), and (c) the ceiling limit (TLV-C) (Table 3-1).

TLVs are TWA concentrations of airborne chemicals to which nearly all workers may be exposed, day after day, without adverse effect (4). ACGIH has established these concentrations as guidelines for the control of exposures. The basis on which the TLVs are established varies from substance to substance. It may include protection against impairment of health, reasonable freedom from irritation, narcosis, nuisance, or other forms of stress (4). The TLVs cannot be viewed as a relative index of toxicity but rather as guidelines for "acceptable" exposure to a particular substance over a typical workday or workweek.

The TLV-TWA refers to the airborne concentration of a substance to which workers can be continuously exposed in an

TABLE 3-1. Occupational exposure limits

Value	Abbreviation	Definition
Threshold limit value (three types) (ACGIH)	TLV	Refers to airborne concentrations of substances and represents conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect.
Threshold limit value/time-weighted average (ACGIH)	TLV-TWA	The TWA concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.
Threshold limit value/short-term exposure limit	TLV-STEL	The concentration to which workers can be exposed continuously for a short period without suffering from: (a) irritation; (b) chronic or irreversible tissue damage; or (c) narcosis of sufficient degree to increase the likelihood of accidental injury, impair self-rescue, or materially reduce work efficiency, and provided that the daily TLV-TWA is not exceeded. A STEL is defined as a 15-minute TWA exposure that should not be exceeded at any time during a workday even if the 8-hour TWA is within the TLV-TWA. Exposures above the TLV-TWA up to the STEL should not be longer than 15 minutes and should not occur more than four times per day. There should be at least 60 minutes between successive exposures in this range. An averaging period other than 15 minutes may be recommended when this is warranted by observed biological effects. In the absence of a STEL, which takes precedence, excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 minutes during a workday, and under no circumstances should they exceed five times the TLV-TWA for no more than a total of 30 minutes during a workday, provided the TLV-TWA is not exceeded.
Threshold limit value/ceiling (ACGIH)	TLV-C	The concentration that should not be exceeded during any part of the working exposure.
Permissible exposure limit (OSHA)	PEL	Same as TLV-TWA.
Immediately dangerous to life and health (OSHA)	IDLH	A maximum concentration (in air) from which one could escape within 30 minutes without any escape-impairing symptoms or any irreversible health effects.
Recommended exposure limit (NIOSH)	REL	Highest allowable airborne concentration that is not expected to injure a worker; expressed as a ceiling limit or TWA for an 8- to 10-hour workday.

ACGIH, American Conference of Governmental Industrial Hygienists; OSHA, Occupational Safety and Health Administration; NIOSH, National Institute for Occupational Safety and Health.

occupational setting over an 8-hour period or 40-hour workweek (4). The TLV-TWA is calculated as follows:

$$\text{TLV} \approx \text{TWA} = \frac{C_1T_1 + C_2T_2 + \bullet\bullet\bullet + C_nT_n}{8}$$

The TLVs should be viewed as guidelines or recommendations in the control of potential health hazards. They should not be used by anyone untrained in the discipline of industrial hygiene and unaware of their limitations (4). The ACGIH insists that the TLVs are not to be used as fine lines between unsafe and safe levels of exposure. It is acknowledged that a small percentage of workers may experience discomfort from some substances at concentrations at or below the TLV; a smaller percentage may be affected by aggravation of a preexisting condition or by development of an occupational disease (4). Individuals who are hypersusceptible or otherwise unusually responsive to some industrial chemicals because of genetic factors, age, personal habits (e.g., smoking, alcohol or other drugs), or medication may not be adequately protected from adverse health effects from certain chemicals at concentrations at or below the TLVs (4). Known or suspected carcinogens may not be assigned TLVs.

The basis on which certain TLV recommendations have been made has been criticized for being too limited. An analysis of the basis for the TLVs found that many have been developed by ad hoc procedures (5). It was suggested that a more aggressive policy be adopted by the ACGIH regarding TLVs for carcinogens, but not necessarily for substances that produce effects other than cancer. New information regarding the toxicology of chemicals and other agents, especially information pertaining to the human health experience, has provided a better foundation on which to support TLVs and other standards. The annual updating of the TLVs and the publication of recommended exposure limits (RELs) and hazard alert bulletins by the National Institute for Occupational Safety and Health (NIOSH) represent avenues for incorporating and disseminating the most recent information affecting the basis for standards. Health professionals assigned responsibility for the health and welfare of workers should consider all sources of scientific information involved in the standards-setting process when considering acceptable exposure limits for workers.

Conversion of Threshold Limit Values in Parts Per Million to mg/m^3

TLVs for gases and vapors are usually established in terms of ppm of substances in air by volume. TLVs may also be listed in terms of milligrams of substance per cubic meter of air (mg/m^3), where 24.45 = molar volume of air in liters at normal temperature and pressure conditions (25°C and 760 mm Hg), giving a conversion equation of:

$$\text{TLV in mg/m}^3 = \frac{(\text{TLV in ppm})\left(\begin{array}{c}\text{gram molecular}\\ \text{weight of substance}\end{array}\right)}{24.45}$$

Conversely, the equation for converting TLVs in mg/m^3 to ppm is:

$$\text{TLV in ppm} = \frac{(\text{TLV in mg/m}^3)(24.45)}{\text{gram molecular weight of substance}}$$

Values are rounded to two significant figures below 100 and to three significant figures above 100. This is done to avoid increasing or decreasing the TLV significantly by the conversion of units.

When converting TLVs to mg/m^3 for other temperatures and pressures, the reference TLVs should be used as a starting point. When converting values expressed as an element (e.g., as Fe or Ni), the molecular value of the element should be used, not that of the entire compound.

Permissible Exposure Limits

Permissible exposure limits (PELs) are conceptually the same as many TLVs but differ in some specific allowable concentrations. PELs are enforceable standards under the Occupational Safety and Health Administration (OSHA), whereas the TLVs are intended as guidelines. The first occupational safety and health standards were derived from the 1968 TLV list adapted from nearly 400 substances, as well as certain standards of the American National Standards Institute and the Walsh-Healey Public Contracts Act.

Under the authority of the Occupational Safety and Health Act of 1970, the 1968 TLVs and certain American National Standards Institute standards were adopted and promulgated by OSHA as the PELs for all workers covered by the act. The current list of PELs, similar to the ones adopted from the ACGIH, has been expanded by OSHA to include updated regulations for benzene, lead, arsenic, vinyl chloride, acrylonitrile, and asbestos. This expanded group of standards now is used to regulate human exposure in the work environment.

For OSHA to change or add a new PEL, either a lengthy rulemaking procedure or emergency temporary standard process is required. The ACGIH, however, can modify or add new substances listed during its annual updating of the TLV listing. Currently, there are approximately 600 substances listed in the ACGIH's TLV handbook.

Recommended Exposure Limits

NIOSH is the principal federal agency engaged in research at the national level to eliminate on-the-job hazards. Under the authority of the Occupational Safety and Health Act of 1970 (Public Law 91-596), NIOSH continues to develop and periodically revise recommendations for limits of exposure to potentially hazardous substances or conditions in the workplace. The RELs are published annually and transmitted to OSHA or the Mine Safety and Health Administration of the U.S. Department of Labor for use in promulgating legal standards. These published documents specify NIOSH RELs for a variety of chemical agents.

Preventive measures designed to reduce or eliminate health effects of these hazards are also recommended by NIOSH for consideration by OSHA. All known and available scientific information relevant to the potential hazard is evaluated by NIOSH in formulating these recommendations. Exposure limits are based on the best available information from human and animal studies, epidemiologic assessment, and industrial experience. It should be noted that the PELs established by OSHA are not always in agreement with the TLVs proposed by the ACGIH or the RELs recommended by NIOSH.

NIOSH also is involved in preparing documents related to special hazard reviews and occupational hazard assessments. These criteria documents provide safety and health assessments of specific chemical hazards along with recommended control and monitoring methods. NIOSH also evaluates new and emerging occupational health hazard data and publishes bulletins on them. These hazard alert bulletins provide information on previously unrecognized toxic hazards, report updates on current hazards, or disseminate information on hazard control methods and monitoring.

Conditions Immediately Dangerous to Life or Health

Conditions immediately dangerous to life or health (IDLH) are established by NIOSH for the purpose of respirator selection to protect health and life of those entering potentially dangerous situations. IDLH indicates an atmospheric concentration of any toxic corrosive or asphyxiant substance that poses an immediate threat to life or would cause irreversible or delayed effects or would interfere with an individual's ability to escape from a dangerous atmosphere.

Conditions IDLH can be caused by the presence of explosive or flammable materials, a deficiency of oxygen as can occur in a confined space, the presence of a highly toxic compound in high concentration, or the presence of ionizing radiation. Dangerous conditions can also be associated with a variety of processes and reactions involving chemicals as well as physical processes (Table 3-2).

TABLE 3-2. Hazardous processes, reactions, and conditions

Fires and explosions
Flammable liquids
Compressed gases
Confined spaces
Oxygen-deficient areas
Release of chemicals in vapor form
Dust and particulate formation
Fume formation
Release or spill of corrosives
Unknown spilled material
Oxidation reactions
Chemical reactions
Heating chemicals near flashpoints
Release of cryogenic fluids
Sudden release of pressurized gases
Radioactive materials
Thermal reactions
Electrical shock
Loading and unloading processes
Low-pressure operations
Handling large quantities of flammable liquids

Worker Protection

Evaluation of worker exposures is accomplished by determining the concentration of contaminants within the breathing zone of the individual. These concentrations can be compared with established exposure limits (PELs, RELs, TLVs). If detected concentrations are in excess of established limits, engineering or administrative controls can be instituted to control exposures to within acceptable limits. If such controls are not feasible or are unsuccessful in reducing concentrations, personal protective equipment may be required.

EXPOSURE ASSESSMENT

The mere presence of a particular hazard in an environment does not indicate that human exposure has occurred, nor does it provide an adequate basis for determining potential risk. The exposure potential must be assessed for an individual or group to determine the actual risk. The storage of large amounts of chemical solvents in nonleaking containers may constitute a potential hazard to persons or the immediate environment, but is not a potential hazard until human or environmental exposure occurs.

Hazard evaluation involves both the toxicity of the chemical or material and the opportunity for exposure to cause disease. Therefore, the evaluation should include

1. Nature of the chemical or chemicals
2. Quantity of material and its physical form
3. Routes of exposure and potential of multiple exposures
4. Duration of exposure (acute, chronic, long term)
5. Magnitude and frequency of the exposure
6. Representative monitoring data
7. Control measures that limit exposure
8. Toxicity of the material in biological systems
9. Medications used by exposed person that might influence toxicity
10. Exposure-dose-response relationships
11. Prior health status and genetic predisposition

Exposures can be defined using qualitative and quantitative bases. The most useful information is obtained from quantitative data on a specific agent, because these types of data can best be related to established exposure limits (TLVs, PELs, or other reference limits) designed to minimize the occurrence of health effects. Although the intention of most standard-setting bodies is to set exposure limits below which no significant effect is expected to occur over a working lifetime, the difficulty has been the identification of the minimal-risk level for the agent of concern. Standard setting frequently is impeded by the paucity or quality of dose-response information on which decisions regarding appropriate standards are made. Often, the more conservative recommendations or standards are used by practitioners as indices of acceptable exposure.

Exposure Terms

Exposures are generally classified as acute, chronic, or long term. An acute exposure involves a single dose during a short time. Acute exposures can involve either single or multiple chemicals. Health effects may become apparent very quickly. Chronic exposure involves receiving a dose at frequencies over a period that may be days, months, or years. Health effects after chronic exposure are a function of the frequency of the exposure, contaminant concentration, route of exposure, accumulation and metabolism of the chemical, possible synergism among multiple chemicals, and the inherent toxicity of the chemical or material. Chronic exposures usually occur over longer periods and involve lower concentrations. Long-term exposures generally last more than 1 year on a continuous basis.

The biological variability in toxic responses among humans and other animals can be considerable. Toxins may have small or large margins of safety. Exposures may be multiple and erratic in the occupational setting. The overall biological response can be influenced by other environmental exposures that may act synergistically.

DEFINITION OF HAZARD CLASSES

The toxic action of a material is a function of its physical and chemical properties. The form or physical state of a material determines the route of entry as well as the potential hazard associated with a substance. The form of the substance also dictates the method used to monitor or detect the contaminant.

Gas

A gas is defined as a compound that is in the gaseous state at a temperature of 25°C and 760 mm Hg pressure. Normally, a gas is a formless fluid that occupies a space and can be changed to the liquid or solid state only by the combined effort of increased pressure and reduced temperature.

Vapors

Vapors are the gaseous form of substances that are normally in the solid or liquid state at room temperature and pressure (25°C and 760 mm Hg). Vapors can be changed back to the solid or liquid state either by increasing the pressure or decreasing the temperature. Evaporation is the process by which a liquid is changed into the vapor state and mixed with the surrounding atmosphere. Organic solvents with low boiling points volatilize quickly, yielding solvent vapors. Vapors, like gases, diffuse throughout the space they occupy. Concentrations of gases and vapors are typically expressed on a ppm (vol/vol) or mg/m^3 basis. Exposure or area assessments for gases and vapors are generally conducted by using direct reading instrumentation (either grab or continuous monitor types) or indirect (integrative) techniques such as sorbent tubes or passive dosimeters.

Aerosols

Aerosols are liquid or solid particles suspended in air that are of fine enough particle size to remain dispersed for a period. Aerosol concentrations are expressed on a mass per unit volume basis (e.g., mg/m^3) or on a numerical, fiber per cubic centimeter or millions of particles per cubic foot basis. Aerosols include the following contaminant categories:

- Dusts: Solid particles formed from the handling, crushing, grinding, rapid impact, or detonation of organic or inorganic materials such as ores, rocks, metal, coal, wood, or grain. Dusts do not tend to flocculate except under electrostatic forces, but settle under the influence of gravity. Examples include mineral dusts (e.g., asbestos, quartz, or talc) and organic dusts.
- Fumes: Solid particles formed when a volatilized solid, such as a metal, condenses in cool air. This physical change is often accompanied by a chemical reaction, such as oxidation. The solid particles that make up a fume are extremely fine, usually less than 1.0 μm. Fumes flocculate and sometimes coalesce. Examples include lead oxide fumes from smelting and iron oxide fumes from iron welding.
- Smoke: Solid particles generated by incomplete combustion of carbonaceous materials such as coal or oil. Generally, carbon or soot particles are less than 0.1–0.5 μm. Smoke generally contains droplets as well as dry particles. Tobacco, for instance, produces a wet smoke composed of minute, tarry droplets. The size of the particles contained in tobacco smoke is approximately 0.25 μm.
- Mists: Suspended liquid particles generated by condensation from the gaseous to the liquid state or by the breakup of a liquid into a dispersed state by splashing, foaming, or atomizing. Examples of mists include: (a) oil mist produced during cutting and grinding operations, (b) acid mists from electroplating, (c) acid or alkali mist from pickling operations, and (d) paint mists from spraying operations.
- Fog: Liquid particles formed by condensation of water vapor.
- Smog: Mixture of liquid and solid matter in the air generated from the dispersion of incomplete combustion products into a moist atmosphere (the term *smog* is derived from smoke and fog).

Solids

Solids are materials that retain a given shape under standard conditions.

Liquids

A liquid is a state of matter that assumes the shape of its container.

Bioaerosols

Bioaerosols are airborne biological source particles, both viable and nonviable, that include living organisms capable of reproduction or replication, such as bacteria, protozoa, fungi, and viruses. The term includes nonviable components, pieces, and by-products of microorganisms such as endotoxins, toxins, mycotoxins, pollens, spores, and immunogenic macromolecules.

Exposure or area assessments for aerosols are generally accomplished using integrative techniques such as collection on filters either alone or in concert with size-selective precollectors. A less common but convenient approach is the use of direct-reading aerosol monitors.

Solvent Vapor Pressure and Health Hazards

The concept of the vapor pressure of a solvent as it relates to hazards and toxic health effects is important. The vapor pressure of a solvent is directly related to its airborne concentration and its toxic hazard and human exposure. Vapor pressure is the force per unit area exerted by molecules of a vapor that is in equilibrium with a liquid or solid. Vapor pressure is expressed in terms of mm Hg in relation to atmospheric pressure (1 atm = 760 mm Hg). The vapor pressure of a solvent also is directly related to its economical use because of volatilization loss. The toxic hazard of an organic solvent is dependent on its vapor pressure and its intrinsic chemical properties. The vapor pressure directly relates to the concentration of solvent in the breathing zone of exposed individuals.

The vapor pressure of a solvent obeys the same physical laws as other gases:

$$Pv = nRt/V$$

Pv = vapor pressure (mm Hg)
n = moles
V = gas volume (M^3)
R = gas constant (6.236×10^5)
t = absolute gas temperature in K°

Rearrangement of this formula yields an equation that allows the calculation of the vapor concentration from the vapor pressure of a gas (vapor) that is in an equilibrium state:

$$Pv = nRt/V = CRt/MW = (X)(\text{atm})(2 \times 10^6)$$

C = concentration (mg/m^3)
MW = molecular weight
X = concentration in ppm
atm = 760 mm Hg

The vapor hazard ratio of solvents can be compared by this method to help determine the potential of human exposure. The formula expresses the vapor pressure in terms of an equilibrium state or worst-case scenario, as would be achieved in a closed environment. Solvents or chemicals with the same TLV may present two distinctively different health hazards caused by their different vapor pressures. An example of this hazard assessment with two related chemicals is as follows:

Chemical A	TLV = 0.02
	Vapor pressure = 0.00014 at 25°C
Chemical B	TLV = 0.02
	Vapor pressure = 0.00001 at 25°C

Rearranging this equation allows for a calculation of the vapor concentration in ppm of a vapor in an equilibrium state (V_{peq}):

$$V_{peq} = \frac{(Pv) \cdot (1 \cdot 10^6)}{\text{atm}}$$

The equilibrium vapor pressure, as calculated using the above formula, can be used to calculate a vapor hazard ratio (VHR):

$$\text{VHR} = \frac{\text{equilibrium vapor pressure (ppm)}}{\text{threshold limit value (ppm)}}$$

The greater the vapor hazard ratio, the greater the potential hazard for inhalation and dermal contact.

$$V_{peq}\,(\text{Chemical B}) = \frac{(1.4 \cdot 10^{-4})(1 \cdot 10^6)}{760 \text{ mm Hg}} = 0.184 \text{ ppm}$$

$$V_{peq}\,(\text{Chemical A}) = \frac{(1.4 \cdot 10^{-5})(1 \cdot 10^6)}{760 \text{ mm Hg}} = 0.0132 \text{ ppm}$$

$$\text{Chemical A VHR} = \frac{0.184 \text{ ppm}}{0.002 \text{ ppm}} = 92$$

$$\text{Chemical B VHR} = \frac{0.0132 \text{ ppm}}{0.002 \text{ ppm}} = 6.6$$

Chemical B would present much less of a hazard than chemical A in terms of vapor exposure. Chemical B also would have a lower air concentration than its TLV.

MONITORING STRATEGIES

The purpose of a monitoring program is to: (a) characterize the nature of the exposure; (b) determine whether the risk of exposure exists; (c) quantify the amount of the exposure; (d) relate the exposure to possible toxic effects; (e) ensure that concentrations of hazardous substances do not exceed established TLVs, RELs, or regulatory standards; and (f) prevent disease. Monitoring helps determine the protection required for a specific activity or site. It also dictates the types of personal protective equipment required when other control measures are not feasible.

Although some monitoring techniques do not yield an immediate determination of airborne contaminant levels because of the need for laboratory analysis, this approach provides a definitive statement about the identity and magnitude of multiple contaminants over a specified sampling period. Mass spectrometric analysis can be used to confirm the identity of contaminants in a mixed exposure environment.

The nature of the environment being monitored dictates the sampling strategies and kinds of instrumentation to be used. Questions to be addressed in any monitoring program are

- What is the purpose of the monitoring?
- What is the suspected chemical or contaminant?
- What kind of instrumentation is required for specificity and sensitivity?
- Where is the monitoring going to be performed? Ambient air? Personal breathing zone?
- When is it to be performed?
- Over what length of time is the monitoring to occur?
- How many samples are to be collected?

Sampling strategies must include a quality assurance program to account for proper calibration of instruments before and after sampling procedures, adequate flow control during sampling, and use of accepted standards and procedures for determining sampled volumes and analyzing collected contaminants.

Area versus Point-Source Monitoring

Personal air monitoring is preferred for evaluating work exposure to airborne chemicals. Typically, air sampling permits one to estimate an employee's 8-hour or 15-minute TWA exposure to a substance by collecting one or more personal samples over a work shift. The collection of multiple samples over the duration of a work shift allows one to measure exposures for individual tasks and still estimate workers' 8-hour TWA exposure.

Area samples are useful in determining background contaminant levels, evaluating the effectiveness of control measures, and identifying possible sources of exposure. But neither area monitoring nor point-source monitoring provides an estimate of worker exposure because environmental conditions at a fixed site frequently do not represent those experienced by the worker. Under certain conditions, workroom samples may reflect a worker's average exposure. But samples must be collected in the immediate vicinity of the worker's breathing zone during his or her various activities to represent his or her actual exposure. Without vigilant observation of the employee's pattern of work, one cannot obtain a representative estimate of the worker's exposure from area monitoring data. Area sampling, even when carefully designed to estimate a worker's exposure, fails to comply with OSHA regulations that require personal monitoring. For obvious reasons, area monitoring in outdoor environments provides little information with which to estimate personal exposures.

RATIONALE FOR AIR MONITORING

Assessment of occupational exposures serves as the primary reason for conducting air monitoring studies. The magnitude of personal exposures to specific chemical, biological, and physical agents is compared to occupational exposure limits for determining the acceptability of the work environment relative to these exposure guidelines. Other reasons exist for conducting air monitoring. Many of these reasons contribute either directly or indirectly to insights regarding the work environment, control of exposure, and protection of human health. Reasons for initiating air monitoring studies are

- Monitoring of personnel to characterize their exposures and determine compliance with consensus, regulatory, or other occupational exposure limits.
- Response to workers' inquiries or complaints regarding the nature of their work environment.
- Evaluation of point-source emissions to determine their potential contribution to employee exposures, area levels, and compliance with emission standards.
- Evaluation of confined spaces for safety and health hazards before entry.
- Evaluation of the effectiveness of engineering or administrative exposure control measures.
- Support of data for epidemiologic investigation, whether prospective or retrospective in nature.
- Research aimed at characterizing the composition, concentration, and form of exposure agents from new processes, products, and so forth.
- Support of evidence for legal actions directed at characterizing an employee's occupational work history.

Regardless of the reason for initiating an air monitoring study, it is incumbent on the environmental and occupational health specialist to define clearly the purposes of a monitoring exercise or program, and establish protocols to achieve these objectives. Information derived from air monitoring may be of little value unless descriptive criteria pertinent to exposure and other assessments are stated clearly by the professional on field sampling sheets or in survey reports. Assuming air samples are collected and analyzed according to standard or other acceptable protocols, it is critical to describe properly the conditions under which air samples were collected. This information imparts meaning and context to monitoring data. Professionals who are properly trained and experienced in the field of environmental and occupational health often are able to deduce the significance of samples with minimal descriptions of the conditions or situations under which air samples were collected. But to the untrained recipient of data, its meaning may be misconstrued. For example, area or point-source data may be interpreted incorrectly as being representative of personal exposure data when the information actually was intended to evaluate a potential source of emission or conditions at a specific location at one point in time. Professionals should be aware that their data may be interpreted incorrectly if its intended purpose is not stated clearly on sampling data sheets or survey reports.

Descriptive information useful in defining the intended purpose and context of monitoring data include the following elements:

- Statement regarding purpose of monitoring
- Type of monitoring (personal, area, point source)
- Individual's job title and description (if data are personal sample)
- Monitoring location (precise information to fix location)
- Task description (multiple activities and duration of each should be described individually)
- Time and duration of monitoring (if multiple samples are collected, time, duration, and description of each activity should be noted)
- Use of personal protective equipment (respirators, clothing, and eye protection, including specifics on type and model)
- Engineering or administrative controls in use during the monitoring period
- Factors that may affect reliability of data

Although exposure assessments are conducted under a variety of schemes, they all have as their goal a statement about potential human exposure. A set of eight good exposure assessment practices has been proposed that are particularly useful in large- and small-scale exposure assessments (5). Good exposure assessment practice components include the writing of a study protocol for conducting a study, consideration of available resources, specification of an exposure assessment model, and a study design. The design should include sampling and analytical methods and data analysis strategies, quality assurance, archiving of all program elements, communication of personal exposure information, and a statement of overall uncertainty in exposure assessment (5,6).

Monitoring Techniques

Two basic techniques are used to evaluate personnel exposures and contaminant levels in an environment. Direct and indirect monitoring devices are used. Direct or real-time devices give a direct readout of pollutant concentration, often on an instantaneous and continuous basis.

Indirect or integrative monitoring devices are used to collect contaminants over extended periods, ranging from 15 minutes to 8 hours or more. They provide a TWA estimate of contaminant levels over a given sampling period. Laboratory analysis is required to determine the mass of contaminant collected, which is then time-weighted to estimate average exposure concentration of the contaminant. The methods used to analyze such samples may provide additional information regarding the identity and concentration of contaminants.

DIRECT MONITORING

Direct or real-time monitoring instruments can be used at various locations to provide instantaneous information concerning

TABLE 3-3. Direct air sampling instruments

Instrument	Detection method	Chemical	Detection limits
Compound-specific instruments	Electrochemical cell	Hydrogen cyanide	0–100 ppm
		Hydrogen sulfide	0–100 ppm
		Oxygen	0–100%
		Nitrogen dioxide	0.01–50.00 ppm
		Carbon monoxide	0–500 ppm
Portable gas chromatograph	Flame ionization	Organic vapors	0.2 ppm
			0–1,000 ppm
	Photoionization	Compounds with ionization potential less than or equal to the output energy of the ultraviolet lamp	0.1 ppb
Aerosol monitor	Light scattering	Aerosols	0.001 mg/m^3
Mercury vapor analyzer	Ultraviolet light	Mercury vapor	0–1 mg/m^3
Combustible gas detector	Catalytic combustion	Vapors of combustible gases	0–100% LEL
Portable photoionization detector	Photoionization	Compounds with ionization potential less than or equal to the output energy of the ultraviolet lamp	0.05–2,000.00 ppm
Portable infrared analyzer	Infrared absorption	Infrared absorbing compounds	0–9,999 ppm
Portable FID	Flame ionization	Organic vapors	0–1,000 ppm
Gamma radiation detector	Scintillation detector	Gamma radiation	Does not detect beta or alpha

FID, flame ionization detector; LEL, lower explosive limit; ppb, parts per billion; ppm, parts per million.

personal and ambient air concentrations of certain chemicals, radioactive materials, or conditions IDLH.

Direct-reading instruments provide an immediate and continuous readout of contaminant levels in a specific work environment. They can be used to detect emission point sources, the effectiveness of control measures, and changes in an environment over time. These capabilities permit checks for compliance with ceiling and short-term exposure limits and estimates of TWA concentrations, when coupled with data processors (e.g., data loggers). One group of direct-reading devices—portable gas chromatographs—can provide not only a direct readout of contaminant concentration, but also more specific information on the identity of airborne contaminants that other methods cannot furnish.

Direct-reading instruments can provide real-time measurement of potentially hazardous environments. But proper data interpretation is dependent on the user's skill and knowledge of the calibration, principle of operation, application, and limitations of the instrument. Users also should be aware of factors such as instrument specificity, especially as it applies to detection of a substance in the presence of potential chemical interferences.

The sensitivity or limits of detection of direct-reading instruments also impact the validity and usefulness of instrument data. Choice of a particular direct-reading instrument is dependent on the physical and chemical state of the contaminant to be detected. For example, many combustible gas detectors do not indicate a combustible atmosphere in the presence of high vapor or gas concentrations devoid of the oxygen needed for instrument response. The types of direct-reading instruments that are available include

Explosimeters and combustible gas indicators
Photoionization detector (UV)
Portable gas chromatograph
Oxygen meters
Radiation detectors
Portable infrared spectrophotometer

Direct-reading instruments are used to provide immediate insights into contaminant levels and, in certain settings, warnings where dangerous airborne contaminants may exist or appear during work (Table 3-3). They are the primary instruments used to initially characterize an unknown hazardous site. They detect organic vapors, various gases, and other contaminants being released into the atmosphere. They also can detect the presence of explosive conditions and flammable gases, a lack of oxygen, and the presence of ionizing radiation. Contemporary real-time monitors are very sensitive, with detection limits in ppm and, in some cases, parts per billion range (e.g., photoionization detector). Because of problems of specificity when multiple chemicals are present, identification and quantitation can become difficult. False readings can occur because of interference from other chemicals.

Direct-reading instruments have certain limitations in their capacity to detect different families of hazardous substances. They can detect or measure certain specific substances or classes of chemicals, so it is possible to miss other hazards when limited information is available on the types of contaminants potentially present in the work environment. In other instances, these instruments are not designed to detect extremely low air concentrations (e.g., <1 ppm).

It is critical that direct-reading instruments be used by highly qualified persons such as certified industrial hygienists or technicians who are skilled at proper instrument selection, calibration, use, and interpretation of information.

GRAB SAMPLING

Direct-reading devices, such as indicator tubes, often are used for collecting grab samples. Grab samples are taken to measure the concentration of a contaminant over a brief sampling time (several minutes or less) to obtain a general appreciation of environmental conditions at a specific operation or location. Before using such devices, it is important to know the identity of the airborne contaminants. Grab or instantaneous air samples also may be collected in evacuated containers (e.g., canisters, bags, and syringes) followed by laboratory analysis.

ELECTROCHEMICAL DEVICES

Electrochemical cells, which operate on the principle of membrane electrolysis, commonly are used to detect gases such as carbon monoxide (Table 3-4). The gas passes through a membrane and reacts with an electrolyte. This reaction produces a flow of electrons proportional to the partial pressure of the gas in the air. With the addition of chemical filtration mechanisms preceding the cells, instruments may be made more sensitive and specific for a variety of gases.

TABLE 3-4. Electrochemical cells for compound detection

Simple paraffins
Halogenated paraffins
Aliphatic ring compounds
Nitrogen-containing compounds
Unsaturated acids and esters
Chlorinated aromatics
Chlorinated olefins
Aromatics
Organometallics
Carbon-oxygen compounds
Sulfur-containing compounds
Phosphorus compounds

Adapted from Transducer Research, Inc., 1228 Olympus Drive, Naperville, IL.

EXPLOSIMETERS

Combustibility or explosivity is generally detected with an instrument that uses a catalytic combustion process. The gaseous contaminant burns on a heated wire, thus altering resistance to flow of an electric current (Fig. 3-1).

A gas (or vapor) sample is drawn into the instrument across a heated filament and ignited. The resulting change in electrical resistance of the filament is detected by conventional bridge measurement techniques. The degree of induced electrical resistance is directly proportional to the gas (or vapor) concentration of the gas (or vapor) being drawn into the instrument. The heat of combustion—a particular physical characteristic of combustible gases—is used for quantitative detection. This procedure is nonspecific when mixtures of gases are being analyzed. Typically, these instruments read in percentage of the LEL so they are not useful in measuring concentrations in the ppm range. They are not to be used in determining concentrations relative to the PELs.

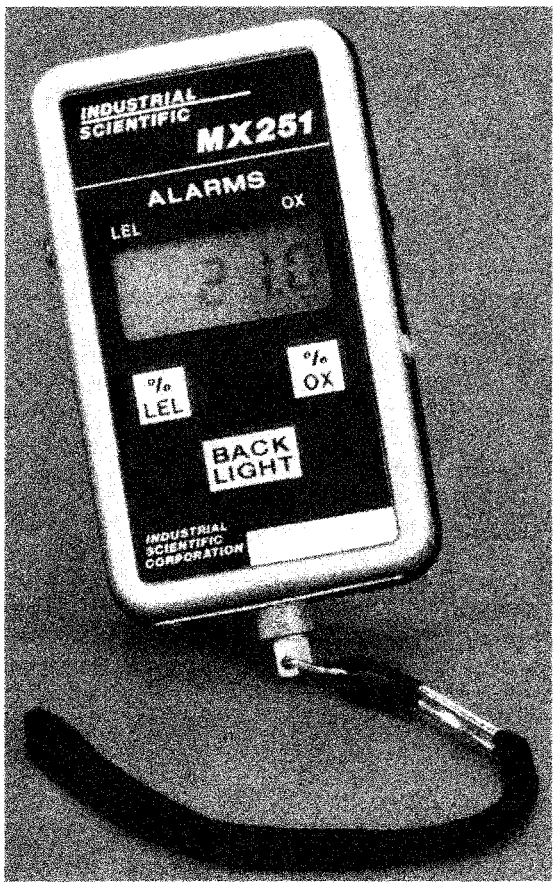

Figure 3-1. Lower explosives limit and O_2 deficiency monitor for conditions immediately dangerous to life or health. (Photograph courtesy of Hazco.)

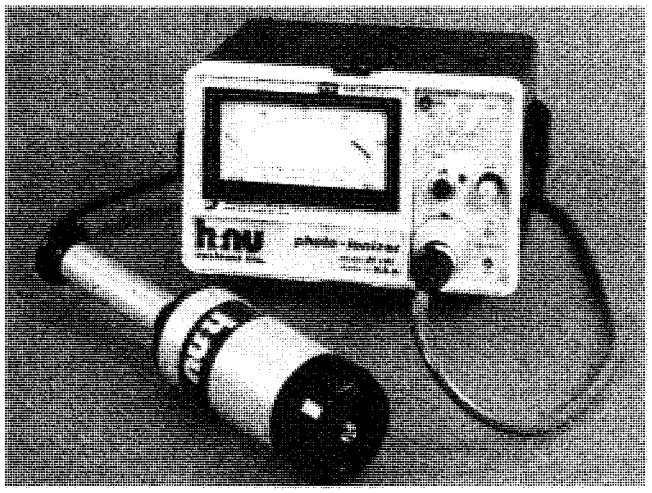

Figure 3-2. Photoionization detector for detection of organic vapors and inorganic gases such as hydrogen sulfide and ammonia. (Photograph courtesy of Hazco.)

ORGANIC VAPOR MONITORS

Monitors with a photoionization detector (PID) represent a nonspecific instrument that uses an ultraviolet lamp (Fig. 3-2). The gas is carried into a ionization chamber and ionized by an ultraviolet beam. The resulting degree of ionization produces an electric signal that can be read on a meter.

Other gas-detecting instruments use a flame ionization detector (FID). These instruments are used to detect a volatile hydrocarbon. The hydrocarbon is drawn into the ionization chamber, and a hydrogen flame ignites the compound. The resulting degree of ionization produces an electrical signal that can be read on a meter. The FID is not as sensitive as other detectors and is less sensitive to compounds containing electronegative atoms such as oxygen, sulfur, and chlorine.

Portable gas chromatographs equipped with FIDs or PIDs can be used to separate and detect multiple gases and vapors (Fig. 3-3). Such instruments greatly increase the specificity of gas and vapor detection.

PID and FID devices are the common direct-reading detection instruments used at industrial and hazardous-materials sites. These instruments do not detect hydrogen sulfide or hydrogen cyanide. Multiple methods of detection are needed at hazardous-materials sites to ensure safety of personnel.

Other instruments use absorption of various wavelengths of infrared energy as a detection method. These may be for personal monitoring also (Fig. 3-4). The gas is drawn into a chamber through which infrared radiation is projected. The gases are selected by adjusting for specific wavelengths of infrared light. The measured absorbance is then converted to a ppm value through appropriate instrument calibration. These instruments allow for the detection of multiple gases such as organic vapors, carbon dioxide, chlorine, hydrogen cyanide, hydrofluoric acid, hydrogen sulfide, formaldehyde, sulfur dioxide, ammonia, and nitrogen dioxide.

MERCURY MONITOR

Elemental mercury, which vaporizes at room temperatures, can be a significant hazard in confined areas. It has no odor. Real-

Figure 3-3. GA-90 infrared gas analyzer for portable use at hazardous sites. (Photograph courtesy of Hazco.)

time airborne concentrations can be measured using a gold-film technology mercury-vapor detector with a sensitivity of 0.003 mg/m^3 (Jerome Instruments, Jerome, AZ).

DETECTOR TUBES

Gas detector (indicator) tubes also can be used on site as direct-reading and grab-sampling instruments. These direct-reading colorimetric tubes contain a reagent that reacts with a standard volume of air and the gaseous contaminant drawn through it (Fig. 3-5). The reagent changes color in the presence of specific hazardous gases. The concentration of the contaminant in the air is read directly on the calibrated tube in ppm. The length or intensity of the color band indicates the quantity of hazardous gas present (Table 3-5).

Long-term detector tubes that require the assistance of a low-slow sampling pump provide an integrative approach to evaluating concentration over extended periods such as an entire work shift. At the end of the monitoring period, the length of the color band provides a direct readout of the TWA concentration.

PARTICLE MONITORS

Real-time monitoring for airborne particulate concentrations can be accomplished using portable direct-reading devices. The principle of operation of these monitors involves light scattering, piezoelectric effects, or beta attenuation. Such instruments should be calibrated against standard particulate monitoring methods to validate their performance.

Figure 3-4. Personal monitor for volatile organic chemicals.

METALS

Information derived from real-time particulate monitors may be used other than for estimating particulate concentrations on a direct numerical or mass basis. For example, if one knows the average concentration of metals in a soil matrix or bulk sample, this value, as a percentage, can be applied to a reading obtained by a direct-reading aerosol monitor in mg/m^3 to obtain an approximate airborne concentration of a metal. This method provides only an approximation of the true airborne metal concentration because the metal content of the source material may vary. The analysis of filter samples for specific metal contaminants provides an accurate estimate of exposure to individual metals.

Indirect (Integrative) Monitoring Methods

INDIRECT MONITORING

Indirect or integrative monitoring is useful for measuring air concentrations of chemicals over a period, typically 15 minutes or longer, to better describe a hazardous environment. Although direct-reading instruments are available for a more limited number of specific toxic agents, indirect analytical techniques simultaneously can collect multiple chemicals at very low concentrations for subsequent analysis. Indirect-reading instruments provide a historical assessment of a site that may have changed since the samples were collected because collection occurs over a specified period and analysis occurs off site.

Indirect-reading instruments or integrative samplers, such as charcoal tubes and passive dosimeters or badges, are used to detect low concentrations of chemicals that may be present in occupational environments. Such monitors collect air samples over extended periods and provide estimates of average exposure or concentration. The measured levels represent TWA concentrations over the specified sampling period. An important concept in the use of these devices is the selection of the proper sampling method and medium to be used, both of which depend on the nature of the substance sampled. The analysis of air samples collected using such methods occurs at a later time in a licensed or certified analytical laboratory. Specific monitoring techniques are described in the following sections.

SOLID SORBENT TUBES

Sampling for gases and vapors with solid sorbent tubes typically is accomplished by drawing contaminant-laden air through a bed of granular sorbent (e.g., charcoal, silica gel, tenax) with a vacuum pump. The contaminant is adsorbed on a granular material. Then it is removed by a chemical or thermal desorptive process. The desorbed material is identified and

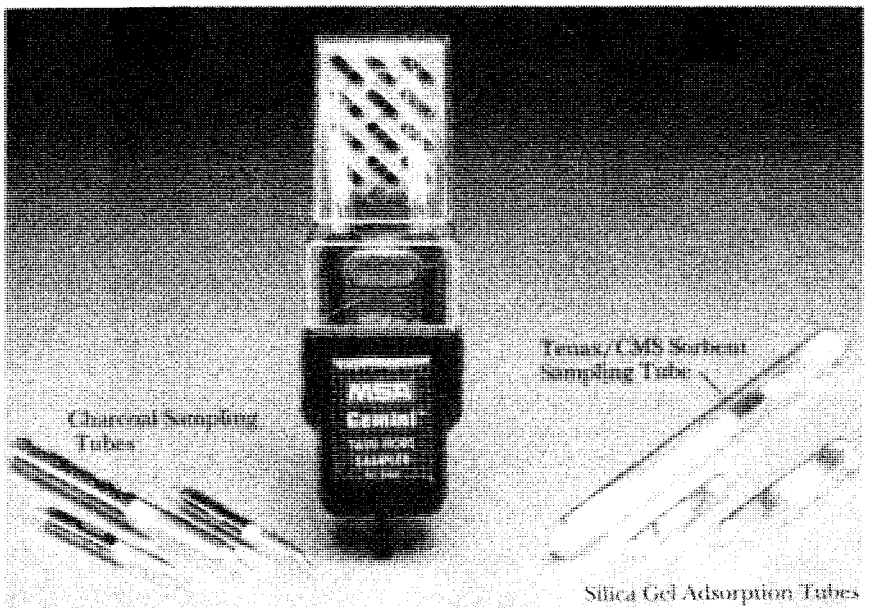

Figure 3-5. Sorbent tube sampling system for airborne chemicals. (Photograph courtesy of Hazco.)

quantified by laboratory procedures. Calibration of pumps before and after monitoring is required to accurately determine the collected air volumes.

PASSIVE DIFFUSIONAL MONITORS

Passive diffusional monitors operate much the same as solid sorbent tubes except that the contaminant is deposited on a sorbent bed by diffusion rather than by actively drawing contaminant-laden air through the collection device. Analysis of the samples is similar to that for solid sorbent tubes.

BUBBLERS (IMPINGERS)

Contaminant-laden air is drawn through a bubbler or impinger containing a liquid media in which the contaminant is soluble. The liquid-media–contaminant matrix then is chemically prepared for laboratory analysis (e.g., spectrophotometry).

ENVIRONMENTAL MONITORING OF BIOLOGICAL AGENTS

Biologicals consist of viable and nonviable agents. Viable agents, which can be grown on culture media or isolated from the environment, include microorganisms such as fungus, bacteria, virus, protozoa, and spores. Nonviable agents are pollen, pieces of microorganisms, and chemical products such as toxins, volatile organic chemicals, mycotoxins, and endotoxins. Biological sampling can be complex and should be performed by professionals for the following reasons:

- The sampling method should be matched to the environmental conditions to characterize the contamination and adverse health effects.
- Sampling should be performed with controls.
- Cultures should be processed by a qualified laboratory.

Bioaerosols are airborne dusts consisting of organic matter, biological material, and inorganic material. Exposure can cause nonallergic and allergic-mediated diseases, including hypersensitivity, pneumonitis, rhinitis, asthma, and airway inflammation.

Indoor biological contamination is defined as the presence of (a) bioaerosols of a kind and concentration likely to cause disease or predispose to disease, (b) inappropriate concentration of outdoor bioaerosols, or (c) microbiological growth that might become aerosolized. Environmental monitoring of bioaerosols usually reveals a diverse mixture of viable and nonviable agents with dynamics of movement determined by

- Particle size related to their diameter
- Shape
- Density
- Hydrophobic or hydrophilic properties
- Electrical charges
- Chemical nature

The primary factors that determine particle aerodynamics are diameter and density. For particles that are more spherical, the aerodynamic properties are related more to the diameter of the sphere. For elongated or spherical particles, the smallest diameter may influence its aerodynamic properties.

Large particles fall faster than smaller ones. Therefore, gravity collection assays may overestimate large particles compared to small. Also, small particles flow around a surface whereas larger particles impact a surface. Hydrophilic particles are collected more easily in a liquid impinger collection method than hydrophobic particles, which pass through the liquid. The electrostatic charge affects particle behavior with respect to surface interaction. Charged particles are more attracted to surfaces with opposite charges. Particle aerodynamics and aerodynamic properties of particles all influence assay systems.

Exposure Guidelines for Biological Agents

No TLVs or PELs exist for interpreting biological contaminants, culturable bioaerosols, countable bioaerosols, or pathogenic agents. Cultural bioaerosols are usually not of a single microbial entity, but rather are complex mixtures. Different sampling methods for bioaerosols can provide different results. Defining human exposure to a single agent or toxin in a bioaerosol is difficult. For these reasons, establishing TLV or PEL standards is not possible currently.

Assays for biochemical markers of biologicals, volatile chemical by-products, mycotoxins, and endotoxins are improving, but field validation is still lacking. The current state-of-the-art biological monitoring and hazard assessment remains professional judgment based on research reports, clinical case studies, and exposure-response relationships.

TABLE 3-5. Detector and indicator tubes

Chemical	Sensitivity/ range (ppm)	OSHA PEL (ppm 1989)	Chemical	Sensitivity/range (ppm)	OSHA PEL (ppm 1989)
Acetaldehyde	100–1,000	100	Ethylene oxide	1–30	1
Acetic acid	5–80	10	Formaldehyde	0.2–5.0	1
Acetone	100–12,000	750		0.5–10.0	1
Acid compounds (air)	Qualitative	—	Formic acid	1–15	5
Acrylonitrile	0.5–20.0	—	*n*-Hexane	100–3,000	50
	5–700	35 (STEL)	Hydrazine	0.2–10.0	0.1
	25–700	35 (STEL)	Hydrocarbons	0.1–0.8	—
Aliphatic hydrocarbons	2–23 mg/L	—	Hydrochloric acid	0.5–25.0	—
Ammonia	2–30	35 (STEL)	Hydrocyanic acid	2–150	—
Aniline	0.5–10.0	2	Hydrogen fluoride	1.5–15.0	3
Arsenic trioxide	0.2 mg AS/m^3	—	Hydrogen peroxide	0.1–3.0	1
Arsine	0.05–60.00	0.05	Hydrogen sulfide	1–200	10
Organic arsines	Qualitative	—	Isopropyl alcohol	100–3,000	400
Basic compounds (air)	Qualitative	—	Mercaptan	0.5–5.0	—
Benzene	2–60	1	Mercury vapor	0.1–2.0 mg/m^3	1 mg/m^3 (ceiling)
	0.5–10.0	1			
Bromine	0.2–30.0	0.1	Methacrylonitrile	1–10	1
n-Butane	0.1–0.8%	800	Methane	Qualitative	—
I-Butylene	1–55 mg/L	—	Methanol	50–3,000	200
Carbon dioxide	1–20 vol %	10,000	Methyl acrylate	5–200	10
	0.5–10.0 vol %	10,000	Methyl bromide	3–100	5
Carbon disulfide	3–95	4	Methyl chloroform	50–600	350
Carbon monoxide	10–3,000	35	Methyl mercaptan	2–100	0.5
Carbon tetrachloride	1–15	2	Methyl methacrylate	50–50,000	100
Carbonyl chloride	0.05–1.50	—	Methylene chloride	50–2,000	500
Chlorine	0.2–30.0	0.5	Monostyrene	50–400	—
Chlorobenzene	5–200	75	Nickel (aerosol)	0.25–1.00 mg/m^3	1 mg/m^3
2-Chloro-1,3-butadiene	5–90	10	Nickel tetracarbonyl	0.1–1.0	—
1-Chloro-2,3-epoxypropane	5–60	2	Nitric acid	1–50	1 (STEL)
Chloroformates	0.2–10.0	—	Nitrogen dioxide	0.5–25.0	1 (STEL)
Chloroprene	5–90	10	Nitrous fumes	0.5–10.0	1 (STEL)
Chromic acid	0.1–0.5 mg/m^3	0.1 (ceiling)	*n*-Octane	100–2,500	300
Cyanogen chloride	0.25–5.00	0.3 (ceiling)	Oil mist	1–10 mg/m^3	5 mg/m^3
Cyclohexane	100–1,500	300	Olefins (butylene, propylene)	1–55 mg/L	—
Cyclohexylamine	2–30	10	Organic basic nitrogens	Qualitative	—
Demeton	0.05	0.1	Oxygen	5–23 vol %	—
Dimethyldichlorovinylphosphate	Qualitative	0.1 mg/m^3	Ozone	0.05–1.40	0.1
p-Dichlorobenzene	2–100	75		10–300	0.1
Dichlorovos	0.05	—	*n*-Pentane	100–1,500	600
Diethyl ether	100–4,000	400	Perchlorethylene	5–50	25
Dioborane	0.05–3.00	0.1	Phenol	5	5
Dimethyl acetamide	10–40	10	Phosgene	0.04–1.5	0.1
Dimethyl formamide	10–40	10	Phosphine	0.1–40.0	0.3
Dimethyl sulfate	0.005–0.050	0.1	Propane	0.5–1.3 vol %	1,000
Epichlorhydrin	5–50	2	*n*-Propanol	100–3,000	200
Ethanol	100–3,000	1,000	Sulfur dioxide	0.5–25.0	2
Ether	100–4,000	—	Sulfuric acid	1–5 mg/m^3	1 mg/m^3
Ethyl acetate	200–3,000	400	Toluene	5–400	100
Ethyl benzene	30–600	100	Toluene diisocyanate	0.02–0.20	0.005
Ethyl ether	100–4,000	400	*o*-Toluidine	1–30	5
Ethyl mercaptan	0.5–5.0	0.5	1,1,1-Trichloroethane	50–600	350
Ethylene	50–2,500	—	Trichloroethylene	2–200	50
	0.1–5.0	—	Triethylamine	5–60	10
Ethylene glycol	10–180 mg/m^3	50 (ceiling)	Vinyl chloride	1–50	1
Ethylene glycol dinitrate	0.25	0.1 mg/m^3 (STEL)	*o*-Xylene	10–400	100

OSHA, Occupational Safety and Health Administration; ppm, parts per million; STEL, short-term exposure limit.

Environmental Sampling for Bioaerosols

Before sampling, the environment should be surveyed for contamination sources, dispersion sources, and exposure of individuals to biologicals. Overgrowth of bacteria or fungi cause musty or foul odors. Observations can result in immediate decisions about the health and safety of an environment and the relationship of signs and symptoms to environmental conditions. Inspection involves detection of odors, and noting of water-damaged areas, moisture in ventilation systems, stagnant water sources, or easily observed areas of mold growth.

Assaying for fungi, fungal elements (spores, hyphae), and bacteria involve three basic methods:

1. Air sampling
2. Swab or surface sampling
3. Bulk sampling

SURFACE OR SWAB SAMPLING

Wiping or swabbing an area of suspected biological contamination helps characterize the genus and species of microorganisms predominantly present. Surfaces are swabbed with a sterile, cotton-tip stick moistened with nutrient media such as 0.1% peptone with 0.01% Tween 80. The swabs are placed in a sterile tube and plated on agar.

Another technique is to place the swab into a 250-mL flask with nutrient broth, place the flasks on a rotary shaker for 20 minutes, then inoculate agar plates with a 0.1–0.2-mL aliquot of the suspension (7–9).

BULK SAMPLING

With bulk sampling, a physical sample is collected from a surface or specifically identified biological source such as the dust in a ventilation system. Such sampling helps determine the amount of an agent per gram of dust or contaminated material. But this does not consider the total amount of contaminant in the environment or the amount that might be aerosolized. To have meaning, bulk samples must be collected from the primary source of the causative agent in the environment. Generally, one gram of dust is extracted in sterile water with nutrient broth and agitated. The suspension is serially diluted and an aliquot is inoculated on appropriate agar (7–9).

AIR SAMPLING

Air sampling uses a device to collect a certain amount of air to determine the colony-forming units per cubic meter (CFU/m^3) of viable biologicals. Three basic sampling methods exist for collecting bacteria or fungi (7–9):

1. Drawing a volume of air through sterile microporous filter
2. Impinging air into a liquid
3. Collecting a fixed volume of air with impaction of viable organisms, spores, or hyphae on agar

Air sampling is more representative of human exposure to bioaerosols than wipe sampling or bulk sampling. But there are many variables in air sampling that affect results. First, collecting a representative sample of bioaerosols in a certain space over time to make health hazard determinations is the goal, but is not always representative. Particle aerodynamics and chemical and electrical nature all affect bioaerosol sampling. The sampling device and culture media also are critical to both collection and growth of microorganisms for identification.

Particle size can vary from smaller than 1 μm to more than 100 μm. Characterizing the sample from such a large range and size of particles can be difficult when using a single collecting device. But bioaerosols of concern generally range from 0.1 μm to 10.0 μm. Focusing on the particle size provides a better human exposure representation.

Choice of culture media is critical for growing bacteria and fungi (Table 3-6). Culture media can be general or nutrient-specific (i.e., designed to grow a particular organism). *Aspergillus* and *Penicillium* are hardy and persist in dry conditions. *Botrytis* and *Stachybotrys chartarum* are not as viable. If found in air sampling, their presence should be evaluated carefully as a potential environmental health problem. The selection of culture media is critical because different microbes may grow poorly or not at all in standard culture media and under certain conditions. Living organisms also can be damaged by the collection technique and fail to grow. Air sampling for culture usually underestimates the true bioaerosol concentration (8). For comparison, air sampling should be conducted outdoors in close proximity to the fresh air intakes to serve as controls. Indoor air samples should be collected simultaneously near suspected sources of contamination before and after agitation of sources. Source agitation can produce a 1,000-fold increase in the indoor air bioaerosol concentrations. Gravity or settling Petri dishes with culture media are of no use in sampling because they underestimate or may fail to detect biological contaminants that can remain in the air for lengthy periods. Summarizing, important issues involving air sampling for viable biologicals include

- Detection of viable organisms by culture
- Choice of appropriate culture media
- Timing of sampling to best characterize the biological exposure
- Choice of sampler device
- Identification of the genera and species of microorganism
- Interpreting the results in terms of exposure and health hazards

TABLE 3-6. Culture media for biologicals

Biological	Culture media
Saprotrophic fungi	Malt extract agar
Xerophilic saprotrophic fungi	Malt-salt agar Dichloren glycerol agar
Stachybotrys atra	Cellulose agar
Bacteria	Blood agar Tryptic soy agar (TSA) Aerobic agar Nutrient agar Sterile peptone water for use with liquid impinger
Actinomycetes	TSA Specific culture medium
Legionella bacteria	Buffered charcoal yeast extract (BCYE) agar with antibiotics or BCYE containing L-cysteine

Air Sampling Devices

Devices for sampling air (7) include (a) suction samplers that impact particles on surfaces or into liquid, or trap particles on filters; (b) rotating impact samplers that impact particles on rapidly moving surfaces; (c) electrostatic samplers that attract particles to electrically charged surfaces; and (d) gravity devices that trap particles falling from the air (Table 3-7).

Impactor sampling is more practical for nonindustrial sampling of bioaerosols. In heavily contaminated environments, impinger sampling is more appropriate.

Sampling time is an important variable when sampling for microorganisms. Continuous sampling over an exposure period of interest might be ideal but may not be achievable. Sampling duration often is constrained by desiccation of media by airflow and the potential of overloading media surface with microorganisms, which can lead to overgrowth during incubation.

CENTRIFUGAL SAMPLER

A centrifugal sampler draws in particles from air and impacts them on an agar surface using centrifugal force. The commonly used Reuter Centrifugal Sampler (Biotest, Danville, NJ) samples air at 280 liters per minute. Another model is designed to sample air rates from 1 to 1,000 liters per minute. Bioaerosols are impacted against agar strips that then are incubated for colony growth (7).

ALL GLASS IMPINGER

The all glass impinger (AGI-30, Ace Glass, Vineland, NJ) concentrates air samples of bioaerosols by drawing air through a curved inlet that simulates nasal passages, then through a jet where particles are impinged on a liquid. The AGI-30 is a frequently used device with an air sampling rate of 12.5 liters per minute. The AGI-30 is used to sample air for bacteria, fungi (spores and hyphae), and viruses (7).

TABLE 3-7. Commonly used samplers for collecting indoor bioaerosols

Sampler	Principle of operation	Sampling rate, 1 pm	Recommended sample time	Minimum CFUs detected	Applications/remarks
Slit to agar impactor	Impaction onto agar on rotating plate or stationary plate	30–700 continuous	Variable; 1–60 min or 7 d	—	Provides information on aerosol concentrations over time
Sieve-type impactors					
Single-stage portable	Impaction onto agar on "rodac" plate	90 or 185	0.5 or 0.3 min	22 or 16	Approximately 40% as efficient as slit sampler; portable, useful as probe
Single-stage impactor	Impaction onto agar, 100-mm plates	28	1 min	35	Nearly as efficient as slit, bulky to handle, AC operation
Two-stage impactor	Impaction onto agar, two 100-mm plates	28	1–5 min	35	Same as single-stage impactor but divides samples into respirable and nonrespirable fractions
Filter cassettes	Filtration	1–2	15–60 min or 8 h	8–33	Some desiccation loss; portable, inexpensive, useful as probe
High-volume filtration	Electrostatic collection into liquid	Up to 1,000	Variable	—	—
All glass impingers	Impingement into liquid	12.5	30 min	3	Fungi require wetting agent; useful over wide range of particle concentrations
Centrifugal sampler	Impaction onto agar, plastic strips	40	0.5 min	50	Cannot be calibrated; small, portable, useful as a probe

AC, alternating current; CFUs, colony-forming units; PM, phase modulation.
With permission from U.S. Environmental Protection Agency. Introduction to indoor air quality: a self-paced learning module. Washington: EPA, Office of Air and Radiation; 1991; EPA publication 400/3-91/002.

CYCLONE SCRUBBER

The cyclone scrubber collects aerosols by tangential impingement into thin layer created by a liquid mist that impacts the sampler wall. Collection fluid is delivered by a controlled flow rate through a jet inlet that creates a mist that traps bioaerosols. This device is used to sample for viruses, bacteria, and *Legionella* bacteria (7).

ANDERSEN MULTIHOLE IMPACTOR

Several types of Andersen multihole impactors are available, including single- and multistage. The device works by pulling air through jet holes below which are Petri dishes of agar. Air sampling rate is fixed at 28.3 liters per minute. Some Andersen samplers are multistage with different jet diameters for each stage. This design allows sampling for coarse particles and fine particles. The six-stage impactor is efficient for collecting bacteria and fungi in indoor air (7).

SURFACE AIR SYSTEM SAMPLER

The surface air system sampler is a portable, multiorifice device that collects microorganisms by inertial impaction. Air drawn through a jet is deflected 90% and agar serves as the obstacle to air flow. Larger particles impact on agar while smaller particles follow the jet stream (7).

SPORE TRAPS

A spore trap can provide a continuous recording of spores that collect on a greased tape. It can run for days. This allows for the recording of spore size and type. It can help detect fluctuation in concentrations in nature of spores during a time course.

Other Assays for Characterization of Biological Contamination

Identification of microbe genus and species along with determination of the relative percentages of fungal, bacterial, and spore species is critical to assessing health risks. Analysis of bioaerosols may also include (9,10)

- Microscopy: Visually characterizing spores, pollen, or particles by microscope
- Assaying for antigen content of dust
- Assaying for endotoxin content of dust (gram-negative bacteria)
- Chemical assays for volatile organic compounds of fungi and bacteria
- Assaying for mycotoxins (fungi)
- Assaying for (1→3)-β-glucan in dust samples (fungi)

BACTERIA

Bacteria are single-celled microbes without a nucleus (procaryotic) usually less than 4 μm in diameter. Bacteria possess a thick cell wall and are divided into two main types based on Gram's stain: gram-positive or gram-negative. Some bacteria are pathogenic. All bacteria can cause health problems if they have a nutrient source and amplify indoors. Culture plate impactors are used for bacterial sampling using general media such as nutrient agar, blood agar, or casein soy peptone agar. Specialized media can be used to grow certain types of bacteria. Pathogenic bacteria grow best at approximately 95°F (35°C). Thermophilic organisms grow best at 122°F (50°C) or higher and most other common organisms grow between 25° and 30°C (77° to 86°F).

The presence of more than 1,000 CFU/m^3 of gram-positive or more than 500 CFU/m^3 of gram-negative bacteria in air samples is a health concern. The presence of any species of pathogenic bacteria, such as *Legionella* and *Pseudomonas*, should raise concerns. Gram-negative bacteria are associated with environmental endotoxins. Positive bacteria have a peptidoglycan present in cell walls. Peptidoglycan is an immunomodulator similar to endotoxin but with less potency. Bacteria can produce spores that are temperature and drought resistant.

Stagnant water is a reservoir for gram-negative bacteria. *Legionella* also grows in stagnant water. *Legionella pneumophila* may not be detected in air samples, which makes sampling from potentially contaminated water sources important to detect this organism.

Many gram-negative bacteria are found in agricultural settings. Composting activities are associated with bioaerosols in excess of 10,000 CFU/m^3.

Pseudomonas can grow in metal-cutting machine fluids. Gram-negative bacteria grow on chronically wet building materials. Levels of biological contaminants indoors must be compared to levels found outdoors. For pathogenic contaminants such as *L. pneumophila*, any finding would be abnormal and indicate contamination and potentially serious health consequences.

Indoor bacteria generally originate from activities of the human occupants. Excessive quantities of human-source bacteria, such as *Bacillus subtilis*, indicate overcrowding or poor, ineffective ventilation. The presence of pathogens, such as actinomycetes, *L. pneumophila*, or *Pseudomonas*, or of an endotoxin indicates potentially serious contamination.

Bacterial air-sampled concentrations of less than 1,000 CFU/m^3 generally are not a concern, provided there is not a preponderance of one organism type. Concern is generated by air-sampled concentrations of gram-negative bacteria or pathogenic bacteria that are greater than 500 CFU/m^3.

Muramic Acid (Peptidoglycan)

The cell walls of gram-positive bacteria contain a chemical called *peptidoglycan* that has toxicity similar to endotoxin (11). Gram-positive bacteria containing peptidoglycan may pose a health problem when they accumulate indoors, because peptidoglycans have inflammatory and respiratory health effects.

Muramic acid is a component of peptidoglycan in bacterial cell walls. It is not found anywhere else (7,11). Therefore, muramic acid is a marker for peptidoglycan presence and indicates contaminating presence of gram-positive bacteria.

Tandem gas chromatography and mass spectrometry (GC-MS) have allowed improved specificity of detection of muramic acid but remains a research tool (12). The presence of muramic acid in air concentrations of dust should be correlated with health effects.

Endotoxins

Endotoxins are lipopolysaccharides (LPSs) derived from the outer membrane of gram-negative bacteria and blue-green algae. Endotoxins are composed of proteins, lipids, and LPSs. *LPS* refers to endotoxin material that is free of protein and other cell wall components. LPSs consist of a lipid component and a polysaccharide component. The lipid component—lipid A—is responsible for most of the toxic and adverse properties of endotoxins (13). The polysaccharide component is hydrophilic. It varies considerably between bacterial species while the lipid component is fairly constant on bacterial species. Most endotoxin exposure is caused by gram-negative bacteria in the environment. Endotoxins also are present in organic dust.

Environmental monitoring for endotoxins is performed by the sampling of water or airborne dust with analysis of aqueous extracts by the limulus amebocyte lysate test (LAL) (7,14,15). Although the LAL assay is standard for endotoxin detection by the U.S. Food and Drug Administration (FDA), there is no generally accepted standard for sampling and extraction (16). Standardization of the LAL assay has been attempted. For environmental dust, the use of the quantitative chromogenic modification of the LAL test is recommended (7,13–16). Reagents and endotoxin standards are available in kit form (Kinetic-QCL, Bio Whittaker, Walkersville, MD). Another method using the kinetic turbidimetric approach (KLARE, *k*inetic-turbidimetric *l*imulus *a*ssay with *r*esistant-parallels-line *e*stimate) yields results that are consistent with gas chromatography and mass spectrometry (17).

The FDA has a standard reference for endotoxin that is 50 endotoxin U/mL (EU/mL), which is approximately 5 ng/mL (7,14–18) (Standard Reference Endotoxin EC-5, No. 23550-3 USP, Customer Service Department 1643, 12601 Twinbrook Parkway, Rockville, MD 20852).

The LAL assay has interferences caused by dust. A wide coefficient of variation also exists in some studies using the assay (17).

Recommendations are emerging for the sampling of endotoxin as it relates to interpreting health effects. More recent versions of the LAL assay are proving to be more sensitive, with ranges of 0.01 to 100 EU/mL, or approximately 1 pg/mL to 10 ng/mL. The detection limit of airborne endotoxin for the LAL method is approximately 5 pg/m^3 (0.05 EU/m^3). The absolute measurement of endotoxin is probably inaccurate because it only assays measurements of endotoxins collected within that period of sampling.

Levels of endotoxin as they relate to illness are difficult to ascertain. Some guidelines are emerging (19). The International Commission on Environmental Health has guidelines for endotoxin of 1 μg/m^3 for pneumonitis and 0.001 μg/m^3 for general airway inflammation (7).

It is important to have an internal standard for endotoxin because different LAL test batches can give different results (7). Using standard endotoxins as part of the procedure is recommended. The FDA uses *Escherichia coli*-5 in its standardization procedures. The *E. coli*-5 reference is based on purified lipopolysaccharides from *E. coli* organisms as expressed in endotoxin units measured by LAL test activity. Commercial LAL tests also include a control standard endotoxin based on *E. coli* and sometimes on *Serratia abortus equi*. Caution should be used to ensure that the LAL test is endotoxin-specific, and does not react with (1→3)-β-glucan, which has a reactive affinity for factor G in the LAL test kit reagent.

No occupational exposure standard for endotoxins exists, although recommendations are being made to establish exposure limits (20).

Air sampling for endotoxin uses standard procedures for collection of airborne dust. Water samples should be collected in sterile containers. Filters should be selected that allow for efficient dust extraction. Polyvinyl chloride filters bind endotoxin. Polyvinyl chloride and cellulose acetate filters provide higher extraction efficiencies compared to glass fiber filters (7). Polycarbonate filters also are efficient in capturing endotoxin. A 100-liter air sample is sufficient to determine endotoxin indoors.

The medical literature reflects no adverse effect levels for inhaled endotoxin ranging from 9 ng/m^3 to 170 ng/m^3 (90 to 1,700 EU/m^3). These calculated "no effect" levels are based on epidemiologic studies of exposed populations with a safety factor of two applied (18).

The Dutch Expert Committee on Occupational Standards has proposed a health-based recommended limit of 50 EU/m^3 (4.5 ng/m^3 over an 8-hour exposure period) (13).

3-HYDROXYLATED FATTY ACIDS

An alternative assay method to determine endotoxin is based on detection of 3-hydroxylated (OH) fatty acids of LPS by GC-MS. These 3-OH fatty acids are linked to the glucosamine disaccharide portion of lipid A (7). GC-MS thus allows for determining chemical markers of gram-negative bacterial populations present indoors.

The LAL assay is more sensitive, but the GC-MS analysis of 3-OH fatty acids allows for identification of bacteria. The chiral configuration of the 3-OH fatty acids can be obtained to separate optically active configurations (R and S) (7).

Viruses

Assaying for the presence of viruses requires specialized culture media. Viral-culture media are generally tissue cultures. If collection is delayed more than 1 hour, the samples should be refrigerated.

FUNGUS

Fungi are eukaryotic—they possess a nucleus—and exist as single cells or multiple cells. Fungi are not photosynthetic. Fungi release enzymes that dissolve organic material on which they grow. These chemicals cause the typical musty odor of damp areas indoors. Fungi have hyphae and produce spores. Sampling of fungi can be performed by plating air, bulk, or liquid samples on appropriate culture media such as potato dextrose, Sabouraud-S dextrose, or malt-extract agar. Malt-extract agar has advantages because it does not support bacterial growth and it also is a medium in which *Aspergillus* species grow. *Aspergillus fumigatus* generally grows at 45°C in incubation. All other cultures for fungi are incubated at room temperature.

High-volume-filtration sampling devices can be used to evaluate airborne antigens and mycotoxins. Volumetric sampling with sieve or slit impactors also can be performed over an interval of time in areas of suspected high fungal spore concentrations.

Fungal concentrations in indoor air samples should be equal to or less than outdoor concentrations while distributions of genus and species should be similar. Air concentrations less than 100 CFU/m^3 are generally not a concern. Those higher than 500 CFU/m^3 should be compared to controls because they could be a concern, while those higher than 1,000 CFU/m^3 definitely are a concern. Disturbing a source of fungus or mold elevates spore counts up to 1,000-fold the baseline level in the air. *Penicillium*, *Cladosporium*, and *Alternaria* are the most prevalent fungal spores found in indoor environments.

Fungal Chemical Markers

Fungi produce toxic and immunoreactive chemical by-products that cause inflammation, respiratory irritancy, fatigue, lassitude, and other constitution symptoms:

- Mycotoxins
- Low-molecular-weight volatile compounds: geosmin, 1-octen-3-ol, 3-methylfuran
- (1→3)-β-glucan
- Enzymes
- Ergosterol

VOLATILES GENERATED BY FUNGI

Volatile chemicals generated by fungi can be used to determine fungal presence and the nature of fungal contamination indoors. Detection of 3-methylfuran indicates fungal growth and amplification (7). Detection of 1-octen-3-ol indicates dormant fungal mass. Geosmin presence indicates fungal mass presence and active growth (7).

Air concentrations of ergosterol measurements can be used to assay fungal mass in indoor dust. Ergosterol is a membrane sterol of fungal filaments. Ergosterol is very stable and is found in living and nonviable spores. Air is collected on a microspore titer and spores are extracted with methanol. Analysis is by GC-MS or high-pressure liquid chromatography. One study showed 3.2 μg of ergosterol per milligram of spores. *Aspergillus* and *Penicillium* produce 1.4 μg/mg to 6.0 μg/mg (21–23).

Fungi release volatile organic chemicals while growing. These chemical by-products can be sampled with a portable air sampler (Anasorb 747 carbon tube). Samples should be obtained in areas of concern and near ventilation intakes outdoors with control samples. GC-MS with selected ion detector is used to analyze for volatile chemicals (24).

INTERPRETING RESULTS OF FUNGAL ASSAYS

Components of the fungal cell wall may be responsible for organic toxic dust syndrome and hypersensitivity pneumonitis, and can be responsible for symptoms of chronic fatigue, fever, nausea, arthralgia, and anorexia (25).

Assaying environments for biological contamination should combine air sampling, bulk sampling, and inspection to characterize the extent of contamination and make decisions regarding health hazards. Comparison with outdoor control samples is important. Results of sampling are as follows:

- A predominance of fungal species in indoor air samples that are not dominant outdoors indicates poor indoor air quality and a potential health hazard.
- Many mycoflora are found commonly indoors. *Cladosporium*, *Alternaria*, and *Penicillium* are common indoors. However, air concentrations of total fungal presence should not exceed 1,000 CFU/m^3.
- *Cladosporium*, *Alternaria*, *Epicoccum*, and *Basidiomycetes* are present outdoors seasonally. In naturally ventilated buildings, the outdoor concentration may equal the indoor concentration. Wetness and moisture cause proliferation of fungi.
- Remediation should follow guidelines for removing and decontamination of fungal overgrowth (26,27).
- Presence of pathogenic fungi requires action. Pathogens include *Aspergillus* fungi (*A. fumigatus*, *A. flavus*), histoplasma capsulatum, and *Cryptococcus neoformans*. *A. fumigatus* grows in warm conditions in composting material. *Fusarium* species, particularly *F. moniliform*, may be found in damp or wet ventilation systems, and can infect immunocompromised individuals.

Fungal spore counts are obtained by drawing air in a sampler and impacting them on a moving, sticky surface. The spores can be examined microscopically. Microporous filters also are used to sample spores. Spores are eluted from the filters and counted microscopically.

MYCOTOXINS

Mycotoxins are chemical components of fungal cell walls and can persist for a long time in the environment after the fungus is dead or no longer viable. Mycotoxins can adhere to dust particles, be present in spores, and disperse in air currents. The presence of mycotoxins is not ruled out by the inability to grow mycotoxin-producing fungal species in culture. Identified mycotoxins include the following:

Diacetoxyscirpenol
Sterigmatocystin
Tannins
T2-toxin
Deoxynivalenol
Fumonisin
Zearalenone
Stachybotrys toxins
Mycophenolic acid
Aflatoxin B1, B2, G1, G2, M1
Ochratoxin A
Satratoxin F, G, H
Verrucarin J
Roridin E
Citrinin
Roquefortine
Patulin
Rubratoxin B

Fungi produce mycotoxins under narrow and strict nutrient and climate conditions. The ability to isolate mycotoxins from cultured fungi does not mean that these fungi are producing mycotoxins in the indoor environment. *Stachybotrys atra*, known

to produce mycotoxins, cannot compete with other fungi like *Penicillium* in culture. Therefore, *Stachybotrys* may be missed in the environment when cultured.

GLUCANS

(1→3)-β-glucan possesses potent immunostimulatory and inflammatory properties through macrophage activation. Measurement of (1→3)-β-glucan is performed using a glucan-specific limulus lysate assay (7,20,25). This biological assay currently is the only one available for measurement of glucans in environmental samples. Demonstration of airborne glucan requires generating air movements to suspend dust in the environment to obtain relevant assay data.

The LAL assay contains an enzyme that reacts with (1→3)-β-glucan. The enzyme was isolated by Sepharose column chromatography to develop an assay for the glucan with pg/mL sensitivity (28). Release of cytokines, such as tumor necrosis factor-2, from macrophages is induced by (1→3)-β-glucan.

The presence of (1→3)-β-glucan in air correlates with illness. Air concentrations of 0.01 to 100 ng/m^3 of (1→3)-β-glucan are associated with chronic respiratory inflammation. Air samples are collected on a cellulose acetate/nitrate membrane filter. Filters are extracted by cold aqueous 0.3N NaOH (29).

ORGANIC AND COTTON DUSTS

Organic dusts consist of particles of vegetable, animal, and microbial origin. Organic dusts contain bacteria and fungi in the range of 10^4 to 10^{12} CFU/m^3 (30). Allergic alveolitis is caused by organic dusts. Causative species include *A. fumigatus, A. flavus, Aspergillus clavatus, Aspergillus niger, Aspergillus terreus, A. versicolor, Cryptostroma corticale, Eurotium rubrum, Penicillium* spp, *Alternaria* spp., *Cladosporium* spp., and *Didynella* spp. (20). Sampling for cotton dusts has provided the experience with organic dust exposure and health effects.

Continuous exposure to microbial concentrations greater than 1×10^5 CFU/m^3 is associated with respiratory illness (20). The cotton dust standard PEL for lint-free dust is 0.2 mg/m^3 for an 8-hour TWA in yarn manufacturing, 0.75 mg/m^3 in weaving and slashing, and 0.5 mg/m^3 in nontextile industries using cotton (31).

Sampling for organic dusts may also involve detection of toxic and pro-inflammatory components such as endotoxin, mycotoxins, and (1→3)-β-glucan (32).

Allergens and Antigen Load in Dust

Analytical assays are available to determine allergen concentrations in dust and bioaerosol samples indoors. Major allergens tested for are cat, dog, dust mite, and cockroaches. Immunoassays are available for detection of select antigens such as latex and fungal and bacterial by-products.

Sampling devices include vacuum cleaners with high-volume pumps and filters. Immunoassays with monoclonal or polyclonal antibodies are used to detect allergens in dust samples. Collection devices are standard vacuum cleaners with high retention bags with 97% efficiency for particles of a diameter greater than 1 μm. Filter cassettes are used with a 0.45-μm pore size attached to standard vacuum as a nozzle. For many allergens, standards or references exist and are available from the World Health Organization and the FDA (Office of Biologics Research and Review, Center for Drugs and Biologics).

Selecting the site for allergen sampling varies depending on the health complaints and presence of animals, dust mites, or roaches. Most samples are obtained from carpet, upholstery, surface dust, kitchens, cabinets, interior wall spaces, bedding, and ventilation ducts. The sampling objective is to characterize human exposure as close as possible.

Because allergens cause adverse health reactions at very low concentrations in sensitized individuals, there is no TLV or PEL (Table 3-8). Individuals vary in terms of their adverse response to allergens. Thresholds can be used only to provide advice to patients to reduce exposure, warn of potential risk, and point out the need to clean or change an environment.

Samples of 500 mg of dust are recommended as the minimum for testing. The antigen is extracted from the dust sample. This can affect the sensitivity and variability of the immunoassay. Coefficients of variation for these assays are approximately 20% (7).

Tannic acid interferes with analysis of dog and cat allergens by immunoassay. Tannic acid is sometimes recommended as an antiallergen treatment for carpet.

TABLE 3-8. Commercially available tests for environmental allergens in dust samples

Antigen	Type of assay	Thresholds reported by testing laboratories
Cat allergen (*Felis domesticus*)	PAb[a]	Low threshold (<20 μg/g)[c]
Fel d I (*Felis domesticus*)	MAb[b]	Threshold for sensitization (8 μg/g)[d]
Dust mites (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*)	PAb	Low threshold (<15 μg/g)[c]
Der p I (from *D. pteronyssinus*)	MAb	Threshold for sensitization (2 μg/g) Dose for symptoms (10 μg/g)[d]
Der f I (from *D. farinae*)	MAb	Threshold for sensitization (2 μg/g) Dose for symptoms (10 μg/g)[d]
Dog allergen (*Canis familiaris*)	PAb	Low threshold (<20 μg/g)[c]
Can f I (*C. familiaris*)	MAb	Threshold for sensitization (10 μg/g)[c]
Cockroach (*Blattella germanica* and *Periplaneta americana*)	PAb	Low threshold (5 μg/g)[c]
Bla g I (from *B. germanica*)	MAb	Threshold for sensitization (2 U/g)[c]

[a]Polyclonal antibody enzyme immunoassay (EIA) with specificity for multiple antigens from the indicated species.
[b]Monoclonal antibody EIA with specificity for individual antigenic determinants from these various organisms.
[c]These low thresholds are based on an arbitrary classification scheme in which allergen concentrations are defined as low, medium, or high.
[d]Thresholds based on epidemiologic studies designed to estimate what level of allergen was likely to result in sensitization in patients with atopic tendencies. For the two mite epitopes (Der f I and Der p I) the dose of allergen that elicited symptoms in clinically sensitive individuals was also determined.
From American Industrial Hygiene Association Biosafety Committee. Allergens. In: Dillon H, Heinsohn P, Miller J, eds. Field guide for the determination of biological contaminants in environmental samples. Fairfax, VA: American Industrial Hygiene Association, 1996:151, with permission.

TABLE 3-9. Guidelines for assessing health hazards of biologicals

Biological agent	No health concern	Health concern	Reference source
Bacteria	<1,000 CFU/m^3 (gram-positive) <500 CFU/m^3 (gram-negative)	>1,000 CFU/m^3 >500 CFU/m^3 (gram-negative) Presence of pathogenic bacteria	7, 8, 31
Fungus	<100 CFU/m^3 or less than outdoor control	>1,000 CFU/m^3 Concentration of species-specific fungus Presence of pathogenic fungi or mycotoxin-producing fungi	7, 8, 31
Muramic acid	No data	Presence indicates gram-positive bacteria; correlate with symptoms	7, 11, 12
Ergosterol	No data	3.2 µg/mg of spores 1.4-6.0 µg/mg spores, *Aspergillus* and *Penicillium*	7, 23–25
Endotoxin	9–170 ng/m^3 (900–1,700 EU/m^3)	4.5 ng/m^3 8-h exposure period (50 EU/m^3) Endotoxin: 1 µg/m^3 for toxic pneumonitis, 0.001 µg/m^3 for airway inflammation	Dutch Expert Commission on Occupational Standards International Commission of Occupational Health 11, 13–20
Antigen	Below sensitization threshold	Dust mite (Der p I/g of dust) Low: <2 µg/g Moderate: 2–10 µg/g of dust High: >10 µg/g dust Threshold for sensitization = 2 µg/g Cat allergen Fel D I/g of dust Low: <1 µg/g Moderate: 1–8 µg/g High: >8 µg/g Threshold for sensitization = 2 µg/g Cockroach (*Blattella germanica*) Threshold for sensitization = 2 U/g	7, 8
(1→3)-β-glucan	None detected	0.01–100.00 ng/m^3	7, 20, 21, 25, 28, 29
Mycotoxin	Correlate with signs and symptoms	0–10^2 ng/m^3, correlate with signs and symptoms	7, 21, 25, 27, 28
Protozoa	Absent	Any present	8, 9
Organic dust spores	Low levels decrease risk	10^6–10^{10} spores/m^3 Allergic alveolitis, hypersensitivity, organic dust toxic syndrome	20, 21
Microorganisms in organic dust	Low levels decrease risk	1×10^5 CFU/m^3 Allergic alveolitis, hypersensitivity, organic dust toxic syndrome	20, 21

CFU, colony-forming unit.

Integrated Monitoring Strategy for Toxic Chemical Markers of Biologicals

An integrated approach that characterizes chemical biomarkers of biologicals involves assaying for 3-OH fatty acids, muramic acid (peptidoglycan and fungal mass), and ergosterol by tandem GC-MS (7,12).

Assessing the health hazards of biologicals and products of biologicals is difficult because of the lack of standards. However, guidelines exist to assist decision making (Table 3-9).

INORGANIC DUST AND PARTICULATES

Inorganic dusts are broadly classified as

- Mineral dusts (silica and silicates)
- Metallic dusts
- Asbestiform dusts
- Carbon dusts

Health problems secondary to inorganic particulates relate to their size, chemical makeup, airborne concentration, and length of exposure. Inorganic dust and related particulates are derived mainly from silica, silicates, metals, asbestiform minerals, and synthetic crystalline fibers (Fig. 3-6).

Mineral dust health hazards include:

- Silica
- Asbestos
- Silicates
- Talc (magnesium silicate)
- Clay (aluminum silicate)
- Kaolin (aluminum silicate)
- Mica (aluminum silicate)
- Feldspar (potassium silicate, NaCa silicate)

Particulate size determines whether aerosols are respirable. In general, particles approximately 10 µm in diameter lodge in the upper airway. Particles smaller than 5 µm in diameter penetrate to lower areas of the respiratory tract where they can deposit and remain for long periods. Those particles that are smaller than 1 µm in diameter generally are able to penetrate into the lower terminal bronchioles, and those that are smaller than 0.5 µm in diameter may be able to reach the terminal alveolar sacs (Fig. 3-7).

Inorganic particulates are divided broadly into metallic and nonmetallic categories. Nonmetallic particles containing silica are divided further into crystalline or amorphous types.

Metallic particulates exist in the form of dusts or fumes. They range in toxicity. Metal fume fever is the acute febrile respiratory illness caused by inhalation of metal fumes. Metal particulates can also cause dermal lesions such as contact dermatitis, allergic dermatitis, and granulomas. Some metal dusts are systemically

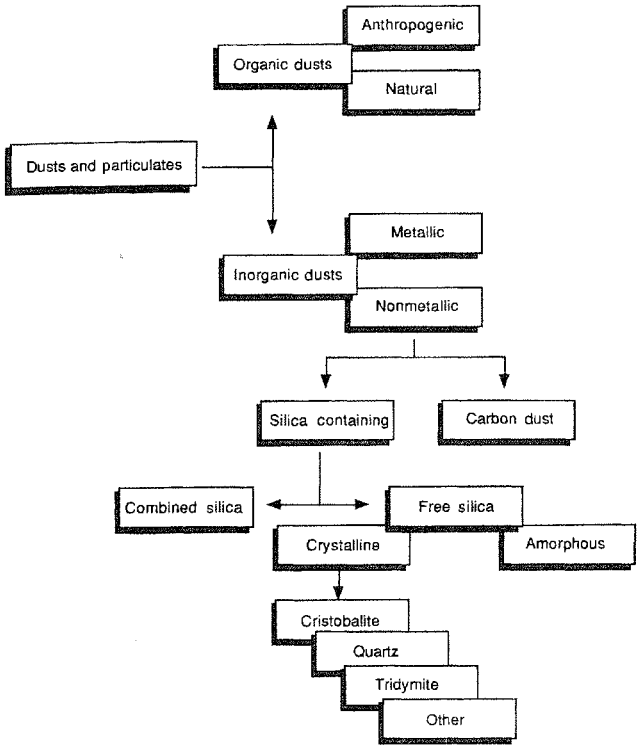

Figure 3-6. Dust and particulates classification.

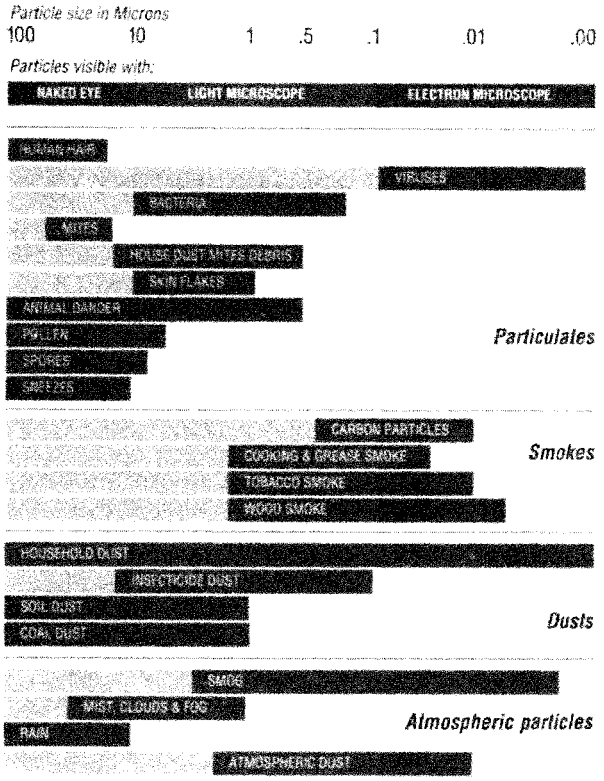

Figure 3-7. Particulate size determines whether aerosols are respirable. (Courtesy: Honeywell, Inc., Home and Building Control, Golden Valley, MN.)

absorbed, resulting in clinical toxicity (e.g., cadmium, manganese, beryllium, lead, arsenic, chromium, and copper).

Particles suspended in air are usually not visible unless they are highly concentrated or approximately 50 μm in diameter. Dust particles settle according to their diameter size. Particles larger than 10 μm settle more quickly than particles that have a diameter smaller than 10 μm. Respirable particles are generally 5 μm or smaller and remain suspended in air for hours. In comparison, pollens have diameters from 18 to 25 μm. Particles of 0.5 μm or smaller in diameter remain airborne for 3 to 6 hours.

The U.S. Environmental Protection Agency (EPA) currently regulates particles of 10-μm diameter (PM_{10}) under National Ambient Air Quality Standards for outdoor air. Health risks from ambient air pollution is associated with particulate pollution 10 μm or smaller in diameter in ambient outdoor air. The PM_{10} standard in the National Ambient Air Quality Standards is 150 mg/m^3, with a yearly average of 50 mg/m^3 (33).

Silica

Silicon refers to the element Si. *Silicon dioxide* (SiO_2) refers to natural amorphous silica (noncrystallized), crystalline silica (quartz), and silicates (clay or aluminum silicate). Silica occurs naturally in either the crystalline or amorphous form. Silica is found in rocks of all varieties. Silicone is synthetic amorphous polymers of SiO_2. Silica is divided into crystalline and noncrystalline forms. Crystalline silica can be further subdivided (see Fig. 3-6). Amorphous SiO_2 is less of a health hazard than crystalline silica (31).

Silicates are composed of silicon and oxygen combined with cations of aluminum, magnesium, sodium, calcium, and potassium. The chemical makeup of silicates also dictates their health risks (fibrous, platy, or granular):

Fiber: Material with length to breadth ratio of at least 3

Platy: Composed of continuous layers of tetrahedral silicate sheets sandwiching octahedral cations such as Al^{+3} or Mg^{+2}

Granule: Large, visible particles such as sand or clay

The crystalline or free silica found in quartz, tridymite, and cristobalite causes silicosis. Crystallized SiO_2 is sand. The percentage of SiO_2 in materials varies (32):

Clay: 0% to 40%
Mica: 0% to 10%
Talc: 0% to 5%
Limestone: 0% to 3%
Feldspar: 12% to 25%
Brick/tile: 10% to 35%
Pottery: 15% to 25%
Sand: 50% to 90%

Clay is a diverse group of hydrated aluminum silicate minerals with a particulate size smaller than 2 μm in diameter. Magnesium silicates are talc. Aluminum silicates are mica and kaolin. Certain silicates, such as talc, may contain crystalline silica and asbestos. Clay minerals include kaolin, bentonite, Fuller's earth, and feldspar. Diatomaceous earth is a gritty amorphous silica made up of skeletons of small aquatic plants (diatoms). Under temperature and pressure, it may contain significant amounts of crystalline tridymite and cristobalite. Therefore, appreciable environmental dust levels should be controlled for crystalline silica.

The OSHA PEL for dusts containing crystalline silica takes into account the percentage of silica present in a sample (31,34):

$$\text{PEL } (mg/m^3) \text{ of dust} = \frac{10 \text{ mg/m}^3}{(\%\ SiO_2 + 2)}$$

This formula is based on dust collection by a size-selective sampling device. It represents the fraction of dust that is respirable, which then can penetrate and remain in the alveoli (32). The PEL for the concentration of free dust with less than 1% crystalline silica is 5 mg/m^3 (this is the reason for the constant "2") (31).

The TLV-TWA for crystalline silica is 0.1 mg/m^3 of respirable quartz in air, regardless of the total dust concentration. For other silicas, the TLVs are as follows (34):

Cristobalite = 0.05 mg/m^3
Tridymite = 0.05 mg/m^3

Asbestos

Asbestos refers to a family of fibrous, hydrated mineral silicates that are fire and heat resistant and insoluble in strong acids and alkalis. Asbestos minerals are classified in two groups: amphiboles and serpentines. Asbestos is used in insulation materials of all varieties. The term *asbestiform* refers to fibrous material of 5 μm or longer with a length to width ratio of 3. The adverse health properties of long, thin fibers longer than 5 μm and less than 0.5 μm in breadth have been established.

In an effort to avoid the use of asbestos fibers because of their health effects, newer generations of fibers have been developed: rock wool, slag wool, glass wool, and ceramic fibers. Such synthetic mineral fibers have been found to have their own health effects. These fibers can withstand very high temperatures of approximately 1,000°C. They are amalgamated from silicon dioxide or aluminum silicates with additives such as aluminum oxide, titanium dioxide, zinc oxide, magnesium oxide, lithium oxide, barium oxide, calcium oxide, sodium oxide, and potassium oxide.

Amphibole fibers are made up of crystalline subfibrils consisting of hydrated magnesium silicates. They are held together by electrostatic bonds to form rigid, nearly indestructible log-like fibers. Serpentine chrysotile fibers are made up of subfibrils rolled into scrolls of platy magnesium silicate or chrysotile fibers. Serpentine subfibrils are bound loosely by electrostatic fones, making them pliable and flexible.

Amphiboles are subdivided into:

- Commercial amphiboles
  Amosite: $(FeMg)SiO_3$
  Crocidolite: $NaFe[SiO_3][2H_3O]$
- Noncommercial amphiboles
  Tremolite: $Ca_2Mg_5Si_8O_{22}[OH]_2$
  Anthophyllite: $[MgFe]_7Si_8O_{22}$
  Actinolite: $CaO \cdot 3(MgFe)O \cdot SiO_2$

OSHA has regulated asbestos since 1971 (40 *CFR* 763, EPA, 1987) in response to the Asbestos Hazard Emergency Response Act. Asbestos PELs are

0.1 fiber/cc of air (8-hour TWA)
1.0 fiber/cc of air (STEL)

The long, thin fibers (longer than 5-μm length and smaller than 0.5-μm diameter) cause clinical disease. Amphiboles with these physical characteristics cause inflammatory pulmonary reactions.

Scanning and transmission electron microscopy are used to identify and quantify asbestos fiber exposures. EPA requires these methods to be used through protocols developed under the Asbestos Hazard Emergency Response Act.

Other Mineral Dusts

Limestone and marble are other building materials that produce dust when ground. Limestone is mainly calcium carbonate and magnesium carbonate. Limestone arises from natural metamorphosis of the cytoskeletons of crustaceans, corals, and mollusks.

Carbon dusts include coal dust, graphite, lignite, peat, and carbon black. Coal dust contains a variety of organic compounds, such as benzenes, naphthalenes, polynuclear aromatic hydrocarbons, and phenols, in addition to carbon. Coal dust also contains inorganic material components. Anthracite coal has the highest carbon content, approximately 95%. Lignite has the lowest carbon content, approximately 65% to 75%, with a higher percentage of quartz, ash, and volatile material (31). The carbon content of bituminous coal is between anthracite and lignite. Pneumoconiosis occurs with chronic lifetime exposure to respirable coal dust.

Natural graphite is different from synthetic graphite. Natural graphite is composed of crystalline carbon with variable amounts of quartz and impurities such as silicates. Synthetic graphite is produced from coal. Carbon black is hard crystalline carbon.

Particulates Not Otherwise Classified

A number of specific exposure limits have been established for certain classes of organic and inorganic dusts with recognized toxicologic properties. Even in the absence of such properties, it has been shown that substantial burdens of dust deposits in the lungs can have adverse health effects. At lower concentrations, dust particles without recognized toxic properties can impede the clearance of more toxic dust particles from the lung by decreasing the mobility of alveolar macrophages. A potentially fatal condition known as *alveolar proteinosis* can be caused by exposure to high concentrations of such dusts (34). As a consequence, the ACGIH has established TLVs for particulates not otherwise classified (PNOC), which were formerly classified as "nuisance dusts." The shift to the PNOC designation was aimed at emphasizing that all materials are potentially toxic and that, even in the absence of specifically recognized toxic effects, it is dangerous to consider materials harmless at all exposure concentrations. The ACGIH TLV-TWA for total inhalable PNOC currently is set at 10 mg/m^3. The TLV-TWA for respirable PNOC [smaller than 10-μm aerodynamic diameter (a 3.5-μm particle has a 50% chance of deposition)] is set at 3 mg/m^3. The OSHA PEL for total dust is 15 mg/m^3, and a PEL for respirable dust is 5 mg/m^3.

Assessing Particle Exposure

Sometimes it is necessary to sample airborne dust and analyze it for size and chemical composition to evaluate the health hazard it presents. Particles larger than 10 μm in diameter are usually not considered a health hazard because they do not remain suspended in air very long nor do they penetrate airways. Particles smaller than 10 μm are a health hazard.

It is critical to differentiate respirable dust from nonrespirable dust with sampling methods. The cyclone sampler is used to sample for respirable dust. Dust and particulate monitoring is performed using cyclone separators that collect dusts and separate particles by their sizes. The cyclone separator uses a filter and filter cassettes. Air is drawn past the filter with a pump. Particles are collected on the filter membrane. Filter selection depends on the size of particles to be collected. Pore sizes vary:

- Silica and metal fumes (0.8 to 37.0 μm)
- Nuisance dust (5.0 to 37.0 μm)

Horizontal elucidators placed in front of a cyclone sampler remove coarse particles by gravity.

Because particles of 5 μm or smaller deposit and stay in deeper areas of the lung, health concerns are directed at measuring these smaller particles. Gravimetric and chemical analyses usually are performed on the particles to better characterize their health hazards. Atomic absorption is used to identify metals. X-ray diffraction is used to determine inorganic compounds and their crystalline structure.

The total dust concentration by weight in an environment does not provide enough information on its health hazard. To

better characterize health risks, it is important to determine both the respirable dust and its chemical and physical nature. Personal-breathing-zone dust analysis provides the best characterization of health risk. It can be performed by personal sampling devices taken over a period, usually 8 hours. The free silica content is important to determine separate from the total dust collected (31).

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CHAPTER 4
Principles of Toxicology

I. Glenn Sipes and Drew Badger

DEFINITION AND SCOPE OF TOXICOLOGY

Toxicology is a broad field of study encompassing multiple scientific disciplines, including biology, chemistry, and environmental sciences. Its primary focus is to determine the adverse effects of chemicals on biological systems. Historically, toxicologic studies were performed to identify those agents that can elicit abnormal physical or behavioral signs of injury. Investigators have extended their efforts to also determine the mechanisms underlying the development of toxicity. Because of the increased awareness of the number and quantities of toxicants generated, and of their potential for causing adverse effects, several subdisciplines of toxicology have emerged (Table 4-1).

Toxicologic Model Systems

To assess the potential toxicity of a chemical, several different model systems have been used. These include whole animal models, isolated perfused organ systems, precision-cut tissue slices, isolated cell cultures, organella subfractions, and so forth. With animal models, toxicity can be assessed by monitoring effects ranging from appetite depression, body weight loss, or behavioral changes to more fatal conditions such as tumor formation or death. Likewise, *in vitro* systems can reveal the potential for toxicity, but are also important in elucidating molecular and cellular mechanisms of toxicity.

In Vitro Model Systems

Several different *in vitro* systems are used to assess toxicity. In such systems, toxicologic endpoints may often be determined readily. For example, chemical-induced toxicity to cells can often be determined easily, either by microscopic evaluation of cells or by measuring biochemical events associated with the cells (e.g., dye exclusion or protein synthesis). *In vitro* systems have also provided important mechanistic information to certain models of injury (1,2).

Animal Models

Although *in vitro* studies are useful for understanding toxicologic mechanisms, animal studies are still required to understand the full range of chemical-mediated effects that can occur in the whole organism. This is because effects seen *in vivo* may not agree with findings established using *in vitro* studies. For example, certain chemicals may cause injury to a particular cell type *in vivo* by eliciting a deleterious inflammatory response. However, this same cell type may be much less susceptible to injury when it is exposed to a chemical as a primary isolated cell culture in which recruitment and activation of inflammatory cells do not occur. On the contrary, *in vitro* studies can show effects that do not occur *in vivo*. For example, several

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