CHAPTER 14

# RISK ASSESSMENT

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Structure of risk analysis.

## 14.1 THE CONCEPT OF RISK ASSESSMENT

Risk, which is common to all life, is an inherent property of everyday human existence. It is therefore a key factor in all decision making. Risk assessment or analysis, however, means different things to different people: Wall Street analysts assess financial risks and insurance companies calculate actuarial risks, while regulatory agencies estimate the risks of fatalities from nuclear plant accidents, the incidence of cancer from industrial emissions, and habitat loss associated with increases in human populations. What all these seemingly disparate activities have in common is the concept of a measurable phenomenon called risk that can be expressed in terms of probability. Thus, we can define **risk assessment** as the process of estimating both the probability that an event will occur, and the probable magnitude of its adverse effects—economic, health/safety-related, or ecological—over a specified time period. For example, we might determine the probability that a chemical reactor will fail and the probable effect of its sudden release of contents on the immediate area in terms of injuries and property loss over a period of days. In addition, we might estimate the probable incidence of cancer in the community where the chemical was spilled. Or, in yet another type of risk assessment, we might calculate the health risks associated with the presence of pathogens in drinking water or pesticide in food.

There are, of course, several varieties of risk assessment. Risk assessment as a formal discipline emerged in the 1940s and 1950s, paralleling the rise of the nuclear industry. Safety-hazard analyses have been used since at least the 1950s in the nuclear, petroleum-refining, and chemical-processing industries, as well as in aerospace. Health-risk assessments, however, had their beginnings in 1976 with the EPA's publication of the *Carcinogenic Risk Assessment Guidelines*.

In this chapter, we are concerned with two types of risk assessment:

- **Health-based risks**. For these risks, the focus is on general human health, mainly outside the workplace. Health-based risks typically involve high-probability, low-consequence, chronic exposures whose long latency periods and delayed effects make cause-and-effect relationships difficult to establish. This category also includes microbial risks, which usually have acute short-term effects. However, the consequences of microbial infection can persist throughout an individual's lifetime.
- **Ecological risks**. For these risks, the focus is on the myriad interactions among populations, communities, and ecosystems (including food chains) at both the micro and the macro level. Ecological risks typically involve both short-term catastrophes, such as oil spills, and long-term exposures to hazardous substances.

Whatever its focus, the **risk assessment process** consists of four basic steps:

- **Hazard identification**—Defining the hazard and nature of the harm; for example, identifying a chemical contaminant, say, lead or carbon tetrachloride, and documenting its toxic effects on humans.
- **Exposure assessment**—Determining the concentration of a contaminating agent in the environment and estimating its rate of intake in target organisms. An example would be finding the concentration of aflatoxin in peanut butter and determining the dose an "average" person would receive.
- **Dose–response assessment**—Quantifying the adverse effects arising from exposure to a hazardous agent based on the degree of exposure. This assessment is usually expressed mathematically as a plot showing the response in living organisms to increasing doses of the agent.
- **Risk characterization**—Estimating the potential impact of a hazard based on the severity of its effects and the amount of exposure.

Once the risks are characterized, various regulatory options are evaluated in a process called **risk management**, which includes consideration of social, political, and economic issues, as well as the engineering problems inherent in a proposed solution. One important component of risk management is **risk communication**, which is the interactive process of information and opinion exchange among individuals, groups, and institutions. Risk communication includes the transfer of risk information from expert to nonexpert audiences. In order to be effective, risk communication must provide a forum for balanced discussions of the nature of the risk, lending a perspective that allows the benefits of reducing the risk to be weighed against the costs.

In the United States, the passage of federal and state laws to protect public health and the environment has expanded the application of risk assessment. Major federal agencies that routinely use risk analysis include the Food and Drug Administration (FDA), the Environmental Protection Agency (EPA), and the Occupational Safety and Health Administration (OSHA). Together with state agencies, these regulatory agencies use risk assessment in a variety of situations (Information Box 14.1).

Risk assessment provides an effective framework for determining the relative urgency of problems and the allocation of resources to reduce risks. Using the results of risk analyses, we can target prevention, remediation, and control efforts toward areas, sources, or situations in which the greatest risk reductions can be achieved with the resources available. However, risk assessment is not an absolute procedure carried out in a vacuum; rather, it is an evaluative, multifaceted, comparative process. Thus, to evaluate risk, we must inevitably compare one risk to a host of others. In fact, the comparison of potential risks associated with several problems or issues has developed into a subset of risk assessment called **comparative risk assessment**. Some commonplace risks are shown in Table 14.1. Here we see, for example, that risks from chemical exposure are fairly small relative to those associated with driving a car or smoking cigarettes.

Comparing different risks allows us to comprehend the uncommon magnitudes involved and to understand the

## INFORMATION BOX 14.1

**Applications of Risk Assessment**

- Setting standards for concentrations of toxic chemicals or pathogenic microorganisms in water or food.
- Conducting baseline analyses of contaminated sites or facilities to determine the need for remedial action and the extent of cleanup required.
- Performing cost/benefit analyses of contaminated-site cleanup or treatment options (including treatment processes to reduce exposure to pathogens).
- Developing cleanup goals for contaminants for which no federal or state authorities have promulgated numerical standards; evaluating acceptable variance from promulgated standards and guidelines (*e.g.*, approving alternative concentration limits).
- Constructing "what-if" scenarios to compare the potential impact of remedial or treatment alternatives and to set priorities for corrective action.
- Evaluating existing and new technologies for effective prevention, control, or mitigation of hazards and risks.
- Articulating community public health concerns and developing consistent public health expectations among different localities.

level, or magnitude, of risk associated with a particular hazard. But comparison with other risks cannot itself establish the *acceptability* of a risk. Thus, the fact that the chance of death from a previously unknown risk is about the same as that from a known risk does not necessarily imply that the two risks are equally acceptable. Generally, comparing risks along a single dimension is not helpful when the risks

**TABLE 14.1 Examples of some commonplace risks in the United States.***

| RISK | LIFETIME RISK OF MORTALITY |
|---|---|
| Cancer from cigarette smoking (one pack per day) | 1:4 |
| Death in a motor vehicle accident | 2:100 |
| Homicide | 1:100 |
| Home accident deaths | 1:100 |
| Cancer from exposure to radon in homes | 3:1,000 |
| Exposure to the pesticide aflatoxin in peanut butter | 6:10,000 |
| Diarrhea from rotavirus | 1:10,000 |
| Exposure to typical EPA maximum chemical contaminant levels | 1:10,000–1:10,000,000 |

*Based on data in Wilson and Crouch (1987) and Gerba and Rose (1992). From *Pollution Science* © 1996, Academic Press, San Diego, CA.

are widely perceived as qualitatively different. Rather, we must take into account certain qualitative factors that affect risk perception and evaluation when selecting risks to be compared. Some of these qualifying factors are listed in Table 14.2. We must also understand the underlying premise that *voluntary risk is always more acceptable than involuntary risk.* For example, the same people who cheerfully drive their cars every day—thus incurring a 2:100 lifetime risk of death by automobile—are quite capable of refusing to accept the 6:10,000 involuntary risk of eating peanut butter contaminated with aflatoxin.

In considering risk, then, we must also understand another principle—the *de minimis* principle, which means that there are some levels of risk so trivial that they are not worth

**TABLE 14.2 Factors affecting risk perception and risk analysis.**

| FACTOR | CONDITIONS ASSOCIATED WITH INCREASED PUBLIC CONCERN | CONDITIONS ASSOCIATED WITH DECREASED PUBLIC CONCERN |
|---|---|---|
| Catastrophic potential | Fatalities and injuries grouped in time and space | Fatalities and injuries scattered and random |
| Familiarity | Unfamiliar | Familiar |
| Understanding | Mechanisms or process not understood | Mechanisms or process understood |
| Controllability (personal) | Uncontrollable | Controllable |
| Voluntariness of exposure | Involuntary | Voluntary |
| Effects on children | Children specifically at risk | Children not specifically at risk |
| Effects manifestation | Delayed effects | Immediate effects |
| Effects on future generations | Risk to future generations | No risk to future generations |
| Victim identity | Identifiable victims | Statistical victims |
| Dread | Effects dreaded | Effects not dreaded |
| Trust in institutions | Lack of trust in responsible institutions | Trust in responsible institutions |
| Media attention | Much media attention | Little media attention |
| Accident history | Major and sometimes minor accidents | No major or minor accidents |
| Equity | Inequitable distribution of risks and benefits | Equitable distribution of risks and benefits |
| Benefits | Unclear benefits | Clear benefits |
| Reversibility | Effects irreversible | Effects reversible |
| Origin | Caused by human actions or failures | Caused by acts of nature |

Source: Covello et al. (1988). From *Pollution Science* © 1996, Academic Press, San Diego, CA.

bothering about. However attractive, this concept is difficult to define, especially if we are trying to find a *de minimis* level acceptable to an entire society. Understandably, regulatory authorities are reluctant to be explicit about an "acceptable" risk. (How much aflatoxin would you consider acceptable in *your* peanut butter and jelly sandwich? How many dead insect parts?) But it is generally agreed that a lifetime risk on the order of one in a million (or in the range of $10^{-6}$ to $10^{-4}$) is trivial enough to be acceptable for the general public. Although the origins and precise meaning of a one-in-a-million acceptable risk remain obscure, its impact on product choices, operations, and costs is very real—running, for example, into hundreds of billions of dollars in hazardous waste site cleanup decisions alone. The levels of acceptable risk can vary within this range. Levels of risk at the higher end of the range ($10^{-4}$ rather than $10^{-6}$) may be acceptable if just a few people are exposed rather than the entire populace. For example, workers dealing with food additives can often tolerate higher levels of risk than can the public at large. These higher levels are justified because workers tend to be a relatively homogeneous, healthy group and because employment is voluntary; however, the sum level of risks would not be acceptable for those same food additives in general.

## 14.2 THE PROCESS OF RISK ASSESSMENT

### 14.2.1 Hazard Identification

The first step in risk assessment is to determine the nature of the hazard. For pollution-related problems, the hazard in question is usually a specific chemical, a physical agent (such as irradiation), or a microorganism identified with a specific illness or disease. Thus the hazard identification component of a pollution risk assessment consists of a review of all relevant biological and chemical information bearing on whether or not an agent poses a specific threat. For example, in the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 1986), the following information is evaluated for a potential carcinogen:

- Physical/chemical properties, routes, and patterns of exposure
- Structure/activity relationships of the substance
- Absorption, distribution, metabolism, and excretion characteristics of the substance in the body
- The influence of other toxicological effects
- Data from short-term tests in living organisms
- Data from long-term animal studies
- Data from human studies

Once these data are reviewed, the animal and human data are both separated into groups characterized by degree of evidence:

- Sufficient evidence of carcinogenicity
- Limited evidence of carcinogenicity
- Inadequate evidence
- No data available
- No evidence of carcinogenicity

The available information on animal and human studies is then combined into a weight-of-evidence classification scheme to assess the likelihood of carcinogenicity. This scheme—which is like that developed by the EPA—gives more weight to human than to animal evidence (when it is available) and includes several groupings (Table 14.3).

Clinical studies of disease can be used to identify very large risks (between 1/10 and 1/100), most epidemiological studies can detect risks down to 1/1,000, and very large epidemiological studies can examine risks in the 1/10,000 range. However, risks lower than 1/10,000 cannot be studied with much certainty using epidemiological approaches. Since regulatory policy objectives generally strive to limit risks below 1/100,000 for life-threatening diseases like cancer, these lower risks are often estimated by extrapolating from the effects of high doses given to animals.

### 14.2.2 Exposure Assessment

Exposure assessment is the process of measuring or estimating the intensity, frequency, and duration of human exposure to an environmental agent. Exposure to contaminants can occur via inhalation, ingestion of water or food, or absorption through the skin upon dermal contact. Contaminant sources, release mechanisms, transport, and transformation characteristics are all important aspects of exposure assessment, as are the nature, location, and activity patterns of the exposed population. This explains why it is critical to understand the factors and processes influencing the transport and fate of a contaminant (see Chapters 6, 7, 8, and 17).

An **exposure pathway** is the course that a hazardous agent takes from a source to a receptor (*e.g.*, human or animal) via environmental carriers or media—generally, air (volatile compounds, particulates) or water (soluble compounds) (Figure 14.1). An exception is electromagnetic radiation, which needs no medium (see Chapter 21). The **exposure route**, or intake pathway, is the mechanism by which the transfer occurs—usually by inhalation, ingestion, and/or dermal contact. Direct contact can result in a local effect at the point of entry and/or in a systemic effect.

**TABLE 14.3 EPA categories for carcinogenic groups.**

| CLASS | DESCRIPTION |
|---|---|
| A | Human carcinogen |
| B | Probable carcinogen |
| $B_1$ | Linked human data |
| $B_2$ | No evidence in humans |
| C | Possible carcinogen |
| D | No classification |
| E | No evidence |

From U.S. EPA, 1986.

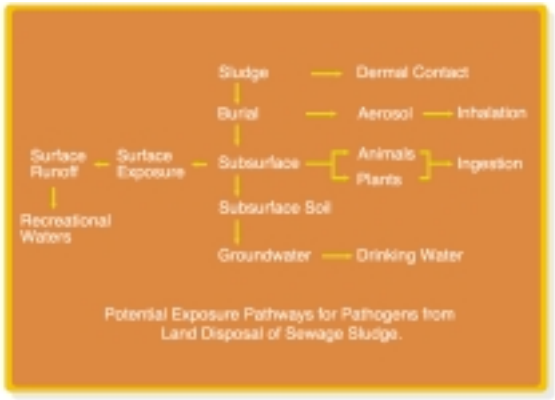



**Figure 14.1** Exposure pathways for potential contaminants. Modified from Straub et al., 1993.

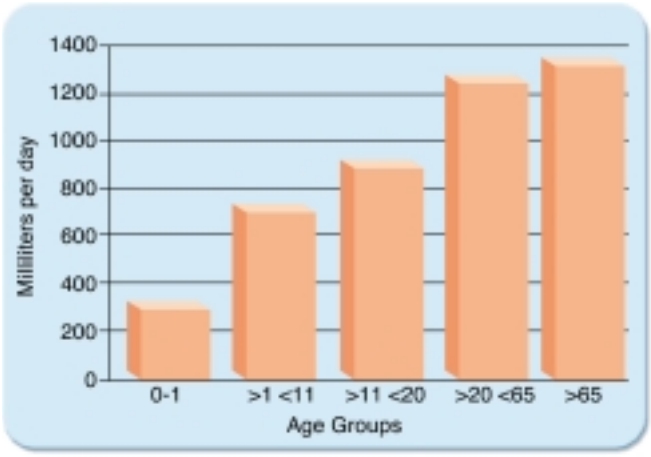



**Figure 14.2** Average tap water ingestion rates in the United States by age. From Roseberry and Burmaster, 1992.

The quantification of exposure, intake, or potential dose can involve equations with three sets of variables:

- Concentrations of chemicals or microbes in the media
- Exposure rates (magnitude, frequency, duration)
- Quantified biological characteristics of receptors (*e.g.*, body weight, absorption capacity for chemicals; level of immunity to microbial pathogens)

Exposure concentrations are derived from measured and/or modeled data. Ideally, exposure concentrations should be measured at the points of contact between the environmental media and current or potential receptors. It is usually possible to identify potential receptors and exposure points from field observations and other information. However, it is seldom possible to anticipate all potential exposure points and measure all environmental concentrations under all conditions. In practice, a combination of monitoring and modeling data, together with a great deal of professional judgment, is required to estimate exposure concentrations.

In order to assess exposure rates via different exposure pathways, we have to consider and weigh many factors. For example, in estimating exposure to a substance via drinking water, we first have to determine the average daily consumption of that water. But this isn't as easy as it sounds. Studies have shown that daily fluid intake varies greatly from individual to individual. Moreover, tap water intake depends on how much fluid is consumed as tap water, and how much is ingested in the form of soft drinks and other non-tap-water sources. Tap water intake also changes significantly with age (Figure 14.2), body weight, diet, and climate. Because these factors are so variable, the EPA has suggested a number of very conservative "default" exposure values that can be used when assessing contaminants in tap water, vegetables, soil, and the like (Table 14.4).

One important route of exposure is the food supply. Toxic substances are often bioaccumulated, or concentrated, in plant and animal tissues, thereby exposing humans who ingest those tissues as food. Moreover, many toxic substances tend to be biomagnified in the food chain, so that animal tissues contain relatively high concentrations of toxins. Take fish, for example. It is relatively straightforward to estimate concentrations of contaminants in water. Thus, we can use a **bioconcentration factor (BCF)** to estimate the tendency for a substance in water

**TABLE 14.4 EPA standard default exposure factors.**

| LAND USE | EXPOSURE PATHWAY | DAILY INTAKE | EXPOSURE FREQUENCY (DAYS/YEAR) | EXPOSURE DURATION (YEARS) |
|---|---|---|---|---|
| Residential | Ingestion of potable water | 2 L $day^{-1}$ | 350 | 30 |
| | Ingestion of soil and dust | 200 mg (child) | 350 | 6 |
| | | 100 mg (adult) | | 24 |
| | Inhalation of contaminants | 20 $m^3$ (total) | 350 | 30 |
| | | 15 $m^3$ (indoor) | | |
| Industrial and commercial | Ingestion of potable water | 1 liter | 250 | 25 |
| | Ingestion of soil and dust | 50 mg | 250 | 25 |
| | Inhalation of contaminants | 20 $m^3$ (workday) | 250 | 25 |
| Agricultural | Consumption of homegrown produce | 42 g (fruit) | 350 | 30 |
| | | 80 g (vegetable) | | |
| Recreational | Consumption of locally caught fish | 54 g | 350 | 30 |

Modified from Kolluru (1993). From *Pollution Science* ©1996, Academic Press, San Diego, CA.

to accumulate in fish tissue. The concentration of a chemical in fish can be estimated by multiplying its concentration in water by the BCF. The greater the value of the BCF, the more the chemical accumulates in the fish and the higher the risk of exposure to humans.

The units of BCF—liters per kilogram (L $kg^{-1}$) —are chosen to allow the concentration of a chemical to be expressed as milligrams per liter (mg $L^{-1}$) of water and the concentration in fish to be in milligrams per kilogram (mg $kg^{-1}$) of fish body weight. In Table 14.5, we see the BCFs of several common organic and inorganic chemicals. Note the high values of BCF for the chlorinated hydrocarbon pesticides like dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs). This exemplifies the concern we have with such compounds, as discussed in Chapter 10.

### 14.2.3 Dose–Response Assessment

Chemicals and other contaminants are not equal in their capacity to cause adverse effects. To determine the capacity of agents to cause harm, we need quantitative toxicity data. Some toxicity data are derived from occupational, clinical, and epidemiological studies. Most toxicity data, however, come from animal experiments in which researchers expose laboratory animals, mostly mice and rats, to increasingly higher concentrations or doses and observe their corresponding effects. The result of these experiments is the *dose–response relationship*—a quantitative relationship that indicates the agent's degree of toxicity to exposed species. Dose is normalized as milligrams of substance or pathogen ingested, inhaled, or absorbed (in the case of chemicals) through the skin per kilogram of body weight per day (mg $kg^{-1}$ $day^{-1}$). Responses or effects can vary widely—from no observable effect, to temporary and reversible effects (*e.g.*, enzyme depression caused by some pesticides or diarrhea caused by viruses), to permanent organ injury (*e.g.*, liver and kidney damage caused by chlorinated solvents, heavy metals, or viruses), to chronic functional impairment (*e.g.*, bronchitis or emphysema arising from smoke damage), to death.

**TABLE 14.5 Bioconcentration factors (BCFs) for various organic and inorganic compounds.**

| CHEMICAL | BCF (L $kg^{-1}$) |
|---|---|
| Aldrin | 28 |
| Benzene | 44 |
| Cadmium | 81 |
| Chlordane | 14,000 |
| Chloroform | 3.75 |
| Copper | 200 |
| DDT | 54,000 |
| Formaldehyde | 0 |
| Nickel | 47 |
| PCBs | 100,000 |
| Trichloroethylene | 10.6 |
| Vinyl chloride | 1.17 |

From U.S. EPA, 1990.

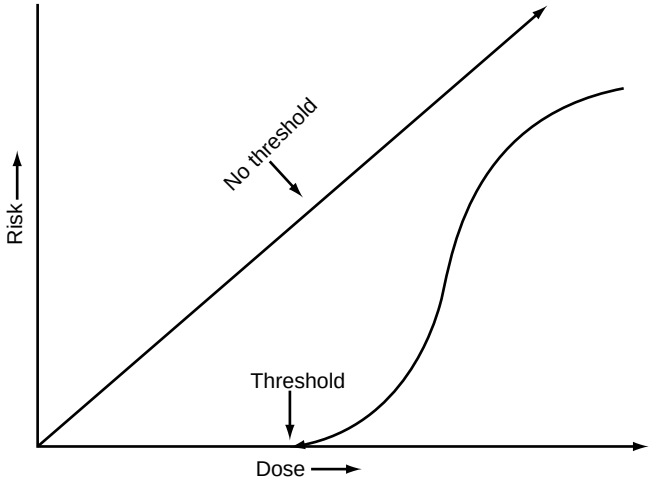



**Figure 14.3** Relationship between a threshold and nonthreshold response.

The goal of a dose–response assessment is to obtain a mathematical relationship between the amount (concentration) of a toxicant or microorganism to which a human is exposed and the risk of an adverse outcome from that dose. The data resulting from experimental studies is presented as a dose–response curve, as shown in Figure 14.3. The abscissa describes the dose, while the ordinate measures the risk that some adverse health effect will occur. In the case of a pathogen, for instance, the ordinate may represent the risk of infection, and not necessarily illness.

Dose–response curves derived from animal studies must be interpreted with care. The data for these curves are necessarily obtained by examining the effects of large doses on test animals. Because of the costs involved, researchers are limited in the numbers of test animals they can use—it is both impractical and cost-prohibitive to use thousands (even millions) of animals to observe just a few individuals that show adverse effects at low doses (e.g., risks of 1:1,000 or 1:10,000). Researchers must therefore extrapolate low-dose responses from their high-dose data. And therein lies the rub: Dose–response curves are subject to controversy because their results change depending on the method chosen to extrapolate from the high doses actually administered to laboratory test subjects to the low doses humans are likely to receive in the course of everyday living.

This controversy revolves around the choice of several mathematical models that have been proposed for extrapolation to low doses. Unfortunately, no model can be proved or disproved from the data, so there is no way to know which model is the most accurate. The choice of models is therefore strictly a policy decision, which is usually based on understandably conservative assumptions. Thus, for noncarcinogenic chemical responses, the assumption is that some *threshold* exists below which there is no toxic response; that is, no adverse effects will occur below some very low dose (say, one in a million) (Figure 14.3). Carcinogens, however, are considered *nonthreshold*—that is, the conservative assumption is

**TABLE 14.6 Primary models used for assessment of nonthreshold effects.**

| MODEL[a] | COMMENTS |
|---|---|
| One-hit | Assumes (1) a single stage for cancer and (2) malignant change induced by one molecular or radiation interaction<br>*Very conservative* |
| Linear multistage | Assumes multiple stages for cancer<br>*Fits curve to the experimental data* |
| Multihit | Assumes several interactions needed before cell becomes transformed<br>*Least conservative model* |
| Probit | Assumes probit (lognormal) distribution for tolerances of exposed population<br>*Appropriate for acute toxicity; questionable for cancer* |

[a]All these models assume that exposure to the pollutant will always produce an effect, regardless of dose.

Modified from Cockerham and Shane, 1994. From *Pollution Science* © 1996, Academic Press, San Diego, CA.

**TABLE 14.7 Lifetime risks of cancer derived from different extrapolation models.**

| MODEL APPLIED | LIFETIME RISK (1.0 mg $kg^{-1}$ $day^{-1}$) OF TOXIC CHEMICAL[a] | |
|---|---|---|
| One-hit | $6.0 \times 10^{-5}$ | (1 in 17,000) |
| Multistage | $6.0 \times 10^{-6}$ | (1 in 167,000) |
| Multihit | $4.4 \times 10^{-7}$ | (1 in 2.3 million) |
| Probit | $1.9 \times 10^{-10}$ | (1 in 5.3 billion) |

[a]All risks for a full lifetime of daily exposure. The lifetime is used as the unit of risk measurement, because the experimental data reflect the risk experienced by animals over their full lifetimes. The values shown are upper confidence limits on risk.

Source: U.S. EPA, 1990. From *Pollution Science* © 1996, Academic Press, San Diego, CA.

that exposure to any amount of carcinogen creates some likelihood of cancer. This means that the only "safe" amount of carcinogen is zero, so the dose–response plot is required to go through the origin (0), as shown in Figure 14.3.

There are many mathematical models to choose from, including the one-hit model, the multistage model, the multihit model, and the probit model. The characteristics of these models for nonthreshold effects are listed in Table 14.6.

The **one-hit model** is the simplest model of carcinogenesis in which it is assumed:

1. That a single chemical "hit," or exposure, is capable of inducing malignant change (*i.e.*, a single hit causes irreversible damage of DNA, leading to tumor development). Once the biological target is hit, the process leading to tumor formation continues independently of dose.
2. That this change occurs in a single stage.

The **multistage model** assumes that tumors are the result of a sequence of biological events, or stages. In simplistic terms, the biological rationale for the multistage model is that there are a series of biological stages that a chemical must pass through (*e.g.*, metabolism, covalent bonding, DNA repair, and so on) without being deactivated, before the expression of a tumor is possible.

The rate at which the cell passes through one or more of these stages is a function of the dose rate. The multistage model also has the desirable feature of producing a linear relationship between risk and dose.

The **multihit model** assumes that a number of dose-related hits are needed before a cell becomes malignant. The most important difference between the multistage and multihit model is that in the multihit model, all hits must result from the dose, whereas in the multistage model, passage through some of the stages can occur spontaneously. The practical implication of this is that the multihit models are generally much flatter at low doses and consequently predict a lower risk than the multistage model.

The **probit model** is not derived from mechanistic assumptions about the cancer process. It may be thought of as representing distributions of tolerances to carcinogens in a large population. The model assumes that the probability of the response (cancer) is a linear function of the log of the dose (log normal). While these models may be appropriate for acute toxicity they are considered questionable for carcinogens. These models would predict the lowest level of risk of all the models.

The effect of models on estimating risk for a given chemical is shown in Table 14.7 and Figure 14.4. As we can see, the choice of models results in order-of-magnitude differences in estimating the risk at low levels of exposure.

The **linear multistage model,** a modified version of the multistage model, is the EPA's model of choice, because this agency chooses to err on the side of safety and overemphasize risk. This model assumes that there are multiple stages for cancer (*i.e.*, a series of mutations or biotransformations) involving many carcinogens, co-carcinogens, and promoters (see Chapter 13) that can best be modeled by a series of mathematical functions. At low doses, the slope of the

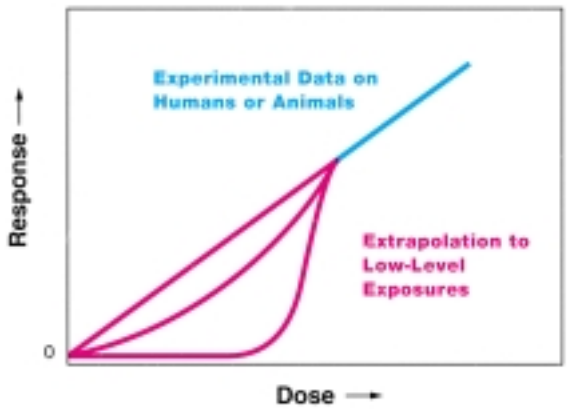



**Figure 14.4** Extrapolation of dose–response curves. Adapted from U.S. EPA, 1990. From *Pollution Science* © 1996, Academic Press, San Diego, CA.

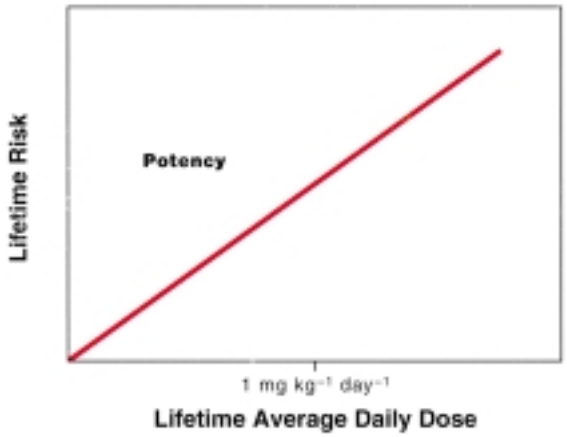



**Figure 14.5** Potency factor is the slope of the dose–response curve at low doses. At low doses, the slope of the dose–response curve produced by the multistage model is called the potency factor. It is the risk produced by a lifetime average dose of 1 mg $kg^{-1}$ $day^{-1}$. Adapted from U.S. EPA, 1990. From *Pollution Science* © 1996, Academic Press, San Diego, CA.

dose–response curve produced by the linear multistage model is called the **potency factor (PF)** or **slope factor (SF)** (Figure 14.5), which is the reciprocal of the concentration of chemical measured in milligrams per kilogram of animal body weight per day, that is, 1/(mg $kg^{-1}$ $day^{-1}$), or the risk produced by a lifetime **average dose (AD)** of 1 mg $kg^{-1}$ $day^{-1}$. Thus the dose–response equation for a carcinogen is

$$\text{Lifetime Risk} = \text{AD} \times \text{PF} \qquad \text{(Eq. 14.1)}$$

The probability of *getting* cancer (not the probability of *dying* of cancer) and the associated dose, consist of an average taken over an assumed 70-year human lifetime. This dose is called the lifetime average daily dose or **chronic daily intake**.

The dose–response effects for noncarcinogens allow for the existence of thresholds, that is, a certain quantity of a substance or dose below which there is **no observable toxic effect (NOAEL**; see Chapter 13) by virtue of the body's natural repair and detoxifying capacity. If a NOAEL is not available, a LOAEL (lowest observed adverse effect level) may be used, which is the lowest observed dose or concentration of a substance at which there is a detectable adverse health effect. When a LOAEL is used instead of a NOAEL, an additional uncertainty factor is normally applied. Examples of toxic substances that have thresholds are heavy metals and polychlorinated biphenyls (PCBs). These thresholds are represented by the **reference dose**, or **RfD**, of a substance, which is the intake or dose of the substance per unit body weight per day (mg $kg^{-1}$ $day^{-1}$) that is likely to pose no appreciable risk to human populations, including such sensitive groups as children (Table 14.8). A dose–response plot for carcinogens therefore goes through this reference point (Figure 14.6).

**TABLE 14.8 Chemical RfDs for chronic noncarcinogenic effects of selected chemicals.**

| CHEMICAL | RfD (mg $kg^{-1}$ $day^{-1}$) |
|---|---|
| Acetone | 0.1 |
| Cadmium | 0.0005 |
| Chloroform | 0.01 |
| Methylene chloride | 0.06 |
| Phenol | 0.04 |
| Polychlorinated biphenyl | 0.0001 |
| Toluene | 0.3 |
| Xylene | 2.0 |

From U.S. EPA, 1990.

In general, substances with relatively high slope factors and low reference doses tend to be associated with higher toxicities. The RfD is obtained by dividing the NOAEL (see Chapter 13) by an appropriate uncertainty factor, sometimes called a **safety factor** or **uncertainty factor**. A 10-fold uncertainty factor is used to account for differences in sensitivity between the most sensitive individuals in an exposed human population. These include pregnant women, young children, and the elderly, who are more sensitive than "average" people. Another factor of 10 is added when the NOAEL is based on animal data that are extrapolated to humans. In addition, another factor of 10 is sometimes applied when questionable or limited human and animal data are available. The general formula for deriving an RfD is

$$\text{RfD} = \frac{\text{NOAEL}}{\text{VF}_1 \times \text{VF}_2 \ldots \times \text{VF}_n} \qquad \text{(Eq. 14.2)}$$

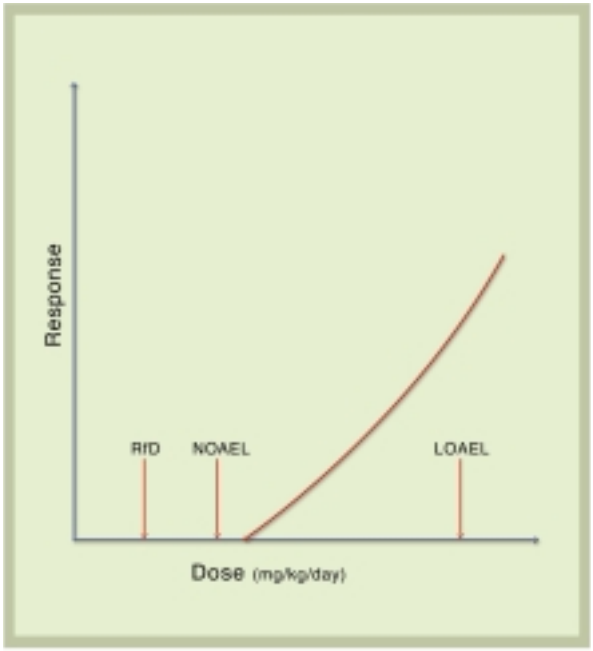



**Figure 14.6** Relationships between RfD, NOAEL, and LOAEL for noncarcinogens.

where $VF_i$ are the uncertainty factors. As the data become more uncertain, higher safety factors are applied. For example, if data are available from a high-quality epidemiological study, a simple uncertainty factor of 10 may be used by simply dividing the original value for RfD by 10 to arrive at a new value of RfD, which reflects the concern for safety. The RfDs of several noncarcinogenic chemicals are shown in Table 14.8.

The RfD (Figure 14.6) can be used in quantitative risk assessments by using the following relationship:

$$\text{Risk} = \text{PF}\ (\text{CDI} - \text{RfD}) \qquad \text{(Eq. 14.3)}$$

where CDI is the chronic daily intake, and the *potency factor (PF)* is the slope of the dose–response curve. Table 14.9 contains potency factors for some potential carcinogens:

$$\text{CDI (mg kg}^{-1}\text{ day}^{-1}) = \frac{\text{Average daily dose (mg day}^{-1})}{\text{Body weight (kg)}} \qquad \text{(Eq. 14.4)}$$

This type of risk calculation is rarely performed. In most cases, the RfD is used as a simple indicator of potential risk in practice. That is, the chronic daily intake is simply compared with the RfD, then, if the CDI is below the RfD, it is assumed that the risk is negligible for almost all members of an exposed population.

### 14.2.4 Risk Characterization

The final phase of risk assessment process is risk characterization. In this phase, exposure and dose–response assessments are integrated to yield probabilities of effects occurring in humans under specific exposure conditions. Quantitative risks are calculated for appropriate media and pathways. For example, the risks of lead in water are estimated over a lifetime assuming: (1) that the exposure of 2 liters of water per day is ingested over a 70-year lifetime; and (2) that different concentrations of lead occur in the drinking water. This information can then be used by risk managers to develop standards or guidelines for specific toxic chemicals or infectious microorganisms in different media, such as the drinking water or food supply.

#### *14.2.4.1 Cancer risks*

If the dose–response curve is assumed to be linear at low doses for a carcinogen, then:

$$\text{Incremental lifetime risk of cancer} = (\text{CDI})\ (\text{PF}) \qquad \text{(Eq. 14.5)}$$

The linearized multistage model assumptions (see Table 14.6) estimates the risk of getting cancer, which is not necessarily the same as the risk of dying of cancer, so it should be even more conservative as an upper-bound estimate of cancer deaths. Potency factors can be found in the EPA database on toxic substances called the Integrated Risk Information System (IRIS) (see Information Box 14.2). Table 14.9 contains the potency factor for some of these chemicals.

**TABLE 14.9 Toxicity data for selected potential carcinogens.**

| CHEMICAL | POTENCY FACTOR ORAL ROUTE (mg kg day$^{-1}$) |
|---|---|
| Arsenic | 1.75 |
| Benzene | $2.9 \times 10^{-2}$ |
| Carbon tetrachloride | 0.13 |
| Chloroform | $6.1 \times 10^{-3}$ |
| DDT | 0.34 |
| Dieldrin | 30 |
| Heptachlor | 3.4 |
| Methylene chloride | $7.5 \times 10^{-3}$ |
| Polychlorinated biphenyls (PCBs) | 7.7 |
| 2,3,7,8-TCDD (dioxin) | $1.56 \times 10^{5}$ |
| Tetrachloroethylene | $5.1 \times 10^{-2}$ |
| Trichloroethylene (TCE) | $1.1 \times 10^{-2}$ |
| Vinyl chloride | 2.3 |

From U.S. EPA, www.epa.gov/iris.

The mean exposure concentration of contaminants is used with exposed population variables and the assessment determined variables to estimate contaminant intake. The general equation for chemical intake is

$$\text{CDI} = \frac{\text{C} \times \text{CR} \times \text{EFD}}{\text{BW}} \times \frac{1}{\text{AT}} \qquad \text{(Eq. 14.6)}$$

where:

- CDI = chronic daily intake; the amount of chemical at the exchange boundary (mg/kg-day)
- C = average exposure concentration over the period (*e.g.*, mg/L for water or mg/m$^3$ for air)
- CR = contact rate, the amount of contaminated medium contacted per unit time (L/day or m$^3$/day)
- EFD = exposure frequency and duration, a variable that describes how long and how often exposure occurs. The EFD is usually divided into two terms: EF = exposure frequency (days/year) and ED = exposure duration (years)
- BW = average body mass over the exposure period (kg)
- AT = averaging time; the period over which the exposure is averaged (days)

Determination of accurate intake data is sometimes difficult; for example, exposure frequency and duration vary among individuals and must often be estimated; site-specific information may be available; and professional judgment may be necessary. Equations for estimating daily contamination intake rates from drinking water, the air, and contaminated food, and for dermal exposure while swimming, have been reported by the EPA. Two of the most common routes of exposure are

## INFORMATION BOX 14.2

**Integrated Risk Information System (IRIS)**

**The Integrated Risk Information System (IRIS)**, prepared and maintained by the U.S. Environmental Protection Agency (U.S. EPA), is an electronic database containing information on human health effects that may result from exposure to various chemicals in the environment (www.epa.gov/iris). IRIS was initially developed for EPA staff in response to a growing demand for consistent information on chemical substances for use in risk assessments, decision-making, and regulatory activities. The information in IRIS is intended for those without extensive training in toxicology, but with some knowledge of health sciences. The heart of the IRIS system is its collection of computer files covering individual chemicals. These chemical files contain descriptive and quantitative information in the following categories:

· Oral reference doses and inhalation reference concentrations (RfDs) for chronic noncarcinogenic health effects.
· Hazard identification, oral slope factors, and oral and inhalation unit risks for carcinogenic effects.

**Oral RfD Summary for Arsenic.**

| CRITICAL EFFECT | EXPERIMENTAL DOSES* | UF | RFD |
|---|---|---|---|
| Hyperpigmentation, keratosis and possible vascular complications<br>Human chronic oral exposure<br>Tseng, 1977; Tseng et al., 1968 | NOAEL: 0.009 mg/L converted to 0.0008 mg/kg-day<br>LOAEL: 0.17 mg/L converted to 0.014 mg/kg-day | 3 | 3E-4 mg/kg-day |

*Conversion Factors—NOAEL was based on an arithmetic mean of 0.009 mg/L in a range of arsenic concentration of 0.001 to 0.017 mg/L. This NOAEL also included estimation of arsenic from food. Since experimental data were missing, arsenic concentrations in sweet potatoes and rice were estimated as 0.002 mg/day. Other assumptions included consumption of 4.5 L water/day and 55 kg body weight (Abernathy et al., 1989). NOAEL = [(0.009 mg/L × 4.5 L/day) + 0.002 mg/day]/55 kg = 0.0008 mg/kg-day. The LOAEL dose was estimated using the same assumptions as the NOAEL starting with an arithmetic mean water concentration from Tseng (1977) of 0.17 mg/L. LOAEL = [(0.17 mg/L × 4.5 L/day) + 0.002 mg/day]/55 kg = 0.014 mg/kg-day.
UF = Uncertainty Factor or Safety Factor.

through drinking contaminated water and breathing contaminated air. The intake for ingestion of waterborne chemicals is

$$CDI = \frac{CW \times IR \times EF \times ED}{BW \times AT} \qquad \text{(Eq. 14.7)}$$

where

- CDI = chronic daily intake by ingestion (mg/kg-day)
- CW = chemical concentration in water (mg/L)
- IR = ingestion rate (L/day)
- EF = exposure frequency (days/year)
- ED = exposure duration (years)
- BW = body weight (kg)
- AT = averaging time (period over which the exposure is averaged—days)

Some of the values used in Equation 14.5 are

- CW: site-specific measured or modeled value
- IR: 2 L/day (adult, 90$^{th}$ percentile); 1.4 L/day (adult, average)
- EF: pathway-specific value (dependent on the frequency of exposure-related activities)
- ED: 70 years (lifetime; by convention); 30 years [national upper-bound time (90$^{th}$ percentile) at one residence]; 9 years [national median time (50$^{th}$ percentile) at one residence]
- BW: 70 kg (adult, average); Age-specific values
- AT: pathway-specific period of exposure for noncarcinogenic effects (*i.e.*, ED × 365 days/year), and 70-year lifetime for carcinogenic effects (*i.e.*, 70 years × 365 days/year), averaging time.

### *EXAMPLE 14.1*

*Estimation of an Oral Chronic Daily Intake*

The mean concentration of 1,2-dichlorobenzene in a water supply is 1.7 μg/L. Determine the chronic daily intake for a 70-kg adult. Assume that 2 L of water are consumed per day.

*Solution*

The chronic daily intake (CDI) may be calculated using Equation 14.7.

$$CDI = \frac{C \times CR \times EF \times ED}{BW \times AT}$$

where

CDI = chronic daily intake (mg/kg-day)
C = 1.7 μg/L = 0.0017 mg/L
CR = 2 L/day
EF = 365 days/year
ED = 30 years (standard exposure duration for an adult exposed to a noncarcinogenic)
BW = 70 kg
AT = 365 days/year × 30 years = 10,950 days

Substituting values into the equation yields the chronic daily intake.

$$\text{CDI} = \frac{0.0017 \times 2 \times 365 \times 30}{70 \times 10{,}950} = 4.86 \times 10^{-5} \text{ mg/kg-day}$$

### 14.2.4.2 Noncancer risks

Noncancer risks are expressed in terms of a hazard quotient (HQ) for a single substance, or hazard index (HI) for multiple substances and/or exposure pathways.

$$\text{Hazard quotient (HQ)} = \frac{\text{Average daily dose during exposure period (mg kg}^{-1}\text{ day}^{-1})}{\text{RfD (mg kg}^{-1}\text{ day}^{-1})} \quad \text{(Eq. 14.8)}$$

Unlike a carcinogen, the toxicity is important only during the time of exposure, which may be one day, a few days, or years. The HQ has been defined so that if it is less than 1.0, there should be no significant risk or systemic toxicity. Ratios above 1.0 could represent a potential risk, but there is no way to establish that risk with any certainty.

When exposure involves more than one chemical, the sum of the individual hazard quotients for each chemical is used as a measure of the potential for harm. This sum is called the hazard index (HI):

$$\text{HI} = \text{Sum of hazard quotients} \quad \text{(Eq. 14.9)}$$

### 14.2.4.3 Uncertainty analysis

Uncertainty is inherent in every step of the risk assessment process. Thus, before we can begin to characterize any risk, we need some idea of the nature and magnitude of uncertainty in the risk estimate. Sources of uncertainty include:

- Extrapolation from high to low doses
- Extrapolation from animal to human responses
- Extrapolation from one route of exposure to another
- Limitations of analytical methods
- Estimates of exposure

Although the uncertainties are generally much larger in estimates of exposure and the relationships between dose and response (*e.g.*, the percent mortality), it is important to include the uncertainties originating from all steps in a risk assessment in risk characterization.

### EXAMPLE 14.2

*Application of Hazard Index and Incremental Carcinogenic Risk Associated with Chemical Exposure*

A drinking water supply is found to contain 0.1 mg $L^{-1}$ of acetone and 0.1 mg $L^{-1}$ of chloroform. A 70-kg adult drinks 2 L per day of this water for 5 years. What would be the hazard index and the carcinogenic risk from drinking this water?

First, we need to determine the average daily doses (ADDs) for each of the chemicals and then their individual hazard quotients.

**For Acetone**

$$\text{ADD} = \frac{(0.1 \text{ mg L}^{-1})\,(2\text{L day}^{-1})}{70 \text{ kg}} = 2.9 \times 10^{-3} \text{ mg kg}^{-1}\text{ day}^{-1}$$

From Table 14.5, the RfD for acetone is 0.1 mg $kg^{-1}$ $day^{-1}$

$$\text{Hazard quotient (HQ)} = \frac{2.9 \times 10^{-3} \text{ mg kg}^{-1}\text{ day}^{-1}}{0.1} = 0.029$$

**For Chloroform**

$$\text{ADD} = \frac{(0.1 \text{ mg L}^{-1})\,(2\text{L day}^{-1})}{70 \text{ kg}} = 2.9 \times 10^{-3} \text{ mg kg}^{-1}\text{ day}^{-1}$$

From Table 14.5, the RfD value for chloroform is 0.01 mg $kg^{-1}$ $day^{-1}$

$$\text{HQ} = \frac{2.9 \times 10^{-3} \text{ mg kg}^{-1}\text{ day}^{-1}}{0.01} = 0.029$$

Thus,

$$\text{Hazard index} = 0.029 + 0.29 = 0.319$$

Since the hazard index is less than 1.0, the water is safe. Notice that we did not need to take into consideration that the person drank the water for 5 years.

The incremental carcinogenic risk associated with chloroform is determined as follows.

$$\text{Risk} = (\text{CDI})\,(\text{Potency factor})$$

$$\text{CDI} = \frac{(0.1 \text{ mg L}^{-1})\,(2 \text{ L day}^{-1}\,(365 \text{ days yr}^{-1})\,(5 \text{ yrs})}{(70 \text{ kg})\,(365 \text{ days yr}^{-1})\,(70 \text{ yrs})} = 4.19 \times 10^{-5} \text{ mg kg}^{-1}\text{ day}^{-1}$$

From Table 14.6, the potency factor for chloroform is $6.1 \times 10^{-3}$

$$\text{Risk} = (\text{CDI})\,(\text{Potency factor})$$

$$\text{Risk} = (4.19 \times 10^{-5} \text{ mg kg}^{-1}\text{ day}^{-1})\,(6.1 \times 10^{-3} \text{ mg kg}^{-1}\text{ day}^{-1}) = 2.55 \times 2.55 \times 10^{-7}$$

From a cancer risk standpoint, the risk over this period of exposure is less than the $10^{-6}$ goal.

Two approaches commonly used to characterize uncertainty are sensitivity analyses and Monte Carlo simulations. In **sensitivity analyses**, we simply vary the uncertain quantities of each parameter (*e.g.*, average values, high and low estimates), usually one at a time, to find out how changes in these quantities affect the final risk estimate. This procedure gives us a range of possible values for the overall risk and tells us which parameters are most crucial in determining the size of the risk. In a **Monte Carlo simulation**, however, we assume that all parameters are random or uncertain.

Thus, instead of varying one parameter at a time, we use a computer program to select parameter distributions randomly every time the model equations are solved, the procedure being repeated many times. The resulting output can be used to identify values of exposure or risk corresponding to a specified probability, say, the 50$^{th}$ percentile or 95$^{th}$ percentile.

#### *14.2.4.4 Risk projections and management*

The final phase of the risk assessment process is risk characterization. In this phase, exposure and dose–response assessments are integrated to yield probabilities of effects occurring in humans under specific exposure conditions. Quantitative risks are calculated for appropriate media and pathways. For example, the risks of lead in water are estimated over a lifetime, assuming (1) that the exposure is 2 liters of water ingested per day over a 70-year lifetime and (2) that different concentrations of lead occur in the drinking water. This information can then be used by risk managers to develop standards or guidelines for specific toxic chemicals or infectious microorganisms in different media, such as the drinking water or food supply.

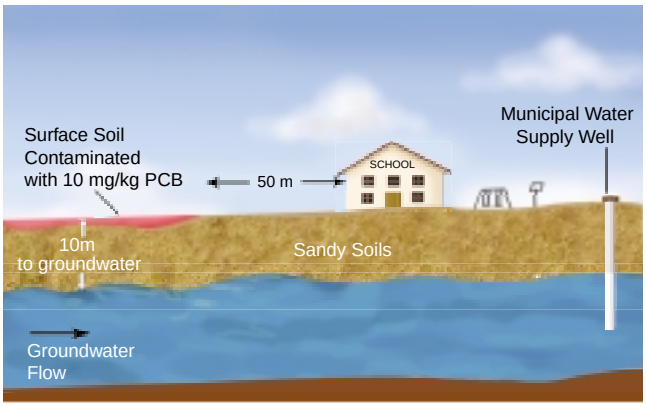
#### *14.2.4.5 Hazardous waste risk assessment*

Hazardous waste risk assessments are a key part of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). Risk assessments are performed to assess health and ecological risks at Superfund sites and to evaluate the effectiveness of remedial alternatives in attaining a **record of decision (ROD)**. Since specific cleanup requirements have not been established for most contaminants under CERCLA, each site is assessed on an individual basis and cleaned up to a predetermined level of risk, such as 1 cancer case per 1,000,000 people. Risks may be different from one site to the next, depending on characteristics of the site and the potential for exposure.

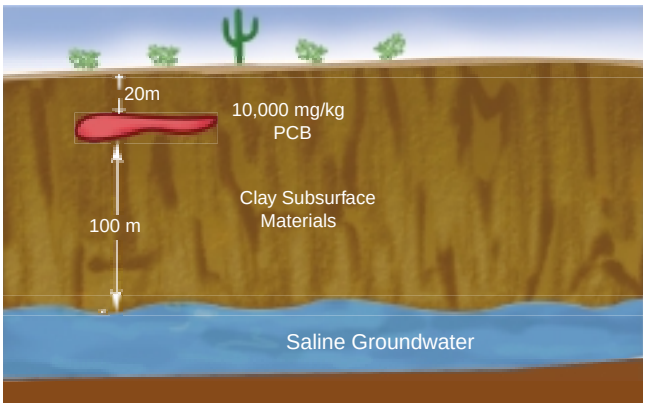
For example, at one site, a high level of contaminants may be present (10,000 mg per kg of soil), but there is no nearby population, there is a large distance to groundwater, and the soils are of low permeability. Based on a risk assessment, the best remedial action for the site may be to leave the contaminated soil in place, where natural attenuation processes will eventually result in its degradation. Removing the contaminated soil with disposal in a landfill or *in situ* treatment may result in a high risk due to release of wind-blown dusts that may expose workers at the site (Watts, 1998). In contrast, a soil contaminated with 10 mg of hazardous material per kg of soil may be considered a greater risk if the site has sandy soil, shallow groundwater, and nearby drinking water wells, and is located near a school. Cleanup to low levels would be necessary in this case to protect human health (Figure 14.7).

## 14.3 ECOLOGICAL RISK ASSESSMENT

Ecological risk assessment is a process that evaluates the probability that adverse ecological effects will occur as the result of exposure to one or more stressors. A **stressor** (or agent) is a substance, circumstance, or energy field that has the inherent ability to impose adverse effects upon a biological system. The environment is subject to many different stressors, including chemicals, genetically engineered microorganisms, ionizing radiation, and rapid changes in temperatures. Ecolog-




Site A-High Risk




Site B-Low Risk

**Figure 14.7** Two extremes of potential risk from contaminated sites. Site A is a high-risk site with potential for migration from the source to nearby receptors. Site B, although characterized by a higher source concentration, has minimal potential for contaminant migration and risk. Modified from Watts, 1998.

ical risk assessment may evaluate one or more stressors and ecological components (*e.g.*, specific organisms, populations, communities, or ecosystems). Ecological risks may be expressed as true probabilistic estimates of adverse effects (as is done with carcinogens in human health risk assessment), or they may be expressed in a more qualitative manner.

In the United States, the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) (otherwise known as the Superfund), the Resource Conservation and Recovery Act (RCRA), and other regulations require an ecological assessment as part of all remedial investigation and feasibility studies (see also Section 14.2.4.5). Pesticide registration, which is required under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), must also include an ecological assessment (see Section 14.3). In the CERCLA/RCRA context, a typical objective is to determine and document actual or potential effects of contaminants on ecological receptors and habitats as a basis for evaluating remedial alternatives in a scientifically defensible manner.

The four major phases or steps in ecological assessment (Figure 14.8) are as follows:

- Problem formulation and hazard identification
- Exposure assessment
- Ecological effects/toxicity assessment
- Risk characterization

An ecological risk assessment may be initiated under many circumstances—the manufacturing of a new chemical, evaluation of cleanup options for a contaminated site, or the planned filling of a marsh, among others. The problem-formulation

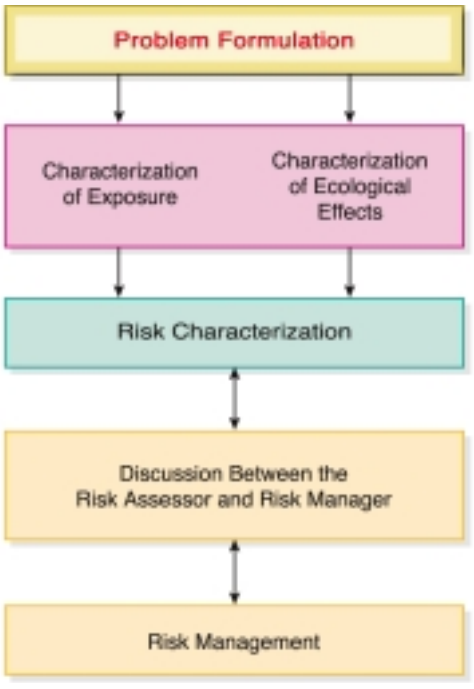



**Figure 14.8** Framework for ecological risk assessment. Adapted from U.S. EPA, 1992a.

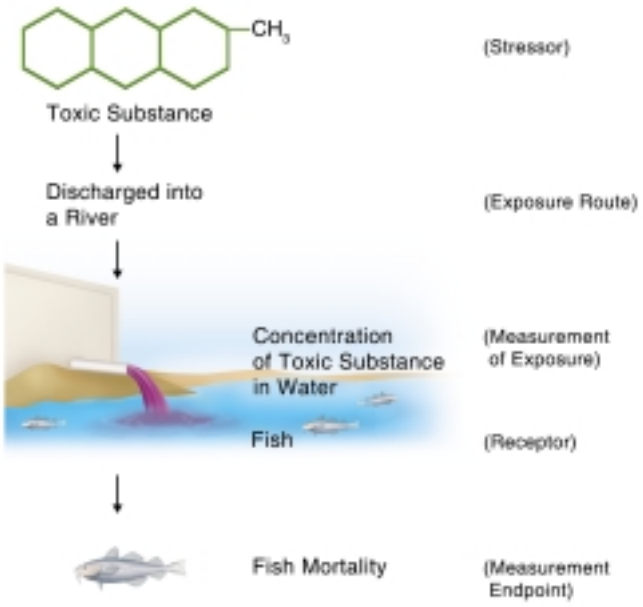



**Figure 14.9** Ecological risk assessment.

process begins with an evaluation of the stressor characteristics, the ecosystem at risk, and the likely ecological effects. An endpoint is then selected. An **endpoint** (Figure 14.9) is a characteristic of an ecological component, *e.g.*, the mortality of fish) that may be affected by a stressor. Two types of endpoints are generally used: assessment endpoints and measurement endpoints. **Assessment endpoints** are particular environmental values to be protected. Such endpoints, which are recognized and valued by the public, drive the decisions made by official risk managers. **Measurement endpoints** are qualitatively or quantitatively measurable factors. Suppose, for example, a community that values the quality of sports fishing in the area is worried about the effluent from a nearby paper mill. In this case, a decline in the trout population might serve as the assessment endpoint, while the increased mortality of minnows, as evaluated by laboratory studies, might be the measurement endpoint. Thus, risk managers would use the quantitative data gathered on the surrogate minnow population to develop management strategies designed to protect the trout population.

Exposure assessment is a determination of the environmental concentration range of a particular stressor and the actual dose received by the *biota* (all the plants and animals) in a given area. The most common approach to exposure analysis is to measure actual concentrations of a stressor and combine these measurements with assumptions about contact and uptake by the biota. For example, the exposure of simple aquatic organisms to chemicals can often be measured simply as the concentration of that chemical in the water because the physiologic systems of these organisms are assumed to be in equilibrium with the surrounding water. Stressor measurements can also be combined with quantitative parameters describing the frequency and magnitude of contact. For example, concen-

trations of chemicals or microorganisms in food items can be combined with ingestion rates to estimate dietary exposure. Exposure assignment is, however, rarely straightforward. Biotransformations may occur, especially for heavy metals such as mercury (see Section 13.5.5). Such transformations may result in the formation of even more toxic forms of the stressor. Researchers must therefore use mathematical models to predict the fate and resultant exposure to a stressor and to determine the outcome of a variety of scenarios.

The purpose of evaluating ecological effects is to identify and quantify the adverse effects elicited by a stressor and, to the extent possible, to determine cause-and-effect relationships. During this phase, toxicity data are usually compiled and compared.

### *EXAMPLE 14.3*

*Examples of a Management Goal, Assessment Endpoint, and Measures*

**Goal:** Viable, self-sustaining coho salmon population that supports a subsistence and sport fishery.
**Assessment Endpoint:** Coho salmon breeding success, fry survival, and adult return rates.
**Measures of Effects**
- Egg and fry response to low dissolved oxygen
- Adult behavior in response to obstacles
- Spawning behavior and egg survival with changes in sedimentation

**Measures of Ecosystem and Receptor Characteristics**
- Water temperature, water velocity, and physical obstructions
- Abundance and distribution of suitable breeding substrate
- Abundance and distribution of suitable food sources for fry
- Feeding, resting, and breeding behavior
- Natural reproduction, growth, and mortality rates

**Measures of Exposure**
- Number of hydroelectric dams and associated ease of fish passage
- Toxic chemical concentrations in water, sediment, and fish tissue
- Nutrient and dissolve oxygen levels in ambient waters
- Riparian cover, sediment loading, and water temperature

Generally, there are acute and chronic data for the stressor acting on one or several species. Field observations can provide additional data, and so can controlled-microcosm and large-scale tests.

The process of developing a stressor–response profile is complex because it inevitably requires models, assumptions, and extrapolations. For example, the relationship between measurement and assessment endpoint is an assumption. It is often expressly stated in the model used, but when it is not specifically stated, it is left to professional judgment. In addition, the stressor–response profile is analogous to a dose–response curve in the sense that it involves extrapolations; in this case, though, a single-species toxicity test is extrapolated to the community and ecosystem level. One of the difficulties in the quantification of the stressor–response profile is that many of the quantitative extrapolations are drawn from information that is qualitative in nature. For example, when we use **phylogenic extrapolation** to transfer toxicity data from one species to another species—or even to a whole class of organisms—we are assuming a degree of similarity based on qualitative characteristics. Thus, when we use green algal toxicity test data to represent all photosynthetic eukaryotes (which we often do), we must remember that all photosynthetic eukaryotes are not, in fact, green algae. Because many of the responses are extrapolations based on models ranging from the molecular to the ecosystem level, it is critically important that uncertainties and assumptions be clearly delineated.

Risk assessment consists of comparing the exposure and stressor–response profiles to estimate the probability of effects, given the distribution of the stressor within the system. As you might expect, this process is extraordinarily difficult to accomplish. In fact, our efforts at predicting adverse effects have been likened to the weather forecaster's prediction of rain (Landis and Ho-Yu, 1995). Thus, the predictive process in ecological risk assessment is still very much an art form, largely dependent on professional judgment.

Conceptual model diagrams can be used to better visualize potential impacts (Figure 14.10). They may be based on theory and logic, empirical data, mathematical models, or probability models. These diagrams are useful tools for communicating important pathways in a clear and concise way. They can be used to ask new questions about relationships that help generate plausible risk hypothesis.

## 14.4 MICROBIAL RISK ASSESSMENT

Outbreaks of waterborne disease caused by microorganisms usually occur when the water supply has been obviously and significantly contaminated. In such high-level cases, the exposure is manifest, and cause and effect are relatively easy to determine. However, exposure to low-level microbial contamination is difficult to determine epidemiologically. We know, for example, that long-term exposure to microbes can have a significant impact on the health of individuals within a community, but we need a way to measure that impact.

For some time, methods have been available to detect the presence of low levels (1 organism per 1000 liters) of pathogenic organisms in water, including enteric viruses, bacteria, and protozoan parasites. The trouble is that the risks posed to the community by these low levels of pathogens in a water supply over time are not like those posed by low levels of chemical toxins or carcinogens. For example, it takes just one amoeba in the wrong place at the wrong time to infect one individual, whereas that same individual would have to consume some quantity of a toxic chemical to be comparably harmed. Microbial risk assessment is therefore a process that allows us to estimate responses in terms of the *risk of infection* in a quantitative fashion. Microbial risk gen-

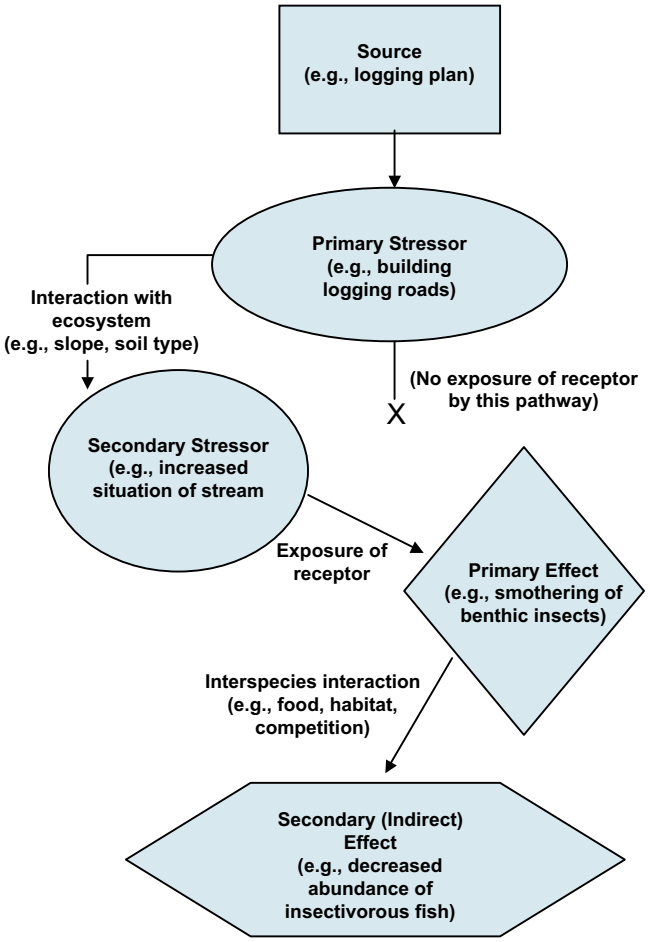



**Figure 14.10** Conceptual model for logging. Source: www.epa.gov.

erally follows the steps used in other health-based risk assessments—hazard identification, exposure assessment, dose–response, and risk characterization. The differences are in the specific assumptions, models, and extrapolation methods used.

Hazard identification in the case of pathogens is complicated because several outcomes—from asymptomatic infection to death (see Figure 14.11) —are possible, and these outcomes depend upon the complex interaction between the pathogenic agent (the "infector") and the host (the "infectee"). This interaction, in turn, depends on the characteristics of the host as well as the nature of the pathogen. Host factors, for example, include preexisting immunity, age, nutrition, ability to mount an immune response, and other nonspecific host factors. Agent factors include type and strain of the organism as well as its capacity to elicit an immune response.

Among the various outcomes of infection is the possibility of **subclinical infection.** Subclinical (asymptomatic) infections are those in which the infection (growth of the microorganism within the human body) results in no obvious illness such as fever, headache, or diarrhea. That is, individuals can host a pathogen microorganism—and transmit it to

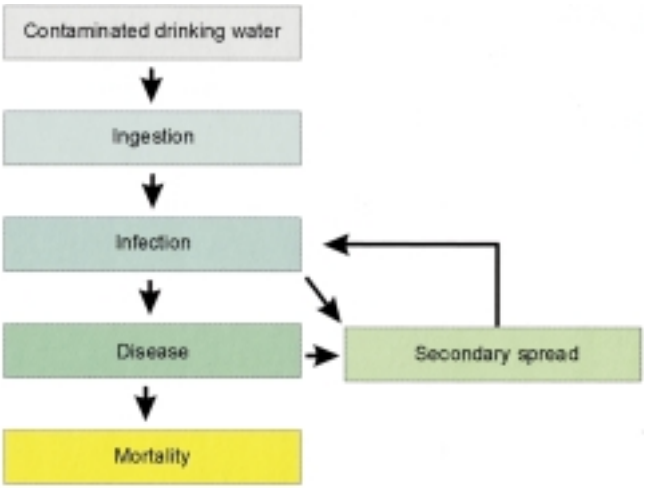



**Figure 14.11** Outcomes of enteric viral exposure. From *Pollution Science* © 1996, Academic Press, San Diego, CA.

others—without ever getting sick themselves. The ratio of clinical to subclinical infection varies from pathogen to pathogen, especially in viruses, as shown in Table 14.10. Poliovirus infections, for instance, seldom result in obvious clinical symptoms; in fact, the proportion of individuals developing clinical illness may be less than 1%. However, other enteroviruses, such as the coxsackie viruses, may exhibit a greater proportion. In many cases, as in that of rotaviruses, the probability of developing clinical illness appears to be completely unrelated to the dose an individual receives via ingestion. Rather, the likelihood of developing

**TABLE 14.10 Ratio of clinical to subclinical infections with enteric viruses.**

| VIRUS | FREQUENCY OF CLINICAL ILLNESS[a] (%) |
|---|---|
| Poliovirus 1 | 0.1–1 |
| Coxsackie | |
| A16 | 50 |
| B2 | 11–50 |
| B3 | 29–96 |
| B4 | 30–70 |
| B5 | 5–40 |
| Echovirus | |
| Overall | 50 |
| 9 | 15–60 |
| 18 | Rare–20 |
| 20 | 33 |
| 25 | 30 |
| 30 | 50 |
| Hepatitis A (adults) | 75 |
| Rotavirus | |
| (Adults) | 56–60 |
| (Children) | 28 |
| Astrovirus (adults) | 12–50 |

[a]The percentage of the individuals infected who develop clinical illness.

From Gerba and Rose (1993). From *Pollution Science* © 1996, Academic Press, San Diego, CA.

clinical illness depends upon the type and strain of the virus as well as host age, nonspecific host factors, and possibly preexisting immunity. The incidence of clinical infection can also vary from year to year for the same virus, depending on the emergence of new strains.

Another outcome of infection is the development of clinical illness. Several host factors play a major role in this outcome. The age of the host is often a determining factor. In the case of hepatitis A, for example, clinical illness can vary from about 5% in children less than 5 years of age to 75% in adults. Similarly, children are more likely to develop rotaviral gastroenteritis than are adults. Immunity is also an important factor, albeit a variable one. That is, immunity may or may not provide long-term protection from reinfection, depending on the enteric pathogen. It does not, for example, provide long-term protection against the development of clinical illness in the case of the Norwalk virus or *Giardia*. However, for most enteroviruses and for the hepatitis A virus, immunity from reinfection is believed to be lifelong. Other undefined host factors may also control the odds of developing illness. For example, in experiments with the Norwalk virus (norovirus), human volunteers who did not become infected upon an initial exposure to the virus also did not respond to a second exposure. In contrast, those volunteers who developed gastroenteritis upon the first exposure also developed illness after the second exposure.

The ultimate outcome of infection—mortality—can be caused by nearly all enteric organisms. The factors that control the prospect of mortality are largely the same factors that control the development of clinical illness. Host age, for example, is significant. Thus, mortality for hepatitis A and poliovirus is greater in adults than in children. In general, however, one can say that the very young, the elderly, and the immunocompromised are at the greatest risk of a fatal outcome of most illnesses (Gerba et al., 1996). For example, the case-fatality rate (%) for *Salmonella* in the general population is 0.1%, but it has been observed to be as high as 3.8% in nursing homes (Table 14.11). In North America and Europe, the reported case-fatality rates (*i.e.*, the ratio of cases to fatalities reported as a percentage of persons who die) for enterovirus infections range from less than 0.1 to 0.94%, as shown in Table 14.12. The case-fatality rate for common enteric bacteria ranges from 0.1 to 0.2% in the general population. Enteric bacterial diseases can be treated with antibiotics, but no treatment is available for enteric viruses.

**TABLE 14.11 Case fatality observed for enteric pathogens in nursing homes versus general population.**

| ORGANISM | CASE FATALITY (%) IN GENERAL POPULATION | CASE FATALITY (%) IN NURSING HOMES |
|---|---|---|
| *Campylobacter jejuni* | 0.1 | 1.1 |
| *Escherichia coli* 0157:H7 | 0.2 | 11.8 |
| *Salmonella* | 0.1 | 3.8 |
| Rotavirus | 0.01 | 1.0 |

Modified from Gerba et al. (1996).

**TABLE 14.12 Case-fatality rates for enteric viruses and bacteria.**

| ORGANISM | CASE-FATALITY RATE (%) |
|---|---|
| **Viruses** | |
| Poliovirus 1 | 0.90 |
| Coxsackie | |
| A2 | 0.50 |
| A4 | 0.50 |
| A9 | 0.26 |
| A15 | 0.12 |
| Cosxsackie B | 0.59–0.94 |
| Echovirus | |
| 6 | 0.29 |
| 9 | 0.27 |
| Hepatitis A | 0.30 |
| Rotavirus | |
| (Total) | 0.01 |
| (Hospitalized) | 0.12 |
| Norwalk | 0.0001 |
| Astrovirus | 0.01 |
| **Bacteria** | |
| *Shigella* | 0.2 |
| *Salmonella* | 0.1 |
| *Escherichia coli* 0157:H7 | 0.2 |
| *Campylobacter jejuni* | 0.1 |

From Gerba and Rose (1993) and Gerba et al. (1996). From *Pollution Science* © 1996, Academic Press, San Diego, CA.

Recognizing that microbial risk involves a myriad of pathogenic organisms capable of producing a variety of outcomes that depend on a number of factors—many of which are undefined—one must now face the problem of exposure assessment, which has complications of its own. Unlike chemical-contaminated water, microorganism-contaminated water does not have to be consumed to cause harm. That is, individuals who do not actually drink, or even touch, contaminated water also risk infection because pathogens—particularly viruses—may be spread by person-to-person contact or subsequent contact with contaminated inanimate objects (such as toys). This phenomenon is described as the **secondary attack rate**, which is reported as a percentage. For example, one person infected with poliovirus can transmit it to 90% of the persons with whom he or she associates. This secondary spread of viruses has been well documented for waterborne outbreaks of several diseases, including that caused by Norwalk virus, whose secondary attack rate is about 30%.

The question of dose is another problem in exposure assessment. How does one define "dose" in this context? To answer this question, researchers have conducted a number of studies to determine the infectious dose of enteric microorganisms in human volunteers. Such human

experimentation is necessary because determination of the infectious dose in animals and extrapolation to humans is often impossible. In some cases, for example, humans are the primary or only known host. In other cases, such as that of *Shigella* or norovirus, infection can be induced in laboratory-held primates, but it is not known whether the infectious dose data can be extrapolated to humans. Much of the existing data on infectious doses of viruses has been obtained with attenuated vaccine viruses or with avirulent laboratory-grown strains, so that the likelihood of serious illness is minimized. An example of a dose–response curve for a human feeding study with rotavirus is shown in Figure 14.12.

In the microbiological literature, the term **minimum infectious dose** is used frequently, implying that a threshold dose exists for microorganisms. In reality, the term used usually refers to the $ID_{50}$ dose at which 50% of the animals or humans exposed became infected or exhibit any symptoms of an illness. Existing infectious dose data are compatible with nonthreshold responses, and the term "infectivity" is probably more appropriate when referring to differences in the likelihood of an organism causing an infection. For example, the probability of a given number of ingested rotaviruses causing diarrhea is greater than that for *Salmonella*. Thus, the infectivity of rotavirus is greater than that of *Salmonella*.

Next, one must choose a dose–response model, whose abscissa is the dose and whose ordinate is the risk of infection (see Figure 14.12). The choice of model is critical so that risks are not greatly overestimated or underestimated. A modified exponential (beta-Poisson distribution) or a log-probit (simple lognormal, or exponential, distribution) model may be used to describe the probability of infection in human subjects for many enteric microorganisms (Haas, 1983). These models have been found to best fit experimental data. For the beta-Poisson model, the probability of infection from a single exposure, $P$, can be described as follows:

$$P = 1 - (1 + N/\beta)^{-\alpha} \qquad \text{(Eq. 14.10)}$$

where N is the number of organisms ingested per exposure and $\alpha$ and $\beta$ represent parameters characterizing the host-virus interaction (dose–response curve). Some values for $\alpha$ and $\beta$ for several enteric waterborne pathogens are shown in Table 14.13; these values were determined from human studies. For some microorganisms, an **exponential model** may better represent the probability of infection.

$$P = 1 - \exp(-rN) \qquad \text{(Eq. 14.11)}$$

In this equation, r is the fraction of the ingested microorganisms that survive to initiate infections (host-microorganism interaction probability). Table 14.13 shows examples of results of both models for several organisms.

These models define the probability of the microorganisms overcoming the host defenses (including stomach pH, finding a susceptible cell, nonspecific immunity, and so on) to establish an infection in the host. When one uses these models, one estimates the probability of becoming infected after ingestion of various concentrations of pathogens. For example, Example 14.5 shows how to calculate the risk of acquiring a viral infection from consumption of contaminated drinking water containing echovirus 12 using Equation 14.10.

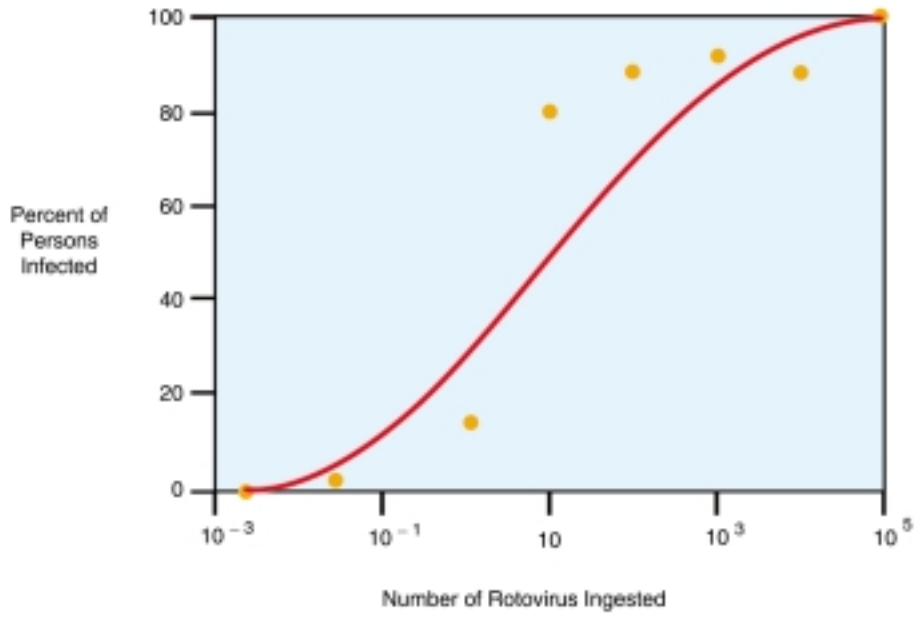



**Figure 14.12** Dose–response for human rotavirus by oral ingestion.

**TABLE 14.13 Best-fit dose-response parameters for enteric pathogen ingestion studies.**

| MICROORGANISM | BEST MODEL | MODEL PARAMETERS |
|---|---|---|
| Echovirus 12 | Beta-Poisson | $\alpha = 0.374$<br>$\beta = 186{,}69$ |
| Rotavirus | Beta-Poisson | $\alpha = 0.26$<br>$\beta = 0.42$ |
| Poliovirus 1 | Exponential | $r = 0.009102$ |
| Poliovirus 1 | Beta-Poisson | $\alpha = 0.1097$<br>$\beta = 1524$ |
| Poliovirus 3 | Beta-Poisson | $\alpha = 0.409$<br>$\beta = 0.788$ |
| *Cryptosporidium* | Exponential | $r = 0.004191$ |
| *Giardia lamblia* | Exponential | $r = 0.02$ |
| *Salmonella* | Exponential | $r = 0.00752$ |
| *Escherichia coli* | Beta-Poisson | $\alpha = 0.1705$<br>$\beta = 1.61 \times 10^{6}$ |

Modified from Regli et al. (1991). From *Pollution Science* © 1996, Academic Press, San Diego, CA.

### EXAMPLE 14.4

*Application of a Virus Risk Model to Characterize Risks from Consuming Shellfish*

It is well known that infectious hepatitis and viral gastroenteritis are caused by consumption of raw or, in some cases, cooked clams and oysters. The concentration of echovirus 12 was found to be 8 plaque-forming units per 100 g in oysters collected from coastal New England waters. What are the risks of becoming infected and ill from echovirus 12 if the oysters are consumed? Assume that a person usually consumes 60 g of oyster meat in a single serving:

$$\frac{8 \text{ PFU}}{100 \text{ g}} = \frac{N}{60 \text{ g}} \quad N = 4.8 \text{ PFU consumed}$$

From Table 14.13, $\alpha = 0.374$, $\beta = 186.64$. The probability of infection from Equation 14.10 is then

$$P = 1 - \left(1 + \frac{4.8}{186.69}\right)^{-0.374} = 9.4 \times 10^{-3}$$

If the percent of infections that result in risk of clinical illness is 50%, then from Equation 14.14 one can calculate the risk of clinical illness:

$$\text{Risk of clinical illness} = (9.4 \times 10^{-3})\,(0.50) = 4.7 \times 10^{-3}$$

If the case-fatality rate is 0.001%, then from Equation 14.15

$$\text{Risk of mortality} = (9.4 \times 10^{-3})\,(0.50)\,(0.001) = 4.7 \times 10^{-6}$$

If a person consumes oysters 10 times a year with 4.8 PFU per serving, then one can calculate the risk of infection in one year from Equation 14.12

### EXAMPLE 14.5

*Risk Assessment for Rotavirus in Drinking Water*

| | |
|---|---|
| Pathogen identified | Rotavirus |
| ↓ | ↓ |
| Dose Response Model (based on human ingestion studies) | best fit for data is the Beta Poisson Model<br>$P = (1 + N/\beta)^{-\alpha}$<br>$\alpha = 0.2631$<br>$\beta = 0.42$ |
| ↓ | ↓ |
| Exposure (field studies on concentration in drinking water) | 4 rotavirus/1,000 liters |
| ↓ | ↓ |
| Risk Characterization | Risk of Infection<br>Assumes: 2 liters/day of drinking water ingested.<br>Thus,<br>$N = 0.008$/day<br>Risk of Infection/day = 1:200<br>Risk of Infection/year<br>$P_A = 1 - (1 - P)^{365}$<br>$P_A = 1{:}2$ |

Annual and lifetime risks can also be determined, again assuming a Poisson distribution of the virus in the water consumed (assuming daily exposure to a constant concentration of viral contamination), as follows:

$$P_A = 1 - (1 - P)^{365} \qquad \text{(Eq. 14.12)}$$

where $P_A$ is the annual risk (365 days) of contracting one or more infections, and

$$P_L = 1 - (1 - P)^{25{,}550} \qquad \text{(Eq. 14.13)}$$

where $P_L$ is the lifetime risk (assuming a lifetime of 70 years = 25,550 days) of contracting one or more infections.

Risks of clinical illness and mortality can then be determined by incorporating terms for the percentage of clinical illness and mortality associated with each particular virus:

$$\text{Risk of clinical illness} = PI \qquad \text{(Eq. 14.14)}$$

$$\text{Risk of mortality} = PIM \qquad \text{(Eq. 14.15)}$$

where $I$ is the percentage of infections that result in clinical illness and $M$ is the percentage of clinical cases that result in mortality.

Application of this model allows estimation of the risks of infection, development of clinical illness, and mortality for different levels of exposure. As shown in Table 14.14, for example, the estimated risk of infection from 1 rotavirus in 100 liters of drinking water (assuming ingestion of 2 liters per day) is $1.2 \times 10^{-3}$, or almost 1 in 1,000 for a single-day

**TABLE 14.14 Risk of infection, disease, and mortality for rotavirus.**

| VIRUS CONCENTRATION PER 100 LITERS | RISK DAILY | RISK ANNUAL |
|---|---|---|
| **Infection** | | |
| 100 | $9.6 \times 10^{-2}$ | 1.0 |
| 1 | $1.2 \times 10^{-3}$ | $3.6 \times 10^{-1}$ |
| 0.1 | $1.2 \times 10^{-4}$ | $4.4 \times 10^{-2}$ |
| **Disease** | | |
| 100 | $5.3 \times 10^{-2}$ | $5.3 \times 10^{-1}$ |
| 1 | $6.6 \times 10^{-4}$ | $2.0 \times 10^{-1}$ |
| 0.1 | $6.6 \times 10^{-5}$ | $2.5 \times 10^{-2}$ |
| **Mortality** | | |
| 100 | $5.3 \times 10^{-6}$ | $5.3 \times 10^{-5}$ |
| 1 | $6.6 \times 10^{-8}$ | $2.0 \times 10^{-5}$ |
| 0.1 | $6.6 \times 10^{-9}$ | $2.5 \times 10^{-6}$ |

Modified from Gerba and Rose (1992). From *Pollution Science* © 1996, Academic Press, San Diego, CA.

100 liters of drinking water (assuming ingestion of 2 liters per day) is $1.2 \times 10^{-3}$, or almost 1 in 1,000 for a single-day exposure. This risk would increase to $3.6 \times 10^{-1}$, or approximately one in three, on an annual basis. As can be seen from this table, the risk of developing a clinical illness also appears to be significant for exposure to low levels of rotavirus in drinking water.

The EPA recommends that any drinking water treatment process should be designed to ensure than human populations are not subjected to risk of infection greater than 1:10,000 for a yearly exposure. To achieve this goal, it would appear from the data shown in Table 14.10 that the virus concentration in drinking water would have to be less than 1 per 1,000 liters. Thus, if the average concentration of enteric viruses in untreated water is 1,400/1,000 liters, treatment plants should be designed to remove at least 99.99% of source in terms of the concentration of a disease-causing organism in that supply. Thus, the more contaminated the raw water source, the more treatment is required to reduce the risk to an acceptable level. An example of this application is shown in Figure 14.13. The plausibility of validation of microbial risk assessment models has been examined by using data from foodborne outbreaks in which information has been available on exposure and outcomes (Rose et al., 1995; Crockett et al., 1996). These studies suggest that microbial risk assessment can give reasonable estimates of illness from exposure to contaminated foods (Table 14.15).

**TABLE 14.15 Comparison of outbreak data to model predictions for assessment of risks associated with exposure to *Salmonella*.**

| FOOD | DOSE CFU | AMOUNT CONSUMED | ATTACK RATE (%) | PREDICTED P (%) |
|---|---|---|---|---|
| Water | 17 | 1 L | 12 | 12 |
| Pancretin | 200 | 7 doses | 100 | 77 |
| Ice cream | 102 | 1 portion | 52 | 54 |
| Cheese | 100–500 | 28 g | 28–36 | 53–98 |
| Cheese | $10^5$ | 100 g | 100 | >99.99 |
| Ham | $10^6$ | 50–100 g | 100 | >99.99 |

Source: Rose et al., 1995. From *Environmental Microbiology* © 2000, Academic Press, San Diego, CA.

In summary, risk assessment is a major tool for decision making in the regulatory arena. This approach is used to explain chemical and microbial risks, as well as ecosystem impacts. The results of such assessments can be used to inform risk managers of the probability and extent of environmental impacts resulting from exposure to different levels of stress (contaminants). Moreover, this process, which allows the quantification and comparison of diverse risks, lets risk managers utilize the maximum amount of complex information in the decision-making process. This information can also be used to weigh the cost and benefits of control options and to develop standards or treatment options (see Example 14.6).

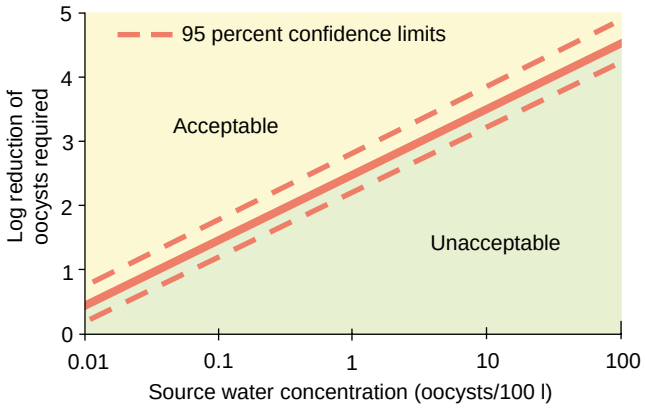



**Figure 14.13** Relationship of influent *Cryptosporidium* concentration and log reduction by treatment necessary to produce acceptable water. From Haas et al., 1996.

### *EXAMPLE 14.6*

*How Do We Set Standards for Pathogens in Drinking Water?*

In 1974, the U.S. Congress passed the Safe Drinking Water Act, giving the U.S. Environmental Protection Agency (EPA) the authority to establish standards for contaminants in drinking water. Through a risk analysis approach, standards have been set for many chemical contaminants in drinking water. Setting standards for microbial contaminants proved more difficult because (1) methods for the detection of many pathogens are not available, (2) days to weeks are sometimes required to obtain results, and (3) costly and time-consuming methods are required. To overcome these difficulties, coliform bacteria had been used historically to assess the microbial quality of drink-

ing water. However, by the 1980s it had become quite clear that coliform bacteria did not indicate the presence of pathogenic waterborne *Giardia* or enteric viruses. Numerous outbreaks had occurred in which coliform standards were met, because of the greater resistance of viruses and *Giardia* to disinfection. A new approach was needed to ensure the microbial safety of drinking water.

To achieve this goal a new treatment approach was developed called the Surface Treatment Rule (STR). As part of the STR, all water utilities that use surface waters as their source of potable water would be required to provide filtration to remove *Giardia* and enough disinfection to kill viruses. The problem facing the EPA was how much removal should be required. To deal with this issue, the EPA for the first time used a microbial risk assessment approach. The STR established that the goal of treatment was to ensure that microbial illness from *Giardia lamblia* infection should not be any greater than 1 per 10,000 exposed persons annually ($10^{-4}$ per year). This value is close to the annual risk of infection from waterborne disease outbreaks in the U. S. ($4 \times 10^{-3}$). Based on the estimated concentration of *Giardia* and enteric viruses in surface waters in the United States from the data available at the time, it was required that all drinking water treatment plants be capable of removing 99.9% of the *Giardia* and 99.99% of the viruses. In this manner it was hoped that the risk of infection of $10^{-4}$ per year would be achieved. The STR went into effect in 1991.

To better assess whether the degree of treatment required is adequate, the EPA developed the Information Collection Rule, which required major drinking water utilities that use surface waters to analyze these surface water for the presence of *Giardia, Cryptosporidium*, and enteric viruses for a period of almost 2 years. From this information, the EPA set treatment control requirements to ensure that the $10^{-4}$ yearly risk is met. Utilities that have heavily contaminated source water are required to achieve greater levels of treatment (see Figure 14.13).

## QUESTIONS AND PROBLEMS

1. List the four steps in a formal risk assessment.
2. Why do we use safety factors in risk assessment?
3. What is the most conservative dose–response curve? What does it mean?
4. What is the difference between risk assessment and risk management?
5. What are some of the differences between the risks posed by chemicals and those posed by microorganisms?
6. Suppose a 50-kg individual drinks 2 L $day^{-1}$ of chloroform and 0.1 mg $L^{-1}$ phenol. What is the hazard index? Is there cause for concern?
7. Estimate the cancer risk for a 70-kg individual consuming 1.5 liters of water containing trichloroethylene (TCE) per day for 70 days.
8. Calculate the risk of infection from rotavirus during swimming in polluted water. Assume 30 ml of water is ingested during swimming and the concentration of rotavirus was 1 per 100 liters. What would the risk be in a year if a person went swimming 5 times and 10 times in the same water with the same concentration of virus?
9. What is a NOAEL and how does it differ from a LOAEL?
10. If 10 oocysts of *Cryptosporidium* are detected in 100 L of surface water, how much reduction (in $\log_{10}$) by a water treatment plant is required to achieve a 1:10,000 annual risk of infection?
11. Give an example of a nonthreshold response for a chemical toxin.
12. What is the difference between a stressor and a receptor? Give an example of a chemical stressor and a receptor in an aquatic system. What endpoint would you use?
13. Draw an exposure pathway for pathogens for the disposal of raw sewage into the ocean. Consider likely routes of ingestions and inhalation. As a risk manager, what options may you have to reduce the risks of exposure?
14. Using the U.S. Environmental Protection Agency IRIS database (www.epa.gov/iris), find the critical effect, uncertainty factor, and NOAEL, LOAEL, and RfD for mercury, chromium, and chloroform. In drinking water, which one would be the most toxic?

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