# Chapter 7
# Principal Elements of a Public Health Risk Assessment for Chemical Exposure Problems

In planning for public health protection from the likely adverse effects caused by human exposure to chemicals, the first concern usually relates to whether or not the substance in question possesses potentially hazardous and/or toxic properties. As a corollary, once a 'social chemical' has been determined to present a potential health hazard, then the main concern becomes one of the likelihood for, and the degree of human exposure. In the final analysis, risk from human exposure to a chemical of concern is determined to be a function of dose or intake and potency of the substance, *viz*.:

$$Risk\ from\ chemical\ exposure = [Dose\ of\ chemical] \times [Chemical\ potency] \quad (7.1)$$

In effect, risk to an exposed population is understood by examining the exposure the population experiences relative to the hazard and the chemical potency information. Indeed, such formulations of the risk assessment paradigm are generally employed to help characterize health risks under existing exposure conditions, as well as to examine how risks might change if actions are taken to alter exposures, etc. (USEPA 2012). In general, both exposure and toxicity information are necessary to fully characterize the potential hazard of a chemical agent—or indeed any other hazardous agent for that matter. This chapter discusses the principal elements and activities necessary for obtaining and integrating the pertinent information that will eventually allow effective public health risk management decisions to be made about chemical exposure problems.

## 7.1 Characterization of Chemical Exposure Problems

Human exposure to a chemical agent is considered to be an episode comprised of the contacting at a boundary between a human body or organ and the chemical-containing medium, at a specific chemical concentration, for a specified time



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interval. Upon exposure, a receptor generally receives a dose of the chemical—and at relative measures/levels that may be quite different from the actual exposed amount; in fact, dose is different from (but occurs as a result of) an exposure (NRC 1991c)—with the dose defined as the amount of the chemical that is absorbed or deposited in the body of an exposed individual over a specified time. A clear understanding of such differences in the exposure parameters is indeed critical to the design of an adequate exposure characterization plan.

The characterization of chemical exposure problems is a process used to establish the presence or absence of chemical hazards, to delineate the nature and degree of the hazards, and to determine possible threats posed by the exposure or hazard situation to human health. The exposure routes (which may consist of inhalation, ingestion, and/or dermal contacts) and duration of exposure (that may be short-term [acute] or long-term [chronic]) will significantly influence the degree of impacts on the affected receptors. The nature and behavior of chemical substances also form a very important basis for evaluating the potential for human exposures to the possible toxic or hazardous constituents of the substance.

Now, whereas the need for and/or reliance on models and default assumptions is almost always inevitable in most chemical exposure characterization problems, the use of applicable empirical data in exposure assessments is strongly recommended whenever possible. In this regard, information obtained (through monitoring studies) from assessment of direct exposure (e.g., drinking contaminated water) and/or indirect exposure (e.g., accumulation of contaminants via the food chain) should preferably be used. Ideally, the assessment will include monitored levels of the chemical agent in the chemical-containing media, and in human tissues and fluids—in particular, estimates of the dose at a biologic target tissue(s) where an effect(s) may occur. Such information is necessary to accurately evaluate the potential health risk of exposed populations. Of course, in the absence of complete monitoring information, mathematical exposure assessment models may be employed. These models provide a methodology through which various factors, such as the temporal/spatial distribution of a chemical agent released from a particular source, can be combined to predict levels of human exposures. Even so, modeling may not necessarily be viewed as a fully satisfactory substitute for adequate data—but rather as a surrogate to be employed when confronted by compelling needs and inadequate data. In the end, uncertainty associated with these and indeed all other methods must be carefully documented and elucidated to the extent feasible.

### *7.1.1 Factors Affecting Exposure Characterization*

Several chemical-specific, receptor-specific, and even environmental factors need to be recognized and/or evaluated as an important part of any public health risk management program that is designed to address problems that could arise from exposure of the public to various chemical substances. The general types of data

and information necessary for the investigation of potential chemical exposure problems relate to the following:

- Identities of the chemicals of concern;
- Concentrations contacted by potential receptors of interest;
- Receptor characteristics;
- Characteristics of the physical and environmental setting that can affect behavior and degree of exposure to the chemicals; and
- Receptor response upon contact with the target chemicals.

In addition, it is necessary to generate information on the chemical intake rates for the specific receptor(s), together with numerous other exposure parameters. Indeed, all parameters that could potentially impact the human health outcomes should be carefully evaluated; this includes the following especially important categories, as annotated/expounded below.

- *Exposure duration and frequency.* A single high-dose exposure to a hazardous agent may result in toxic effects quite different from those following repeated lower dose exposures. Thus, in evaluating chemical risks associated with a given problem situation, adequate consideration should be given to the duration—namely, acute (usually $\leq$14 days) *vs.* intermediate (usually 15–364 days) *vs.* chronic (usually $\geq$365 days); the intensity (i.e., dose rate *vs.* total dose); and the frequency (continuous or intermittent) of exposure. These exposure parameters have to be carefully evaluated, alongside any relevant pharmacokinetic parameters for the constituents of concern.
- *Exposure media and routes.* Exposure to hazardous substances is often a complex phenomenon—entailing exposures via multiple routes and/or media. Thus, all possible exposure media, pathways, and routes should be appropriately investigated and accounted for in the characterization of a chemical exposure situation.
- *Target receptor attributes.* Receptor behavior and activity patterns, such as the amount of time a receptor spends indoors compared with that spent outdoors, as well as its underlying variability in assessing potential human health effects should be carefully evaluated. Also, it should be recognized that factors such as nutritional status and lifestyle variables (e.g., tobacco smoking, alcohol consumption, and occupation) might all affect the health risks associated with the particular chemical exposure problem under consideration. Broadly stated, cultural issues/attributes of the target population should be carefully addressed; indeed, conducting a scientifically-supported exposure assessment for certain sub-populations would typically require development of appropriate ethnographic information—recognizing that certain culture-specific exposure assessments require unique approaches. As a matter of fact, because of unique cultural heritages, etc. of some groups within certain exposure evaluation zones, these receptors may experience exposures that may not be adequately characterized if an analyst simply resorts a use of the 'mainstream' methods of evaluation only. Under such circumstances of 'non-typical' exposure scenarios, it becomes

particularly important to obtain relevant, site-specific information—in order to be able to conduct an adequate and defensible exposure assessment.

- *Potential receptor exposures history*. Chemical exposure effects may occur in populations not only as a result of current exposure to agents but also from past exposures. Thus, past, current, and potential future exposure to hazardous substances should all be carefully evaluated as part of an overall long-term public health risk assessment program.

Indeed, the above listing is by no means complete for the universe of potential exposure possibilities—albeit represents the critical ones that must certainly be examined rather closely.

On the whole, most chemical exposure outcomes depend on the conditions of exposure such as the amount, frequency, duration, and route of exposure (i.e., ingestion, inhalation, and dermal contact). Also, for most environmental chemicals, available health effects information is generally limited to high exposures in studies of humans (e.g., occupational studies of workers) or laboratory animals; thus, evaluation of potential health effects associated with low levels of exposure generally encountered in the human living and work environments involves inferences based on the understanding of the mechanisms of chemical-induced toxicity. Furthermore, one should be cognizant of the fact that, in general, chemicals frequently affect more than one organ or system in the human body (e.g., liver, kidney, nervous system), and can also produce a variety of health endpoints (e.g., cancer, respiratory allergies, infertility). For all these reasons, among perhaps several others, uncertainty issues should be very carefully and comprehensively addressed in such evaluation efforts.

## 7.2 The Risk Assessment Process

Risk assessment is a scientific process that can be used to identify and characterize chemical exposure-related human health problems. Specific forms of risk assessment generally differ considerably in their levels of detail. Most risk assessments, however, share the same general logic—consisting of four basic elements, namely, hazard assessment, dose-response assessment, exposure assessment, and risk characterization (Fig. 7.1).

*Hazard assessment* describes, qualitatively, the likelihood that a chemical agent can produce adverse health effects under certain environmental exposure conditions. *Dose-response assessment* quantitatively estimates the relationship between the magnitude of exposure and the degree or probability for occurrence of a specific health effect. *Exposure assessment* determines the extent of human exposure. *Risk characterization* integrates the findings of the first three components to describe the nature and magnitude of health risk associated with environmental exposure to a chemical substance, or a mixture of substances. A discussion of these fundamental elements follows—with more detailed elaboration given in Chaps. 8–12 of this title,

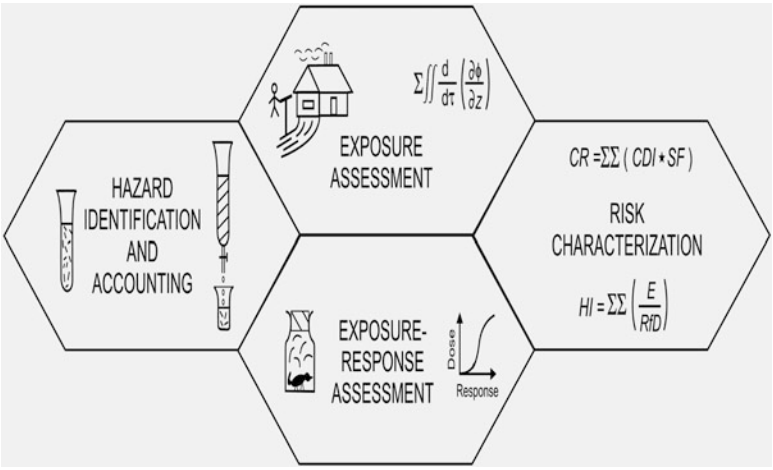


**Fig. 7.1** Illustrative elements of a risk assessment process

and also elsewhere in the risk analysis literature (e.g., Asante-Duah 1998; Cohrssen and Covello 1989; Conway 1982; Cothern 1993; Gheorghe and Nicolet-Monnier 1995; Hallenbeck and Cunningham 1988; Huckle 1991; Kates 1978; Kolluru et al. 1996; LaGoy 1994; Lave 1982; McColl 1987; McTernan and Kaplan 1990; Neely 1994; NRC 1982, 1983, 1994a, b; Paustenbach 1988; Richardson 1990; Rowe 1977; Suter 1993; USEPA 1984b, 1989a, b, c, d, e, f; Whyte and Burton 1980).

### *7.2.1 Hazard Identification and Accounting*

*Hazard identification and accounting* involves a qualitative assessment of the presence of, and the degree of hazard that an agent could have on potential receptors. The hazard identification consists of gathering and evaluating data on the types of health effects or diseases that may be produced by a chemical, and the exposure conditions under which public health damage, injury or disease will be produced. It may also involve characterization of the behavior of a chemical within the body and the interactions it undergoes with organs, cells, or even parts of cells. Data of the latter types may be of value in answering the ultimate question of whether the forms of toxic effects shown to be produced by a substance in one population group or in experimental settings are also likely to be produced in the general human population.

Hazard identification is not a risk assessment *per se*. This process involves simply determining whether it is scientifically correct to infer that toxic effects observed in one setting will occur in other settings—e.g., whether substances found to be carcinogenic or teratogenic in experimental animals are likely to have the

same results in humans. In the context of public health risk management for potential chemical exposure problems, this may consist of:

- Identification of chemical exposure sources;
- Compilation of the lists of all chemical stressors present at the locale and impacting target receptors;
- Identification and selection of the specific chemicals of potential concern (that should become the focus of the risk assessment), based on their specific hazardous properties (such as persistence, bioaccumulative properties, toxicity, and general fate and behavior properties); and
- Compilation of summary statistics for the key constituents selected for further investigation and evaluation.

Indeed, a major purpose of the hazard identification step of a public health risk assessment is to identify a subset of 'chemicals of potential concern' (CoPCs) from all constituents detected during an investigation. The CoPCs are a subset of the complete set of constituents detected during an investigation that are exclusively carried through the quantitative risk assessment process. On the whole, the selection of CoPCs identifies those chemicals observed that have the most potential to be a significant contributor to human health risks—recognizing that most risk assessments tend to be dominated by a few compounds of significant concern (and indeed a few routes of exposure as well); as a matter of fact, the inclusion of all detected compounds in the risk assessment often has minimal influence on the total risk—and thus generally considered an unnecessary burden. In any case, several factors are typically considered in identifying CoPCs for risk assessments—including toxicity and magnitude of detected concentrations, frequency of detection, and essential nutrient status. The so-identified CoPCs are then carried forward for quantitative evaluation in the subsequent (baseline) risk assessment. Overall, the CoPC screening process is intended to identify the following:

(i) Constituents that pose negligible risks—and therefore can be eliminated from further evaluation; and
(ii) Constituents that merit further evaluation, either quantitatively or qualitatively, based on their potential to adversely affect humans depending on specific types of exposures.

Finally, it is noteworthy that, in identifying the CoPCs, an attempt is generally made to select all chemicals that could possibly represent the major part (usually, $\geq$95%) of the risks associated with the relevant exposures.

### *7.2.2 Exposure-Response Evaluation*

The *exposure-response evaluation* (or the *effects assessment*) consists of a process that establishes the relationship between dose or level of exposure to a substance and the incidence-cum-severity of an effect. It considers the types of adverse effects

associated with chemical exposures, the relationship between magnitude of exposure and adverse effects, and related uncertainties (such as the weight-of-evidence of a particular chemical's carcinogenicity in humans). In the context of chemical exposure problems, this evaluation will generally include a 'dose-response evaluation' and/or a 'toxicity assessment'. Dose-response relationships are typically used to quantitatively evaluate the toxicity information, and to characterize the relationship between dose of the contaminant administered or received and the incidence of adverse effects on an exposed population. From the quantitative dose-response relationship, appropriate toxicity values can be derived—and this is subsequently used to estimate the incidence of adverse effects occurring in populations at risk for different exposure levels. The toxicity assessment usually consists of compiling toxicological profiles for the chemicals of potential concern.

*Dose-response assessment* specifically involves describing the quantitative relationship between the amount of exposure to a substance and the extent of toxic injury or disease. Data are characteristically derived from animal studies or, less frequently, from studies in exposed human populations. There may be many different dose-response relationships for a substance if it produces different toxic effects under different conditions of exposure. Meanwhile, it is noteworthy that, even if the substance is known to be toxic, the risks of a substance cannot be ascertained with any degree of confidence unless dose-response relations are quantified.

### *7.2.3 Exposure Assessment and Analysis*

An *exposure assessment* is conducted in order to estimate the magnitude of actual and/or potential receptor exposures to chemicals present in human environments. The process considers the frequency and duration of the exposures, the nature and size of the populations potentially at risk (i.e., the risk group), and the pathways and routes by which the risk group might be exposed. Indeed, several physical and chemical characteristics of the chemicals of concern will provide an indication of the critical exposure features. These characteristics can also provide information necessary for determining the chemical's distribution, intake, metabolism, residence time, excretion, magnification, and half-life or breakdown to new chemical compounds.

In general, exposure assessments involve describing the nature and size of the population exposed to a substance and the magnitude and duration of their exposure. The evaluation could concern past or current exposures, or exposures anticipated in the future. To complete a typical exposure analysis for a chemical exposure problem, populations potentially at risk are identified, and concentrations of the chemicals of concern are determined in each medium to which potential receptors may be exposed. Finally, using the appropriate case-specific exposure parameter values, the intakes of the chemicals of concern are estimated. The

exposure estimates can then be used to determine if any threats exist—based on the prevailing exposure conditions for the particular problem situation.

### 7.2.4 Risk Characterization and Consequence Determination

*Risk characterization* is the process of estimating the probable incidence of adverse impacts to potential receptors under a set of exposure conditions. Typically, the risk characterization summarizes and then integrates outputs of the exposure and toxicity assessments—in order to be able to qualitatively and/or quantitatively define risk levels. The process will usually include an elaboration of uncertainties associated with the risk estimates. Exposures resulting in the greatest risk can be identified in this process—and then mitigative measures can subsequently be selected to address the situation in order of priority, and according to the levels of imminent risks.

In general, risk characterizations involve the integration of the data and information derived/analyzed from the first three components of the risk assessment process (*viz.*, hazard identification, dose-response assessment, and exposure assessment)—in order to ascertain the likelihood that humans might experience any of the various forms of toxicity associated with a substance. [By the way, in cases where exposure data are not available, hypothetical risks can be characterized by the integration of hazard identification and dose-response evaluation data alone.] In the final analysis, a framework to define the significance of the risk is developed, and all of the assumptions, uncertainties, and scientific judgments from the three preceding steps are also presented. Meanwhile, to the extent feasible, the risk characterization should include the distribution of risk amongst the target populations. When all is said and done, an adequate characterization of risks from hazards associated with chemical exposure problems allows risk management and corrective action decisions to be better focused.

## 7.3 General Considerations in Public Health Risk Assessments

Human health risk assessment for chemical exposure problems may be defined as the characterization of the potential adverse health effects associated with human exposures to chemical hazards. In a typical human health risk assessment process, the extent to which potential receptors have been, or could be exposed to chemical hazards is determined. The extent of exposure is then considered in relation to the type and degree of hazard posed by the chemical(s)—thereby permitting an estimate to be made of the present or future health risks to the populations-at-risk.

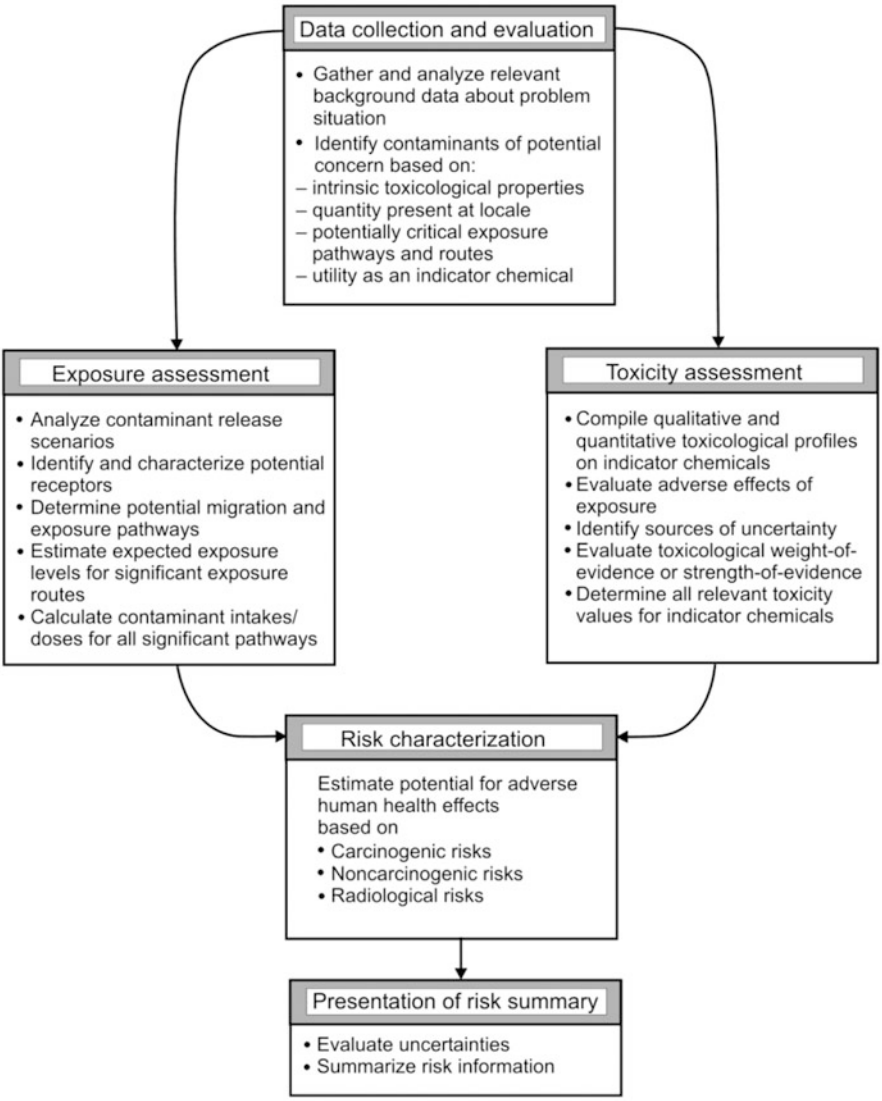


**Fig. 7.2** A general protocol for the human health risk assessment process: fundamental procedural components of a risk assessment for a chemical exposure problem

Figure 7.2 shows the basic components and steps typically involved in a comprehensive human health risk assessment that is designed for use in environmental and public health risk management programs. Several key aspects of the human health risk assessment methodology are presented in the proceeding chapters of this volume—with additional details provided elsewhere in the literature (e.g., Hoddinott 1992; Huckle 1991; NRC 1983; Patton 1993; Paustenbach 1988; Ricci

1985; Ricci and Rowe 1985; USEPA 1984a, b, 1985, 1986a, b, c, d, 1987, 1989d, 1991a, b, c, d, 1992a, b, c, d, e; Van Leeuwen and Hermens 1995).

Invariably, the management of all chemical exposure problems starts with hazard identification and/or a data collection-cum-data evaluation phase. The data evaluation aspect of a human health risk assessment consists of an identification and analysis of the chemicals associated with a chemical exposure problem that should become the focus of the public health risk management program. In this process, an attempt is generally made to select all chemicals that could represent the major part of the risks associated with case-related exposures; typically, this will consist of all constituents contributing $\geq$95% of the overall risks. Chemicals are screened based on such parameters as toxicity, carcinogenicity, concentrations of the detected constituents, and the frequency of detection in the sampled matrix.

The exposure assessment phase of the human health risk assessment is used to estimate the rates at which chemicals are absorbed by potential receptors. Since most potential receptors tend to be exposed to chemicals from a variety of sources and/or in different environmental media, an evaluation of the relative contributions of each medium and/or source to total chemical intake could be critical in a multi-pathway exposure analysis. In fact, the accuracy with which such exposures are characterized could be a major determinant of the ultimate validity of the risk assessment.

The quantitative evaluation of toxicological effects consists of a compilation of toxicological profiles (including the intrinsic toxicological properties of the chemicals of concern, which may include their acute, subchronic, chronic, carcinogenic, and/or reproductive effects) and the determination of appropriate toxicity indices (see Chap. 10 and Appendix C).

Finally, the risk characterization consists of estimating the probable incidence of adverse impacts to potential receptors under various exposure conditions. It involves an integration of the toxicity and exposure assessments, resulting in a quantitative estimation of the actual and potential risks and/or hazards due to exposure to each key chemical constituent, and also the possible additive effects of exposure to mixtures of the chemicals of potential concern.

### *7.3.1 Determining Exposure-Related Health Effects*

Exposure-related health effects of chemical substances introduced into the human living and work environments may be determined within the framework of a public health risk assessment process. In general, when evaluating the health impact of exposure to hazardous substances, the analyst should consider data from studies of human exposures as well as from the results of experimental animal studies. For health assessment purposes, the use of human data is preferred—because it eliminates (or at least reduces) uncertainties involved in extrapolating across species. However, human data are often unavailable, particularly for chronic, low-dose exposures. Furthermore, adequate human data are often not available to establish

a dose-response relationship. In the absence of adequate human data, therefore, the public health analyst must rely on the results of experimental animal studies. Also, in many chemical exposure situations, exposures must often be characterized as chronic and of low dose; meanwhile, it is apparent that health effects data and information for such exposures are often lacking. Again, in these types of situations, the health analyst may have to rely on studies that involve shorter exposures and/or higher dose levels. Ultimately, if such studies are used as the basis for a health assessment, the analyst should acknowledge the qualitative and quantitative uncertainties involved in those extrapolations. In the end, it is generally recommended that estimated chemical exposures be compared to studies or experiments involving comparable routes of exposure—*viz*., ingestion, inhalation, and dermal contact. However, in some instances, it may be necessary to utilize data from studies based on different exposure pathways or routes. Under such circumstances, extra caution should be used when eliciting/deriving conclusions from these 'surrogate' studies because of the uncertainties involved in route-to-route extrapolations—especially because of the likely concomitant differences in chemical absorption, distribution, metabolism, and excretion. In addition, a chemical might exert a toxic effect by one route of exposure, but not by another (e.g., chromium is reported to be carcinogenic by inhalation, but not by ingestion); such differences should be carefully evaluated.

Finally, it is noteworthy here that, to facilitate the development of responsible public health risk management programs, it is important for the public health analyst to use the best medical and toxicological information available to determine the health effects that may arise from exposure to the chemical constituents of concern. Such information can be derived from existing chemical-specific toxicological profiles or databases (*e.g*., 'Toxicological Profiles' from the ATSDR, and IRIS from the US EPA), standard toxicology textbooks, and scientific journals of environmental toxicology or environmental health. Analysts should also consult on-line databases for the most current toxicological and medical information. Furthermore, the analyst should clearly indicate in the health assessment reporting/documentation whether the case-specific health concerns of interest are for acute, intermediate, or chronic exposures.

### *7.3.2 Evaluating Factors That Influence Adverse Health Outcome*

To ensure reliable public health policy decisions, the public health analyst should review the various factors that may enhance or mitigate health effects arising from exposure to chemicals present in the human living and work environments. Indeed, among other things, the analyst should also consider all other pertinent medical and toxicological information; the health implications for sensitive sub-populations; health implications of past and future exposures; and the effects of corrective/

control actions or interventions on human exposure. The particularly important issues are elaborated in the sections below.

#### 7.3.2.1 Public Health Implications of Supplemental Medical and Toxicological Factors

As appropriate, several factors should normally be investigated and their health implications discussed in any given health assessment; typical factors that the public health analyst may generally consider in the evaluation of public health outcomes are annotated in Box 7.1. In general, in addition to the medical and toxicological factors identified here, the public health analyst should also consider population-specific factors that may enhance or mitigate health effects associated with exposure to the constituents of concern. Overall, the health effects identified by comparing dose estimates with toxicity values during a risk characterization should also be evaluated on the basis of other toxicological and medical factors that could potentially amplify or mitigate the effects of a chemical exposure.

**Box 7.1 Typical medical and toxicological factors affecting public health outcomes**

- Distribution of chemical within the body (i.e., the fate of the chemical after ingestion, inhalation, or dermal contact)
- Target organs (i.e., physiologic site of major toxicity)
- Toxicokinetics of substance (including possible transfer to cow's milk or nursing mother's milk)
- Enzyme induction (i.e., chemical induction of various enzyme systems may increase or decrease chemical toxicity)
- Cumulative effect of exposures to chemicals that bioaccumulate in the body (e.g., lead, cadmium, organochlorine pesticides)
- Chemical tolerance (i.e., decreased responsiveness to a toxic chemical effect resulting from previous exposure to that chemical or to a structurally related chemical)
- Immediate *versus* delayed effects (i.e., effects observed rapidly after a single exposure *versus* effects that occur after some lapse of time)
- Reversible *versus* irreversible effects (i.e., ability of affected organs to regenerate)
- Local *versus* systemic effects (i.e., whether the effect occurs at the site of first contact, or if the chemical must be absorbed and distributed before the effect is observed)
- Idiosyncratic reactions (i.e., genetically determined abnormal reactivity to a chemical that is qualitatively similar to reactions found in all persons—

(continued)

**Box 7.1** (continued)

but may take the form of either extreme sensitivity to low doses or extreme insensitivity to high doses)
- Allergic reactions (i.e., adverse reaction to a chemical resulting from previous sensitization to that chemical or a structurally related one)
- Various other related disease effects (i.e., effect of chemical on previously diseased organ)

#### 7.3.2.2 Health Implications for Sensitive Sub-populations

Characteristically, many sub-populations may be identifiable at a given study locale—and each sub-population may have special concerns that must be considered when ascertaining the public health implications of a chemical exposure problem. Perhaps the most crucial set of factors that an analyst must weigh are those that influence differential susceptibility to the effects of specific compounds. Indeed, age, gender, genetic background, nutritional status, health status, and general lifestyle may each influence the effects of chemical exposures; thus, the analyst should carefully consider the impact that each of these factors may have under a specific chemical exposure scenario for a given population. The key factors are elaborated below.

- *Age of Receptor*. Age-related susceptibility to the toxic effects of chemicals is probably more widespread than many public health analysts realize. Indeed, at some point in a human lifetime, every person is at an increased risk from chemical exposures because of age factors. At any rate, it is generally acknowledged that the very young are a particularly high-risk group that must be protected more stringently from the adverse effects of certain compounds. For example, the US EPA primary drinking water standard for nitrate had to be so-established to protect the most susceptible high-risk group—namely, infants in danger of developing methemoglobinemia. Similar age-related sensitivities have been reflected in 'allowable' levels set for lead in ambient air and in drinking water, as well as for mercury in aquatic systems. Then again, the very young are not always the age group necessarily linked with the most amplified risk situation. In fact, in some instances, adults are at greater risk of toxicity than infants or children; for example, past studies have shown that the young seem more resistant (than adults) to the adverse effects of renal toxicants such as fluoride and uranyl nitrate. Furthermore, fairly recent acknowledgment by many experts/investigators that elderly subpopulations may have significantly heightened susceptibility to chemical compounds because of lower functional capacities of various organ systems, reduced capacity to metabolize foreign compounds, and diminished detoxification mechanisms should be recognized.

- *Gender of Receptor*. Although gender-linked differences in toxic susceptibilities have not quite been extensively investigated, there is some scientific evidence to support the fact that certain adverse health effects may be mediated through hormonal influences and other factors that are dependent on the sex of the individual receptor. As an example, it is well documented that pregnant women are often at significantly greater risk from exposure to beryllium, cadmium, lead, manganese, and organophosphate insecticides than other members of the general population; this is because of the various physiologic modifications associated with the pregnancy. Also, a developing fetus is at greater risk from compounds that exert developmental effects.
- *Biochemical and/or Genetic Susceptibilities*. The presence of subpopulations with certain inherent biochemical and/or genetic susceptibilities should be given careful consideration when evaluating the potential health threats from a chemical exposure problem; this is because a number of studies indicate that genetic predisposition is an important determining factor in numerous disease states. Indeed, studies of some of these 'genetically-determined' diseases have shown an increased susceptibility to the toxic effects of certain chemicals. For example, certain percentages of some ethnic groups are known to suffer from inherited serum alpha-1-antitrypsin deficiency—which predisposes them to alveolar destruction and pulmonary emphysema. Persons with this deficiency are especially sensitive to the effects of certain pollutants. In general, this type of information can be used in conjunction with information on the ethnic makeup of populations in the study area, so as to better evaluate potential toxic effects associated with a chemical exposure problem. In addition, persons who have chronic diseases may also be at increased risk from exposure to certain chemicals; for example, individuals with cystic fibrosis are less tolerant of the respiratory and gastrointestinal challenges of some pollutants. Also, persons with hereditary blood disorders, such as sickle-cell anemia, have increased sensitivity to compounds such as benzene, cadmium, and lead—which are suspected 'anemia producers'. Thus, the importance of determining the presence and proximity of facilities such as hospitals or convalescent homes where sensitive subpopulations are likely to be found cannot be overemphasized. On the whole, when identifiable groups are known to be at risk from exposure to a chemical source, then it is quite important to determine the nature and magnitude of adverse health effects that could likely emerge (alongside any confounding factors), by undertaking extensive research of information contained in available medical and toxicological literature/databases, etc.
- *Socioeconomic Factors*. Socioeconomic status is not only an important indicator of human susceptibilities to specific pollutants, but such information may also help identify confounding nutritional deficiencies or behaviors that enhance a person's sensitivity to the toxic effects of chemical materials. For instance, studies have shown that dietary deficiencies of vitamins A, C, and E may increase susceptibility to the toxic effects of polychlorinated biphenyls (PCBs) and other chlorinated hydrocarbons, some pesticides, ozone, and various other substances. Other studies have also indicated that deficiencies in trace metals

such as iron, magnesium, and zinc exacerbate the toxic potential of fluorides, manganese, and cadmium. Meanwhile, it is notable that populations with sensitivities due to nutritional deficiencies have typically been associated with areas of low socioeconomic status and extreme poverty, or in areas with large numbers of indigents. Elderly populations have also been identified as a subgroup at risk of susceptibility because of nutritional deficits.

In general, demographic and land-use information can be used to help identify the relative socioeconomic status of exposed populations; this information may ultimately provide important clues for properly apprising the likely impacts of variant exposed population (sub)groups encountered during a health assessment activity. In fact, as part of the overall public health risk determination process, the public health analyst must carefully examine demographic information for particular groups on or near the study area or exposure source, and who might be especially sensitive to toxic effects. Any suspected high-risk groups should be explicitly identified in any ensuing health assessment report. For instance, locations of daycare centers, schools, playgrounds, recreational areas, hospitals and retirement or convalescent homes on or near a given site should be highlighted as important indications of the presence of sensitive subpopulations. Enumeration of ethnic groups within the population, as well as characterization of socioeconomic status may also indicate sensitive subpopulations near a study area or exposure source. It is noteworthy that, ultimately, information on the number and proximity of people in high-risk subpopulations is vital for developing an optimal public health risk management or mitigation plan.

Overall, subpopulations of special concern should be identified during a public health risk assessment process; those individuals or groups may be at increased risk because of greater sensitivity, compromised health status, concomitant occupational exposures, or indeed a variety of other reasons. Thus, if such individuals or groups really exist, then they should be explicitly identified in the health assessment—and then appropriate recommendations should be made specifically directed at their protection. Furthermore, other groups that are closely affiliated with a high-risk group—such as families of workers who may be (or have been) exposed through contact with work clothing or other secondary means—should perhaps be carefully evaluated as well.

#### 7.3.2.3 Health Implications of Past and Future Exposures

A generally important aspect of the process of determining the public health implications of chemical exposures usually involves establishing a firm difference between that which constitutes ‘actual’ exposures (i.e., expected and/or completed exposures) *vs*. ‘potential’ exposures (i.e., possible but not necessarily complete exposures). When evaluating future ‘actual’ and ‘potential’ exposures, the analyst should also make a determination of the underlying causes for the anticipated exposures (e.g., from the continued use of specific consumer products, etc.)—so

that appropriate mitigative measures for such future exposures can be undertaken *a priori*. At any rate, in the attempt to ascertain the health implications of a chemical exposure problem, and in addressing a population-at-risk's health concerns, the public health analyst should endeavor to include past, current, and potential future exposures in the requisite documentation. Meanwhile, it has to be acknowledged here that, despite the fact that significant exposure may already have occurred, past exposures tend to be difficult to address—especially because they are difficult to quantify. To facilitate requisite efforts in the process of evaluating community health concerns about past hazard exposures, the analyst should review all available community-specific health outcome databases, such as morbidity data and disease registries—in order to determine a possible correlation between past and current health outcomes and past exposures. When past exposures have been documented, but health studies have not been performed, health effects studies or the review of community health records become very important.

#### 7.3.2.4 Health Implications of Corrective Actions and Interventions

In determining the health implications of a chemical exposure situation, it is quite important that the analyst takes the effect(s) of remedial actions and other intervention programs into consideration. This is because previous, current, and/or planned remedial or risk management actions can significantly affect conclusions about exposure-related health concerns.

In general, when remedial response measures or other interventions have occurred previously, the analyst should consider the effect that those measures have had on the health of the target population. Similarly, if intervention is already occurring, the analyst should determine what likely effects this might have, moving forward. Furthermore, the health assessment should be responsive to community health concerns vis-à-vis the remedial actions. In addition, discussion offered in the health assessment with respect to the recognized exposure scenarios should clearly identify and differentiate between those exposure scenarios that still exist *vs.* the exposures that may have occurred in the past (but that have now been eliminated or significantly reduced by remedial action or other intervention programs).

## 7.4 Human Health Risk Assessment in Practice

Quantitative human health risk assessment often becomes an integral part of most environmental and public health risk management programs that are designed to address chemical exposure problems. In the processes involved, four key elements are important in arriving at appropriate risk management solutions—namely, the chemical hazard identification; the chemical toxicity assessment or exposure-response evaluation; the exposure assessment; and the risk characterization. Each

of these elements typically will, among other things, help answer the following fundamental questions:

- Chemical hazard identification step—'what chemicals are present in the human environments of interest?' and 'is the chemical agent likely to have an adverse effect on the potential human receptor?'
- Chemical toxicity assessment or exposure-response evaluation step—'what is the relationship between human exposure/dose to the chemical of potential concern and the response, incidence, injury, or disease as a result of the receptor exposure?' In other words, 'what harmful effects can be caused by the target chemicals, and at what concentration or dose?'
- Exposure assessment step—'what individuals, subpopulations, or population groups may be exposed to the chemical of potential concern?' and 'how much exposure is likely to result from various activities of the potential receptor—i.e., what types and levels of exposure are anticipated or observed under various scenarios?'
- Risk characterization step—'what is the estimated incidence of adverse effect to the exposed individuals or population groups—i.e., what risks are presented by the chemical hazard source?' and 'what is the degree of confidence associated with the estimated risks?'

Typically, the fundamental tasks involved in most human health risk assessments will consist of the key components shown in Box 7.2—revealing a methodical framework; a careful implementation of this framework should generally provide answers to the above questions. Illustrative examples of the practical application of the processes involved are provided in Chaps. 9, 11 and 13. Meanwhile, it cannot be stated enough that there are many uncertainties associated with public health risk assessments. These uncertainties are due in part to the complexity of the exposure-dose-effect relationship, and also the lack of, or incomplete knowledge/information about the physical, chemical, and biological processes within and between human exposure to chemical substances and health effects. On the whole, the major sources of uncertainty in public health risk assessments can be attributed to the following:

(i) Use of a wide range of data from many different disciplines (e.g., epidemiology, toxicology, biology, chemistry, statistics, etc.);
(ii) Use of many different predictive models and methods in lieu of actual measured data; and
(iii) Use of many scientific assumptions and science policy choices (i.e., scientific positions assumed in lieu of scientific data)—in order to bridge the information/knowledge gaps in the risk assessment process.

Ultimately, these diverse elements, along with varying interpretations of the scientific information, can produce divergent results in the risk assessment process—an outcome that often leads to some risk assessment controversies. Thus, it is very important to carefully and systematically identify all sources and types of uncertainty and variability—and then present them as an integral part of risk characterization process.

In closing, it is noteworthy that the scientific information about the hazards used in risk assessments is derived largely from observational epidemiology and experimental animal studies of specific substances or combinations of substances that are designed to identify their hazardous properties (namely, the types of harm they can induce in humans) and the conditions of exposure under which those harms are observed (namely, the dose and duration). Information from these studies will typically be used to develop the hazard identification and dose-response components of a risk assessment—all the while recognizing that the data used to develop these components usually arise from diverse sources and types of study designs that frequently lack strong consistency in methods; thus, reaching valid conclusions about them requires both careful scientific evaluations and experienced/informed judgments (OMB and OSTP 2007). Next, assessing exposure requires an evaluation of the nature of the population that is incurring exposures to the substances of interest and the conditions of exposure that it is experiencing (such as the dose and duration of exposure) (NRC 1991a, b, c). In the end, risk to the exposed population is understood by examining the exposure the population experiences relative to the hazard and dose–response information.

**Box 7.2 Illustrative basic outline for a public health risk assessment report**

| Section Topic | Basic Subject Matter |
|---|---|
| General Overview | |
| | • Background information on the case problem or locale<br>• The risk assessment process<br>• Purpose and scope of the risk assessment<br>• The risk assessment technique and method of approach<br>• Legal and regulatory issues in the risk assessment<br>• Limits of application for the risk assessment |
| Data Collection | |
| | • Chemical exposure sources of potential concern<br>• General case-specific data collection considerations<br>• Assessment of the data quality objectives<br>• Identification of data gathering uncertainties |
| Data Evaluation | |
| | • General case-specific data evaluation considerations<br>• Identification, quantification, and categorization of target chemicals<br>• Statistical analyses of relevant chemical data<br>• Screening and selection of the chemicals of potential concern<br>• Identification of uncertainties associated with data evaluation |

(continued)

**Box 7.2** (continued)

| | |
|---|---|
| Exposure Assessment | |
| | • Characterization of the exposure setting (to include the physical setting and populations potentially at risk)<br>• Identification of the chemical-containing sources/media, exposure pathways, and potentially affected receptors<br>• Determination of the important fate and behavior processes for the chemicals of potential concern<br>• Determination of the likely and significant exposure routes<br>• Development of representative conceptual model(s) for the problem situation<br>• Development of realistic exposure scenarios (to include both current and potential future possibilities)<br>• Estimation/modeling of exposure point concentrations for the chemicals of potential concern<br>• Quantification of exposures (i.e., computation of potential receptor intakes/doses for the applicable exposure scenarios)<br>• Identification of uncertainties associated with exposure parameters |
| Toxicity Assessment | |
| | • Compilation of the relevant toxicological profiles of the chemicals of potential concern<br>• Determination of the appropriate and relevant toxicity index parameters<br>• Identification of uncertainties relating to the toxicity information |
| Risk Characterization | |
| | • Estimation of the human carcinogenic risks from carcinogens<br>• Estimation of the non-carcinogenic effects for systemic toxicants<br>• Sensitivity analyses of relevant parameters<br>• Identification and evaluation of uncertainties associated with the risk estimates |
| Risk Summary Discussion | |
| | • Summarization of risk information<br>• Discussion of all identifiable sources of uncertainties |